Research reports that most young athletes were asymptomatic prior to sudden cardiac death.

Several electrocardiogram criteria such as the European Society of Cardiology Criteria, Seattle Criteria, Refined Criteria, and International Criteria, have sought to improve the accuracy of identifying athletes at risk of sudden cardiac death during pre-participation screening.
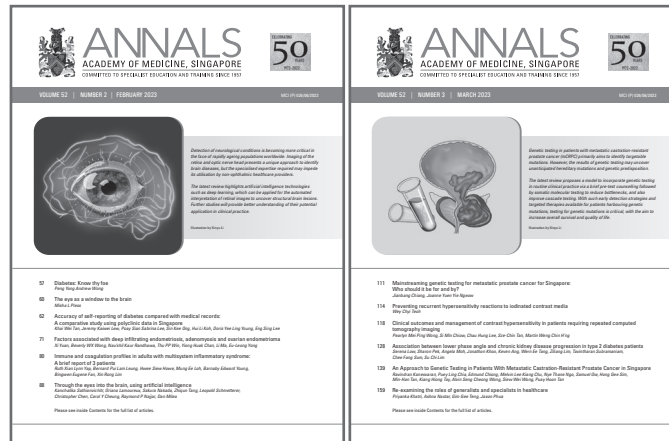
A Singapore study compared the above four criteria in 270 Singapore elite athletes to identify the best in detecting cardiac abnormalities on echocardiography. International Criteria performed the best, with the highest specificity and positive predictive value, joint highest negative predictive value, and lowest false positive rate.

Illustration by Xinyu Li

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Improving electrocardiogram interpretation in Asian athletes: A call to action

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The field of sports cardiology has evolved substantially over the past 2 decades due to improved understanding of the athlete's heart, causes of sudden cardiac death (SCD) in athletes, as well as differentiation between physiological cardiac remodelling and pathological cardiac conditions in athletic individuals. Application of this knowledge forms the basis of pre-participation screening (PPS) in athletes, where the primary aim is to identify conditions predisposing to SCD and mitigate risk to the athlete by appropriate management.

Traditional PPS in athletes comprise a thorough questionnaire on personal and family history and presence of symptoms as well as physical examination. With the 12-lead electrocardiogram (ECG) demonstrating superior sensitivity compared to clinical history and physical examination, it has become a vital tool in PPS for athletes and its importance cannot be understated. This is reflected by the progression of ECG interpretation criteria for athletes over the last 15 years. Early iterations for ECG interpretation in athletes outlined ECG characteristics of specific conditions (e.g. hypertrophic cardiomyopathy) and were derived from the general population. Subsequent accumulation of athlete-specific evidence has facilitated substantial refinements in the years thereafter. These include improved understanding of ECG changes reflecting physiological cardiac remodelling, for instance, the voltage criteria for left ventricular hypertrophy and incomplete right bundle branch block. The impact of age, sex and ethnicity on athletes' ECGs were also recognised, whereby juvenile T wave inversions, gender differences in corrected QT intervals and differences in repolarisation between white and black athletes were incorporated into ECG interpretation criteria. Four major ECG interpretation criteria have been published to date: the European Society of Cardiology (ESC) criteria in 2010, the Seattle Criteria in 2013, the Refined Criteria in 2014 and the International Criteria in 2017.[1-4]

Throughout the evolution of athletes' ECG interpretation criteria, there is a notable absence of evidence from Asian athletes. This is in spite of Asia being the largest and most populous continent in the world with significant representation in international sport. More specifically, while some inroads have been made in West Asian athletes, there remains a dearth of epidemiological data on sudden cardiac death and physiological limits of cardiac remodelling in the diverse population of East, Central and South Asian athletes.[5] This can be attributed to multiple barriers which exist within Asia, including disparity in healthcare resources and access to medical services. Most notably, Asia's unique geography, myriad of ethnicities and cultural diversity may have varying implications with regards to implementation of PPS, SCD risks, and conduct of research in sports cardiology.

Despite these challenges, data from Southeast Asia is emerging, highlighting parallels in the degree of exercise-induced cardiac remodelling between Southeast Asian and white athletes, albeit of smaller magnitudes.[6,7] More recently, the Asian Pacific Society of Cardiology (APSC) recommended using the resting 12-lead ECG for PPS in young competitive athletes, with ECG interpretation via the International Criteria.[8] This was based on available evidence demonstrating high specificity, preserved sensitivity and low interobserver variability in different athletic cohorts. Utilisation of the International Criteria for PPS in athletes also reduced false positive rates compared to older criteria. This is especially pertinent in competitive athletes as a false positive result during screening may lead to unnecessary and costly additional evaluation, delays in resumption of training and even inappropriate stress to the athlete. At the time of publication, performance of the International Criteria in a population of Asian athletes was yet to be evaluated.

In this issue of *Annals*, Lim et al. reviewed the electrocardiograms and echocardiograms of 270 elite

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Southeast Asian athletes who underwent PPS over a period of 7 years.[9] These athletes were young (81% ≤35 years) and male (88%), with football as the predominant sporting discipline (74%). Each ECG was interpreted using four ECG criteria (ESC, Seattle, Refined and International), and the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for each criterion in detecting echocardiographic abnormalities were calculated.

There was a substantial reduction in proportion of abnormal ECG from 35% using the ESC criteria to 3% using the International Criteria. In total, 20 athletes were found to have abnormal echocardiographic findings ranging from mitral valve prolapse, patent foramen ovale to pulmonary hypertension, among others. Among the four ECG interpretation criteria, the International Criteria yielded the best performance with highest specificity (97%), PPV (11%) and NPV (93%) along with lowest false positive rate (3%). These results remained consistent after exclusion of master athletes (12%) from analysis. Sensitivity for all four criteria was poor, achieving 20% at best (by ESC and Refined Criteria).

It should be noted that echocardiograms in the study cohort were performed due to abnormal ECG, physical findings or presence of symptoms rather than part of routine PPS. While routine echocardiographic screening as part of a robust PPS algorithm would indeed be useful, the resources required for mass screening are potentially prohibitive for widespread implementation, especially if the incidence of pathology detectable by echocardiogram is low. These resources include manpower (technicians required to screen, trained healthcare professionals to interpret echocardiographic findings), finances (for purchase of hardware, peripherals, consumables) and time (by the athlete to attend the screening and undergo evaluation). It is unsurprising that the requirement for routine echocardiographic evaluation is limited to larger sporting institutions such as the National Basketball Association (NBA) and Fédération Internationale de Football Association (FIFA). Nonetheless, with point-of-care ultrasound systems becoming more accessible, portable and easy to operate, targeted echocardiography as part of PPS for athletes may be likely in the future.

The applicability of the study findings is also limited by the under-representation of endurance and strength disciplines, as well as female athletes. However, the predominant population of footballers in this study is reflective of football being one of the most popular and common sports in Asia. It is categorised as a largely dynamic sport by the American College of Cardiology and grouped together with sports such as long distance running and tennis, whereas the European Society of Cardiology deems football a mixed sport similar to basketball and hockey. The common theme is the dynamic/endurance component of football leading to a moderate degree of cardiac remodelling. Comparatively, strength/power sports are less common in Asia and also result in lesser degrees of cardiac remodelling. The population of strength-trained athletes remains poorly evaluated and should be considered in future studies.

While structural heart diseases such as hypertrophic cardiomyopathy are historically the most commonly cited causes of SCD in young athletes, there is increasing recognition of sudden arrhythmic death syndrome (SADS) as the predominant culprit in this population.[10] Comprehensive evaluation, including genetic testing, of families with SADS deaths (termed molecular autopsy) revealed a significant proportion of arrhythmic conditions and inherited channelopathies. Prospective SCD registries in Asian athletes are urgently needed to identify the magnitude of SADS in this population, as this finding may have profound implications regarding our understanding of SCD, the conduct of PPS and how ECG criteria are utilised. These include potential modifications to PPS such as more detailed emphasis on palpitations and syncope during history taking as well as lowering the threshold to evaluate athletes with a family history of sudden cardiac death and/or unexplained syncope.

This study by Lim et al.[9] has reinforced that the International Criteria is currently the most appropriate tool in guiding ECG interpretation for Asian athletes based on its highest specificity, NPV and lowest false positive rate compared to other ECG criteria, which is consistent with prevailing APSC consensus recommendations. It has also highlighted the pressing need for further evidence-based refinement of contemporary ECG criteria to improve poor sensitivity and false negative rates, as well as evaluating long-term outcomes based on such a screening protocol in Asian athletes.

The authors deserve commendation for laying the foundation for increased awareness of the Asian athlete's heart. There remains much to be done in Asian athletes: identifying ECG and echocardiographic changes from intensive physical training, and prevalence of pathological cardiac conditions or the true incidence

and predominant causes of SCD. Ethnicity-specific guidelines and recommendations for Asian athletes are overdue, and this call to action aims to encourage systematic research such as prospective PPS and SCD registries focusing on Asian athletes, among the sports cardiology community.

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EDITORIAL

Impact of COVID-19 on mental health and healthcare service delivery

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The COVID-19 pandemic has claimed more than 6.8 million lives globally.[2] While there is yet a cure for the disease, vaccines are now available to minimise transmission risk and protect against severe infection. However, COVID-19 vaccines have had a mixed reception, with concerns of their side effects and of their safety in being quickly developed over a short period.[3]

The COVID-19 pandemic has negatively impacted people's physical and mental health. Fear of contracting the virus, worry about loved ones who are vulnerable to the disease, social isolation, and unemployment have been shown to lead to anxiety and depression, with the global prevalence of 21% and 24%, respectively during the pandemic.[4] In addition, the pandemic has exacerbated symptoms among those with pre-existing mental health problems.[5] The pandemic set an unprecedented challenge on healthcare system, disrupting the delivery of mainstream healthcare while tackling the added challenges of COVID-19-related ailments.[6] The challenges in early diagnosis and treatment of COVID-19 at the time when other important diseases were co-circulating, and the wider use of telemedicine, potentially impacted on the delivery of healthcare aimed at ensuring the mental well-being of patients and healthcare workers.[6] All these have significant impact on the provision of mental and social health services.

Against this background, the study by Goh et al.,[7] in this issue of the *Annals* is timely for a better understanding of the impact of the pandemic on mental health, and on the provision of social and mental health services in Singapore. They found that there has been an increase in the requests for mental health services, hospitalisations for mental health reasons, patients requiring more follow-ups, and patients requiring further referrals to other mental health providers, particularly for social service agencies. These findings point to an increase in mental health issues during the pandemic in Singapore. In a study by the Institute of Mental Health, Singapore, 8.7% of the population met the criteria for clinical depression, 9.4% for anxiety, and 9.3% for mild to severe stress disorders. Stress was mainly attributed to the worry for family members and friends contracting COVID-19, and concerns for financial loss and unemployment.[8]

The findings by Goh et al.[7] also shed light on the change in healthcare provision for mental health services during the pandemic, where it was reported that much of the mental healthcare service delivery had shifted to remote platforms as a measure to reduce the risk of COVID-19 transmissions, and various online tools were used to engage clients such as video conferencing. However, some providers felt that telemedicine services for mental health provision were limited by the difficulty in developing rapport with patients, the lack of assessment of non-verbal cues from patients, and the absence of a "safe space" during these virtual sessions. More than 50% of the providers from restructured hospitals and primary and community health partners in the study reported the need for face-to-face consultation. The limitations of telemedicine were also highlighted in other studies where telemedicine was considered ineffective for first-time patients, follow-up patients,[9] and those experiencing loneliness, domestic abuse, and family conflict. Some patients with learning or cognitive abilities who had difficulties understanding and following social distancing requirements, and those lacking in resources to use these technologies (e.g. older people and those from a lower socio-economic background), could find telemedicine ineffective.[10]

Furthermore, the challenges to provide mental healthcare for patients have significant impact on providers, as they faced difficulties in adjusting to the frequent changing guidelines that required work processes to change constantly, the numerous rules and guidelines that led to confusion and anxiety, and the increased pressure from high workload due to manpower constraints (Goh et al.[7]). These challenges were echoed in another study that reported an increase in the prevalence of anxiety (21.4%), burnout (82.1%), depression (26.6%), and post-traumatic stress disorder

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(8.9%) among general practitioners in Singapore.[11] Other factors that contributed to the mental health sequelae of providers working in the COVID-19 pandemic were worry of infection risk, the pressure to work with reduced leave, the challenge of service provision in the face of essential service restrictions and protocols, covering for colleagues who were ill or self-isolating, and working outside one's main area of expertise.[12]

The world has reached a post-pandemic era, with easing of community and border measures. However, the effects of COVID-19 will continue to stream into social and mental health services through the release of breakthrough infection and reinfection, as well as the long-term impact of COVID-19 on mental health.[13] There is a need to build a resilient and sustainable social and mental health services, and this can be done by prioritising the well-being of social and mental health providers. Among the interventions that have been found to be effective in preserving the mental health of providers are the creation of safe working conditions including shorter duration of shifts, and access to mental health support to support mental well-being.[12]

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Comparison of four electrocardiographic criteria for the detection of cardiac abnormalities in Singapore athletes

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ABSTRACT

Introduction: Sudden cardiac death in athletes is a rare occurrence, the most common cause being hypertrophic cardiomyopathy, which increases the risk of sustained ventricular tachycardia or ventricular fibrillation. Most of these young athletes are asymptomatic prior to the cardiac arrest. Several electrocardiogram criteria such as the European Society of Cardiology group 2 Criteria changes, Seattle Criteria, Refined Criteria, and most recently the 2017 International Criteria, have sought to improve the accuracy of identifying these at-risk athletes during pre-participation screening while minimising unnecessary investigations for the majority of athletes at low risk.We aimed to compare the above four criteria in our Singapore athlete population to identify which criterion performed the best in detecting cardiac abnormalities on echocardiography.

Method: Out of 1,515 athletes included in Changi General Hospital, Singapore registry between June 2007 and June 2014, the electrocardiograms of 270 athletes with further cardiac investigations were analysed. We compared the above four electrocardiographic criteria to evaluate which performed best for detecting cardiac abnormalities on echocardiography in our Southeast Asian athlete population.

Results: The European Society of Cardiology, Seattle, Refined and 2017 International Criteria had a sensitivity of 20%, 0%, 20% and 5%, respectively; a specificity of 64%, 93%, 84% and 97%, respectively; a positive predictive value of 4%, 0%, 9% and 11%, respectively; and a negative predictive value of 91%, 92%, 93% and 93%, respectively for detecting abnormalities on echocardiography.

Conclusion: The latest 2017 International Criteria performed the best as it had the highest specificity and positive predictive value, joint highest negative predictive value, and lowest false positive rate.

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Keywords: Athlete, cardiology, electrocardiogram, pre-participation screening, sports medicine, sudden death

INTRODUCTION

Sudden cardiac death in athletes during exercise is rare, with an estimated incidence of 1–2 per 100,000 people per year in young athletes,[1] and approximately 1 per 7,000 per year in adult athletes.[2] The predominant aetiology of these cases is cardiovascular in nature, with conditions such as hypertrophic cardiomyopathy (HCM), arrhythmogenic right ventricular cardiomyopathy and ion channelopathies among those implicated.[3] These conditions increase the risk of malignant cardiac arrhythmias such as sustained ventricular tachycardia or ventricular fibrillation.

However, most of the affected individuals are young and asymptomatic prior to the event; consequently, the challenge is to detect these at-risk individuals who might benefit from competitive activity restriction while minimising unnecessary investigations for the majority of athletes that are at low risk.

The majority of cardiovascular causes that predispose individuals to sudden cardiac death could potentially be identified by a resting 12-lead electrocardiogram (ECG). The 12-lead ECG is one of the cornerstones of pre-participation screening, in conjunction with screening for cardiovascular-related symptoms, a family

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history of cardiovascular disease with an emphasis on premature sudden cardiac death or inheritable cardiac diseases, and a physical examination.[4]

Over the past 10 years, there have been several modifications to ECG interpretation to sieve out ECG changes that reflect normal physiological changes (the "athlete's heart") from pathological changes that reflect underlying heart disease. In 2009, Corrado et al. published the European Society of Cardiology (ESC) Criteria that listed out group 1 ECG changes—which were common and training-related—as well as group 2 ECG changes—which were uncommon and training-unrelated.[5] This latter group warranted further investigations to rule out underlying cardiac disease. There have also been other publications with similar ECG criteria intending to distinguish normal from abnormal ECG findings.[6] However, the rate of false-positive interpretations and unnecessary secondary investigations appeared unacceptably high especially in Black athletes.[7]

In 2013, Drezner et al. published the Seattle Criteria which added and removed some ECG criteria to the list of abnormal ECG findings, as well as redefining some criteria such as T wave inversion.[8] Subsequent studies showed that the Seattle Criteria had a lower false-positive rate compared to the ESC Criteria.[9] Despite this, the ESC and Seattle Criteria were still based predominantly on data derived from Caucasian athletes. As such, Sheikh et al. published the Refined Criteria in 2014 to take into account both Black and White athletes.[7] This Refined Criteria included a borderline category of ECG variants, which required the presence of 2 or more ECG criteria before recommending further investigation. It was later shown that the Refined Criteria outperformed the ESC and Seattle Criteria in Arabic, Black and Caucasian athletes.[10]

More recently, renowned experts in the field published the International Criteria in 2017, endorsed by international bodies on both sides of the Atlantic.[11] This recommendation largely built on the Refined Criteria and also introduced the concept of juvenile T wave changes, which were considered normal.

The above revisions to ECG interpretation criteria have advanced knowledge of ECG abnormalities in athletes among cardiologists all over the world. However, knowledge gaps remain in athletes of races, other than information of Caucasian, Black and Arabic descent. We had previously presented our data comparing the ESC, Seattle and Refined Criteria in Southeast Asian athletes and found that the Refined Criteria provided the optimum combination of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) among the three criteria for detecting cardiac abnormalities on echocardiography.[12] In this study, we present updated data to compare the above three criteria, in addition to the latest 2017 International Criteria, when applied to our Southeast Asian athlete population.

METHOD

Setting

A total of 1,515 Singapore competitive athletes who underwent pre-participation screening between June 2007 and June 2014 at the Singapore Sport & Exercise Medicine Centre at Changi General Hospital were prospectively included into our registry. They were elite sports athletes, predominantly soccer players funded by Fédération Internationale de Football Association (FIFA) and the Singapore football leagues, participating at the national level. Transthoracic echocardiograms were performed in accordance with the American Society of Echocardiology guidelines either as part of the screening protocols of their sports organisation or on clinical grounds because of abnormal electrocardiograms (ECGs), the presence of symptoms or cardiac murmurs. Other investigations such as computed tomography coronary angiogram, cardiac magnetic resonance imaging and invasive coronary angiography were performed based on clinical indications to arrive at a final diagnosis. Another 270 athletes with further cardiac investigations were included in this analysis and their electronic

medical records reviewed in December 2015. The study was approved by the SingHealth Institutional Review Board in 2015.

Retrospective ECG analysis

The ECGs of all 270 elite athletes were interpreted retrospectively by 2 senior cardiologists (a sports cardiologist and an interventional cardiologist with an interest in sports cardiology) using the ESC Criteria, Seattle Criteria, Refined Criteria, and the 2017 International Criteria (Table 1). The ECG readers were blinded to the results of the cardiac tests during the analysis.

Statistical analysis

The data collected were summarised using frequency with proportion for categorical variables, mean with standard deviation (SD), and median with interquartile range (IQR) for parametric and non-parametric variables, respectively. The accuracy of ESC

Table 1. Summary table of the different electrocardiographic criteria.

ECG abnormality	European Society of Cardiology Criteria	Seattle Criteria	Refined Criteria	2017 International Criteria
Left atrial enlargement	Negative portion of the P wave in lead V1 ≥0.1mV in depth and ≥40ms in duration	Prolonged P wave duration of >120ms in lead I or II with negative portion of the P wave ≥1mm in depth and ≥40ms in duration in lead V1	As per ESC	As per Seattle Criteria
Right atrial enlargement	P wave amplitude ≥2.5mm in lead II, III, or aVF	As per ESC	As per ESC	As per ESC
Left QRS axis deviation	-30° to -90°	As per ESC	As per ESC	As per ESC
Right QRS axis deviation	>115°	>120°	As per ESC	As per Seattle Criteria
Right ventricular hypertrophy	Sum of R wave in V1 and S wave in V5 or V6≥10.5mm	Sum of R wave in V1 and S wave in V5 >10.5mm and right axis deviation >120°	As per ESC	Not applicable
Complete left bundle branch block (LBBB)	QRS≥120ms, predominantly negative QRS complex in lead V1 (QS or rS), and upright monophasic R wave in leads I and V6	As per ESC	As per ESC	As per ESC
Complete right bundle branch block (RBBB)	RSR pattern in anterior precordial leads with QRS duration ≥120ms	Not applicable	As per ESC	As per ESC
Intraventricular conduction delay	Any QRS duration >120ms including RBBB and LBBB	Any QRS duration ≥140ms or complete LBBB	As per ESC	Any QRS duration ≥140ms
Pathological Q wave	>4mm deep in any lead except III, aVR	>3mm deep or >40ms duration in ≥2 leads except III and aVR	≥40ms in duration or ≥25% of the height of the ensuing R wave	Q/R ratio ≥0.25 or ≥40ms in duration in ≥2 contiguous leads (excludes III and aVR)
Significant T wave inversion	≥2mm in ≥2 adjacent leads (deep) or "minor" in ≥2 leads	>1mm in depth in ≥2 leads V2−6, II and aVF, or I and aVL (excludes III, aVR, and V1)	As per Seattle Criteria	Negative portion of T wave ≥1mm in depth in ≥2 contiguous leads (excludes aVR, III and V1). But excludes: 1. Black athletes of African-Caribbean descent with J-point elevation and convex ST segment elevation followed by TWI in V2−4 2. Athletes <16 years with TWI in V1−3 3. Biphasic TWI in only V3
ST segment depression	≥0.5mm deep in ≥2 leads	As per ESC	As per ESC	≥0.5mm in depth in ≥2 contiguous leads

Table 1. Summary table of the different electrocardiographic criteria. (Cont'd)

ECG abnormality	European Society of Cardiology Criteria	Seattle Criteria	Refined Criteria	2017 International Criteria
ST segment depression	≥0.5mm deep in ≥2 leads	As per ESC	As per ESC	≥0.5mm in depth in ≥2 contiguous leads
Ventricular pre-excitation	PR interval <120ms with or without delta wave	PR interval <120ms with delta wave	As per Seattle Criteria	PR interval <120ms with a delta wave (slurred upstroke in the QRS complex) and QRS duration ≥120ms
Epsilon wave	Not applicable	Not applicable	Not applicable	Distinct low amplitude signal (small positive deflection or notch) between the end of the QRS complex and onset of the T wave in leads V1−3
Prolonged QT interval	QTc>440ms for males, >460ms for females	QTc ≥470ms for males, ≥480ms for females. Marked QT prolongation: QTc≥500ms	QTc≥470ms for males, ≥480ms for females	As per Seattle Criteria
Brugada Type 1 pattern	Not defined	Not defined	Not defined	Coved pattern: Initial ST elevation ≥2mm with downsloping ST segment elevation followed by a negative symmetric T wave in ≥1 leads in V1−3
Profound sinus bradycardia	Not applicable	<30 beats per minute or sinus pauses ≥3sec	Not applicable	As per Seattle Criteria
Profound 1st degree atrioventricular block	Not applicable	Not applicable	Not applicable	PR interval ≥400ms
Mobitz Type II 2nd degree atrioventricular block	Not applicable	Not applicable	Not applicable	Intermittently non-conducted P waves with a fixed PR interval
3rd degree atrioventricular block	Not applicable	Not applicable	Not applicable	Complete heart block
Multiple premature ventricular complexes	Not applicable	≥2 premature ventricular complexes per 10 second tracing	As per Seattle Criteria	As per Seattle Criteria
Atrial tachyarrhythmias	Not defined	Not defined	Not defined	Supraventricular tachycardia, atrial fibrillation, atrial flutter
Ventricular tachyarrhythmias	Not defined	Not defined	Not defined	Couplets, triplets, non-sustained ventricular tachycardia

ESC: European Society of Cardiology; LBBB: left bundle branch block; RBBB: right bundle branch block

recommendations, Seattle Criteria, Refined Criteria and the 2017 International Criteria to detect cardiac abnormality was assessed from sensitivity and specificity test by using echocardiography as the gold standard. Statistical analysis was performed using SPSS Statistics software version 20.0 (IBM Corp, Armonk, US).

RESULTS

Of the 270 athletes included in the study, their ages ranged from 11 to 55 years, with the median age being 19. A total of 218 athletes were under the age of 35 years, accounting for 81% of our study cohort. It was a predominantly male population (87.8%), comprising Malay (43.3%), Chinese (36.7%), Indian (8.1%) and other (11.9%) ethnicities. The athletes competed predominantly in soccer. The demographics are presented in Table 2.

The study showed that 94 (34.8%) of the athletes had ECG abnormalities consistent with ESC group 2 changes, 17 (6.3%) consistent with the Seattle Criteria, 45 (16.7%) consistent with the Refined Criteria, and only 9 (3.3%)

Table 2. Study population demographics.

Demographics	n=270
Median age (range), years	19.0 (11.0–55.0)
Age ≤35 years, n (%)	218 (81)
Male, n (%)	237 (87.8)
Races, n (%)	
Chinese	99 (36.7)
Malay	117 (43.3)
Indian	22 (8.1)
Others	32 (11.9)
Sporting discipline, n (%)	
Soccer	201 (74.4)
Long distance running	25 (9.3)
Swimming	12 (4.4)
Bowling	6 (2.2)
Badminton	5 (1.9)
Netball	5 (1.9)
Track and field	4 (1.5)
Golf	3 (1.1)
Sailing	2 (0.7)
Triathlon	2 (0.7)
Cycling	1 (0.4)
Floorball	1 (0.4)
Gymnastics	1 (0.4)
Squash	1 (0.4)
Table tennis	1 (0.4)

consistent with the 2017 International Criteria. Fig. 1 shows the percentage of each ECG abnormality detected by each of the 4 major criteria.

The 2017 International Criteria resulted inmuch fewer T wave inversions and Q waves being classified as abnormal when compared to the ESC group 2 Criteria. T wave inversions were reduced from 36 (ESC group 2 major and minor T wave inversions) to just 4 in the 2017 International Criteria, with a similar reduction in Q waves from 15 to 4, respectively. In addition, the ESC group 2 Criteria picked up 13 athletes with right ventricular hypertrophy ECG changes, whereas the 2017 International Recommendations did not label these 13 cases as beingabnormal since the ECG changes were all in isolation.

There was a total of 20 patients with abnormalities detected on echocardiography. Table 3 lists these 20 patients with their corresponding ECG findings, whether they satisfied any of the 4 ECG criteria, and their final diagnosis after completion of investigations.

Table 4 lists the sensitivities, specificities, positive and negative predictive values, false positive and negative rates for the ESC, Seattle, Refined and 2017 International

Fig. 1. Electrocardiographic abnormalities detected by each criterion.
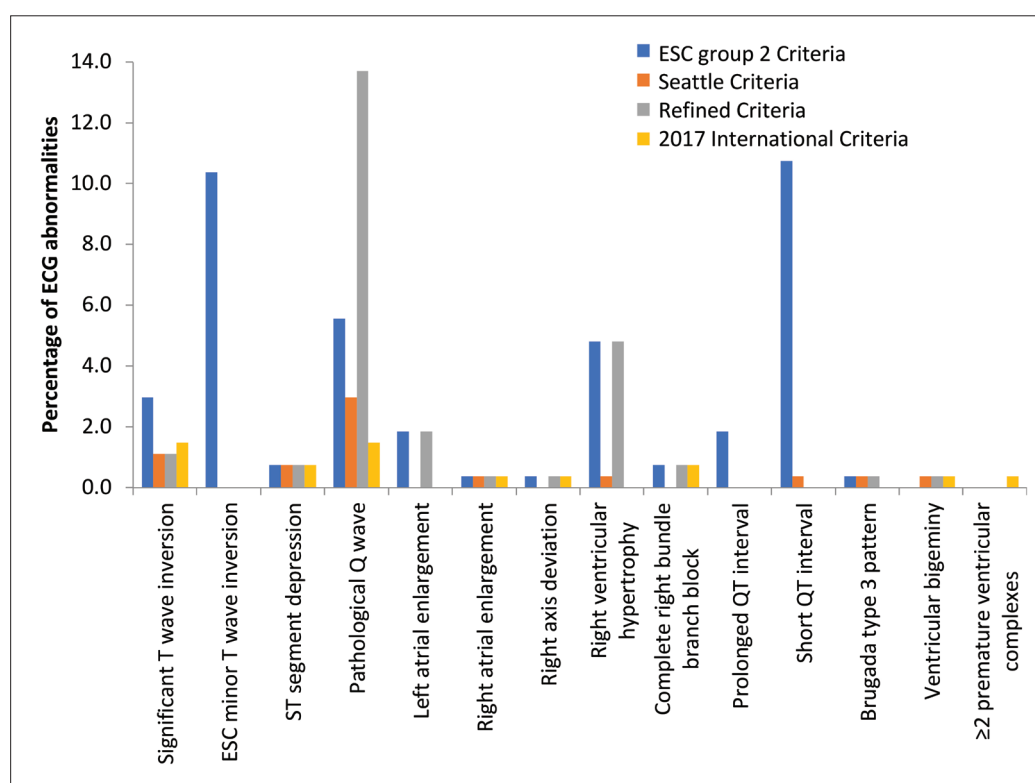ECG: electrocardiogram; ESC: European Society of Cardiology
The columns show the percentage of electrocardiographic abnormalities detected by each of the four criteria (European Society of Cardiology group 2 Criteria in blue, Seattle Criteria in red, Refined Criteria in green and the 2017 International Criteria in purple) in the study population of 270 athletes.

Table 3. List of patients with abnormal echocardiographic finding with their corresponding electrocardiogram (ECG) findings, abnormal ECG criterion satisfied, and final diagnosis.

Patient	ECG findings	Abnormal criterion	Final diagnosis
1	Sinus bradycardia		Previous myocarditis
2	Sinus bradycardia, early repolarisation, Q wave in lead III	Refined	Ischaemic heart disease
3	Sinus bradycardia, early repolarisation, QRS fragmentation, T wave inversion	European Society of Cardiology (ESC)	Ischaemic heart disease
4	Sinus bradycardia, Q wave in lead aVF	Refined	Dilated aortic root
5	Sinus bradycardia, early repolarisation		Pulmonary hypertension
6	Early repolarisation		Mitral valve prolapse
7	Sinus bradycardia, early repolarisation, left ventricular hypertrophy by Sokolov-Lyon criteria		Patent foramen ovale
8	Sinus bradycardia, early repolarisation, QRS fragmentation, left ventricular hypertrophy by Sokolov-Lyon criteria		Perimembranous ventricular septal defect and ventricular septal aneurysm
9	Early repolarisation, left ventricular hypertrophy by Sokolov-Lyon criteria		Atrial septal defect
10	Early repolarisation, QRS fragmentation, first degree heart block		Atrial septal defect
11	Low atrial rhythm, early repolarisation, QRS fragmentation, non-specific ST segment/T wave changes		Ventricular septal defect
12	Sinus bradycardia, early repolarisation, left ventricular hypertrophy by Sokolov-Lyon criteria		Mitral valve prolapse
13	Sinus bradycardia, Q wave in lead aVL	Refined	Left ventricular non-compaction
14	Sinus bradycardia, early repolarisation, left ventricular hypertrophy by Sokolov-Lyon criteria		Patent foramen ovale
15	Sinus bradycardia, non-specific ST segment/T wave changes		Mitral valve prolapse
16	Early repolarisation		Pulmonary stenosis with dilated pulmonary artery
17	Q wave in inferior leads, QRS fragmentation, RVH, left ventricular hypertrophy by Sokolov-Lyon criteria	ESC + Refined + 2017 International Criteria	Pulmonary hypertension
18	Sinus bradycardia, early repolarisation, left ventricular hypertrophy by Sokolov-Lyon criteria		Mitral valve prolapse
19	Left atrial enlargement, left ventricular hypertrophy by Cornell criteria, isolated premature ventricular complex	ESC	Mitral valve prolapse
20	Sinus bradycardia, early repolarisation, T wave inversions	ESC	Mitral valve prolapse and dilated aortic root

criteria. The 2017 International Criteria had a sensitivity of 5%, a specificity of 96.8%, a positive predictive value of 11.1%, and a negative predictive value of 92.7% for detecting abnormalities detected by echocardiography.

The mean duration of follow up was 4.9 ± 1.8 years. During follow-up, none of the 270 athletes had any adverse events such as sudden cardiac death, unexplained syncope (3 had vasovagal syncope and 1 had syncope secondary to heatstroke) or acute myocardial infarction.

Unrelated to his sporting activity, a 56-year-old athlete (patient number 2 in Table 3) had percutaneous coronary intervention performed to his distal left circumflex artery.

DISCUSSION

In this study involving pre-participation screening of competitive and leisure athletes, we compared the ESC, Seattle, Refined and 2017 International Criteria in detecting cardiac abnormalities in Southeast Asian athletes. To the best of our knowledge, these are

Table 4. Sensitivity and specificity using different electrocardiographic criteria to detect cardiac abnormalities in the entire study population (95% confidence interval).

	European Society of Cardiology group 2 Criteria	Seattle Criteria	Refined Criteria	2017 International Criteria
Sensitivity, %	20.0 (5.7–43.7)	0 (0–16.8)	20.0 (5.7–43.7)	5.0 (0.1–24.9)
Specificity, %	64.0 (57.7–70.0)	93.2 (89.3–96.0)	83.6 (78.4–88.0)	96.8 (93.8–98.6)
Positive predictive value, %	4.3 (1.1–10.5)	0 (0–19.5)	8.9 (2.5–21.2)	11.1 (0.3–48.2)
Negative predictive value, %	90.9 (85.7–94.7)	92.1 (88.1–95.1)	92.9 (88.7–95.9)	92.7 (88.9–95.6)
False positive rate, %	36.0 (30.0–42.3)	6.8 (4.0–10.7)	16.4 (12.0–21.6)	3.2 (1.4–6.2)
False negative rate, %	80.0 (56.3–94.3)	100 (83.2–100)	80.0 (56.3–94.3)	95.0 (75.1–99.9)

the first such published data in Southeast Asian athletes and build upon our knowledge base for athletes around the world.

There was a significant reduction in the number of abnormal T wave inversions and pathological Q waves using the 2017 International Criteria due to stricter criteria. The ESC group 2 changes considered deep T wave inversions as ≥2mm in ≥2 adjacent leads, and minor T wave inversions as <2mm in ≥2 adjacent leads. Using these criteria, there were 8 deep and 28 minor T wave inversions in our study. On the other hand, although the 2017 International Criteria considered abnormal T wave inversions as just ≥1mm in ≥2 contiguous leads, it excluded leads aVR, III and V1 from consideration, as well as regarded juvenile T wave inversions in V1-3 as normal findings.[13] Similarly, the ESC group 2 and Seattle Criteria considered pathological Q waves based on an absolute depth on the Q wave, while the Refined Criteria introduced the concept of a Q/R ratio of ≥0.25 to compensate for issues such as physiological left ventricular hypertrophy or thin individuals. The 2017 International Criteria further necessitated that abnormal Q waves had to be present in ≥2 contiguous leads, excluding leads III and aVR, before further investigations are warranted. These reductions, predominantly in athletes with normal cardiac investigations, contributed significantly to the improved specificity of the 2017 International Criteria in our study.

Based on our data, the latest 2017 International Criteria performed the best among the four criteria as it had the highest specificity (97%) and PPV (11%), the joint highest NPV (93%) and the lowest false positive rate (3%). In clinical practice, the relevance of this emerges when the ECG is negative, as clinicians can be reassured that these patients have a very high probability (93%) of truly not having any cardiac condition at that time. However, when the pre-participation ECG is abnormal based on the criteria, only a low probability exists of a truly underlying cardiac condition. This finding is relevant to current clinical practice, which recommends that ECG in pre-participation screening is interpreted according to the 2017 International Recommendations.[14]

The sensitivity by all four criteria is extremely poor, with at best 20% by ESC and Refined Criteria for our Singapore athletes. The issue of improving specificity at the price of sensitivity has been raised by Zorzi et al.,[15] and this is especially disconcerting for our group of athletes. In our previous study on Singapore athletes,[16] we have shown that an elite athlete's heart demonstrated similar morphologic exercise-induced cardiac remodelling as Caucasian athletes, but possibly to a lesser extent than the latter, as we did not observe any absolute left ventricular wall thickness beyond 1.2cm or left ventricular dilatation beyond 5.5cm. A recent study also showed that the upper limits of left ventricular wall thickness was 13mm and left ventricular diameter was 63mm in Southeast Asian athletes.[17] In a separate study, we were not able to find any sports-related sudden cardiac deaths from hypertrophic cardiomyopathy in the Singapore population over 11 years.[18] The low Singapore prevalence of cardiomyopathies might account for the low PPV, while the lower degree of electrical remodelling could explain the poor sensitivity.

There are several limitations to our study with the first being our study population. It was derived from a single centre registry and although our study population

included athletes of all the major ethnic groups in Singapore, we cannot rule out the possibility that other centres in our region may have differences in baseline demographics and ECG characteristics. It was also composed predominantly of males of Malay ethnicity, hence females and other ethnicities are under-represented. In addition, most of our athletes participated in soccer, which is classified as a mixed sporting discipline.[19] Therefore, our study could not assess the utility of these four ECG criteria in other sporting disciplines such as power (e.g. weightlifting, short-distance running and gymnastics) and endurance (e.g. cycling, rowing and swimming). We also acknowledge that our study population only focused on the subset of athletes within our entire registry who had further cardiac investigations performed. Hence, we may not have picked up athletes with normal pre-participation screening who could have underlying cardiac abnormalities, which would then affect the sensitivity, specificity, PPV and NPV.

Secondly, despite ECG screening and further cardiac investigations such as echocardiography, we did not detect any case of HCM. This condition was reported to be the most common cause of sudden cardiac death in athletes, accounting for 36% (and perhaps up to 44%) of sudden cardiac death cases.[3] However, HCM does produce classical deep T wave inversions in the praecordial leads, with less than 10% of HCM patients having a normal ECG.[20] Therefore, we believe that the ECG criteria in the latest 2017 International Recommendations would be able to detect HCM among athletes reliably.

Next, a significant proportion of our athletes only had one echocardiogram performed. Because individuals may only develop HCM at a later stage, we cannot rule out the possibility that the false-negative rate may have been underestimated.

In addition, we recognise that echocardiography would only detect structural heart abnormalities and may miss out arrhythmic conditions. However, our ECG analysis did not pick up any case of Wolff-Parkinson-White syndrome or Brugada type 1 ECG patterns. There was one Brugada type 3 pattern, but this is no longer clinically relevant and does not satisfy the diagnosis of Brugada syndrome. There were 6 cases of long QT detected by ESC Criteria that had a cut-off of 440ms and 460ms for males and females, respectively. However, all 6 cases were less than 470ms and 480ms for males and females, respectively, and were hence not considered abnormal by the other three criteria.

Furthermore, as some of the echocardiograms were performed based on clinical grounds or as part of the screening protocols of the relevant sports organisation, some of the abnormalities detected on echocardiography may be incidental and not related to any ECG abnormality. For example, there were several patients that satisfied other criteria besides the 2017 International Criteria who were subsequently found to have echocardiographic abnormalities. With reference to Table 3, patients 2 (Q wave in lead III) and 3 (T wave inversion) were found to have ischaemic heart disease, patient 4 (Q wave in lead aVF) was found to have a dilated aortic root, patient 13 (Q wave in lead aVL) was found to have left ventricular non-compaction, and patients 19 (left atrial enlargement) and 20 (T wave inversion) were found to have mitral valve prolapse. While it is possible that some of these were incidental

Table 5. Sensitivity and specificity using different electrocardiographic criteria to detect cardiac abnormalities in the study population after excluding master athletes (95% confidence interval).

	European Society of Cardiology group 2 Criteria	Seattle Criteria	Refined Criteria	2017 International Criteria
Sensitivity, %	20.0 (4.3–48.1)	0 (0.0–21.8)	13.3 (1.7–40.5)	6.7 (0.2–31.9)
Specificity, %	60.3 (53.3–67.0)	92.8 (88.4–95.9)	81.8 (75.9–86.8)	96.7 (93.2–98.6)
Positive predictive value, %	3.5 (0.7–9.9)	0 (0–21.8)	5.0 (0.6–16.9)	12.5 (0.3–52.7)
Negative predictive value, %	91.3 (85.3–95.4)	92.8 (88.4–95.9)	92.9 (88.2–96.2)	93.5 (89.4–96.4)
False positive rate, %	39.7 (33.0–46.7)	7.2 (4.1–11.6)	18.2 (13.2–24.1)	3.3 (1.4–6.8)
False negative rate, %	80.0 (51.9–95.7)	100 (78.2–100)	86.7 (59.5–98.3)	93.3 (68.1–99.8)

findings, it is difficult to draw definitive conclusions regarding the positive predictive findings of each criterion in a small sample size.

In contrast to previous studies,[5,8,10,12] our study included both young athletes as well as master athletes—athletes above 35 years old. Traditional pre-participation screening is focused on young athletes below the age of 35 and the four criteria are developed for such a population. We reanalysed our data after excluding the master athletes and had similar results (Table 5)—the 2017 International Criteria had the highest specificity (97%), PPV (13%) and NPV (94%), and the lowest false positive rate (3%). This is not surprising as master athletes only made up 19% of our study population. We also believe that including master athletes reflects real world practice of applying the ECG criteria to all age groups of athletes.

Lastly, even though our study population was recruited between 2007 and 2014, the ECGs were interpreted and analysed according to the four criteria, so would not have been different in an updated group of patients. Nevertheless, further contemporary research enrolling a larger group of patients from multiple centres around our region would help to ensure our athletes are not under-represented when future international pre-participation screening guidelines are being developed.

CONCLUSION

We have compared the latest 2017 International Criteria for ECG interpretation against the ESC group 2 changes, and the Seattle and Refined Criteria in our population of Southeast Asian athletes. The 2017 International Criteria had the highest specificity and PPV, joint highest NPV and lowest false positive rate among the 4 major ECG criteria. However, the sensitivity of all four criteria is very poor in our Singapore population. Further large-scale studies in the Singapore population would add more information into our ever-growing knowledge base of pre-participation ECG interpretation in athletes worldwide.

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Impact of COVID-19 on mental health and social service provision in Singapore: Learnings from a descriptive mixed-methods study for future resource planning

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ABSTRACT

Introduction: COVID-19 restrictions and lockdown measures have led to impact on the mental health and social service delivery, including the rapid adoption of digital solutions to mental healthcare delivery in Singapore. This study aims to rapidly document the quantitative and qualitative impact of the pandemic restrictions on mental health and social services.

Method: This descriptive mixed-methods study consisted of a survey arm and a qualitative arm. Providers and clients from eligible mental health organisations and social service agencies were recruited. The respondents completed a survey on changes to their service delivery and the extent of impact of the pandemic on their clients. In-depth interviews were also conducted with representatives of the organisations and clients.

Results: There were 31 organisation representatives to the survey, while 16 providers and 3 clients participated in the in-depth interviews. In the survey arm, all representatives reported pivoting to remote means of delivering care during the lockdown. An increase in new client referrals and more domestic violence were reported from primary and community health partners respondents who made up 55.5% of health partners respondents. Three distinct response themes were recorded in the in-depth interviews: impact on clients, impact on service provision and impact on mental health landscape.

Conclusion: Two key findings are distilled: (1) mental health and social services have been challenged to meet the evolving demands brought about by the pandemic; (2) more societal attention is needed on mental health and social services. The findings indicate a necessary need for extensive studies on COVID-19 that can inform policies to build a more pandemic-resilient nation.

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Keywords: COVID-19, digital health, mental health, psychiatry, psychology

INTRODUCTION

Coronavirus disease 2019 (COVID-19) was declared a global health emergency by the World Health Organization in January 2020.[1] Singapore reported its first case of COVID-19 on 23 January 2020 and the subsequent emergence of clusters led to a string of restrictions to contain the outbreak and protect the health of the public. The healthcare sector initially ramped down non-emergency services to allow for the redeployment of resources for COVID-19-related services. In response to the widespread COVID-19 clusters,[2] a nationwide lockdown (known as "circuit breaker") was implemented from 7 April to 1 June 2020, during which only essential services could continue operations and be kept open. Home-based learning was implemented, mask-wearing when leaving the home was

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CLINICAL IMPACT

What is New

- This descriptive mixed-methods study documents the extensive quantitative and qualitative impact of the pandemic restrictions on mental health and social services in Singapore during the height of the "circuit breaker" lockdown period.

Clinical Implications

- Findings from this study justifies the need for more societal attention on mental health and social services in the general population.
- The quantitative and qualitative data from this study can potentially inform and guide mental health and social service policies to build a more pandemic-resilient nation.

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made mandatory, and leaving the home was only allowed for essential activities.[3]

The mental health of confirmed COVID-19 patients,[4-6] quarantined cases,[7,8] frontline workers,[9,10] the general public[11-13] and persons with mental illness[14] were inevitable casualties of these necessary public health measures as some studies have demonstrated. Chen et al.[15] showed that the lockdown in the United Kingdom resulted in a decrease in mental health referrals to secondary care services, followed by a longer-term acceleration in the referral rate primarily for urgent or emergency referrals. Despite the restrictions on the provision of mental health and social services, staff working in these sectors innovated to continue service provision remotely, although this provision was only successful in some clinical situations.[16] Singapore faced a similar situation during the circuit breaker" in that community mental health and social service agencies (SSAs) were deemed non-essential services and had to cease face-to-face operations. The impact of such an acute change in services on clients and service providers had not been systematically measured.

There exist abundant reports of the rapid implementation of digital means of mental health services as a way of continuing service provision to high-risk and vulnerable populations.[17,18] These digital adaptations of services include dissemination of mental health surveys, education and communication programmes, counselling services, self-help interventions and artificial intelligence-driven crisis interventions.[19] Users of such services

have reported satisfaction and benefits,[20] and acknowledged them as the inevitable way forward for mental health care,[21,22] although evidence of clinical efficacy remains preliminary.[23] There remain practical challenges on the ground, particularly in the Asian context.[24] Anecdotal experience in Singapore has indicated the pressure experienced by the sector to rapidly convert to online and remote means of continuing mental health and social services despite valid doubts about their utility and acceptability, and fears about their efficacy in preventing and intervening in mental health crises and emergencies.[25]

There was an absence of local and international publications on the impact of COVID-19 on mental health services during the period from late 2020 to early 2021. A qualitative review conducted by Byrne et al.[26] on the impact of COVID-19 pandemic from a mental health perspective indicated a negative impact on people's mental health, mental health services workforce and caregivers given greater strain, as well as the impact on psychiatric education, training and research. Studies on the pandemic and its related measures on mental health and social service provision in Singapore were far fewer. Therefore, a rapid documentation of quantitative and qualitative data on the impact of pandemic restrictions on mental health and social services was needed. By utilising a mixed methods approach, knowledge gaps regarding the utilisation patterns, successes and challenges of mental health and social services can be quantified and contextualised in order to inform policy changes on the current and future infectious disease outbreaks.

The research questions to be addressed in this study were (1) to identify the magnitude of the impact of the pandemic on mental health and social services at the organisational level, and (2) to explore the qualitative impact of the pandemic on the provision of mental health and social services.

METHOD

This descriptive mixed-methods study consisted of a survey arm and a qualitative arm. Ethics approval was obtained from the National Healthcare Group Domain Specific Review Board (ref 2020/00899).

Recruitment

This study adopted a convenience sampling methodology. All organisations and agencies in Singapore that provided mental health services (e.g. psychiatry, psychology) and social services (e.g. family counselling, senior activity centres) were eligible to participate in this study. An email invitation was first

sent to representatives of all eligible mental health organisations and SSAs to respond to the survey. Guidance on data collation was provided to these representatives. The recipients of the invitation could nominate themselves or another staff member to respond to the survey. The representatives were also concurrently invited to participate in the qualitative arm of the study and to refer their suitable clients to participate in the in-depth interviews to describe their experiences of accessing mental health and social services during the pandemic. Separate letters of invitation were provided to the clients to indicate their contact details. The providers and clients who indicated their interest in the qualitative arm of the study were then contacted by the study team members to obtain consent and to conduct the interview.

Data collection

A quantitative survey was administered to quantify the organisational and administrative changes due to the COVID-19 pandemic and the lockdown. The survey was completed either online on FormSG (secured online survey platform for public institutions) or in a Word document which respondents returned to the study team by email. Respondents for the survey first indicated the details of the services that their organisations provided (e.g. sector/department, acute/centre-based service, public/private organisation). Subsequently, they were asked whether there had been changes to their service delivery during the lockdown and the extent of impact of the pandemic on their clients (e.g. increase in crisis situations, need for further escalation).

In-depth interviews were conducted to explore the qualitative impact of the pandemic on the services and clients of the providers. Examples of the questions for the providers include "How has the pandemic impacted your work?", "What COVID-19 measures have caused the most impact on your client?" and "What did you find helpful for you to reach out to your clients effectively?". For clients, the questions were phrased to explore the impact and challenges that they personally face in accessing mental health and social services during the lockdown. The in-depth interviews were conducted using the Zoom platform. Informed consent was obtained individually by the interviewer and all participants consented to voice recording for transcription. One researcher (ZZSG) who had training and experience in qualitative methodologies conducted all the in-depth interviews. The data collection period was from 29 August 2020 to 1 February 2021 for the survey and between 20 October 2020 and 2 February 2021 for the qualitative interviews. The survey and interview

questions are available as Online Supplementary Materials.

Analytical method

Respondent organisations in the survey were categorised and analysed using the following groups: (1) restructured hospitals (comprising the psychiatry and psychology departments from tertiary hospitals), (2) primary and community health partners (PCHPs) (comprising polyclinics and nursing homes), and (3) SSAs. The survey responses were analysed using descriptive statistics.

The in-depth interviews were transcribed with the identifiers anonymised. The transcripts were first given a read-through and then coded inductively by authors ZZSG and KG. Qualitative data were coded using content analysis, in which the codes were categorised and grouped into higher order themes by 3 members of the study team.[27] All qualitative analyses were conducted using NVivo Release 1.0.[28]

The findings from both the quantitative and qualitative arms were first described separately and thereafter combined to generate a more complete understanding of the impact of COVID-19 pandemic and its restrictions on mental health and social service delivery in Singapore.

RESULTS

Survey arm

There were 31 respondent organisations to the survey (9 restructured hospitals, 9 PCHPs, 13 SSAs). Of the PCHPs, 6 were from polyclinics and 3 were nursing homes. A mixture of SSAs participated in the survey (5 in mental health services, 3 family services, 3 dementia care, 1 addiction services, 1 LGBTQ+ services), although most of their services could overlap.

All respondents reported pivoting to remote means of delivering care during the lockdown, compared with about 50% before the lockdown. Comparing with respondents from the restructured hospitals and PCHPs, those from the SSAs group reported a greater proportion of their clients who had requested for an urgent or earlier appointment (restructured hospitals: <25%, PCHPs: <25%, SSAs: 25–50%) or were deemed not suitable for postponement of face-to-face appointment (restructured hospitals: 25–50%, PCHPs: <25%, SSAs: 51–75%).

No respondents from PCHPs reported an increase in clients who completed or attempted suicides. However, respondents from restructured hospitals and SSAs reported an increase in such clients (increase by 15.4–23.1%, Fig. 1). More than half of the respondents from both restructured hospitals and SSAs reported an

increase in hospitalisations for mental health reasons and exacerbations of pre-existing mental illnesses. Notably, the difference in the reporting of domestic violence from more than half of the respondents from PCHPs was more drastic than from the other groups (55.5% in PCHPs vs 22.2% in restructured hospitals and 7.7% in SSAs).

With respect to service use, there was no report of increase in the number of new clients from restructured hospital respondents, whereas more than a third of the respondents in both PCHPs and SSAs reported an increase in new clients (Fig. 2). In all 3 groups, there was a consistent trend in an increase of clients requiring more frequent follow-ups (55.5–66.6%) and reportedly an increase in the need for face-to-face interventions in restructured hospitals and PCHPs (66.6% and 77.7%, respectively). Respondents from SSAs also reported an increase in clients requiring further escalation or referrals to other mental health providers (61.5%).

Qualitative interview arm

A total of 16 providers and 3 clients from mental health and social services were recruited for the in-depth interviews. Of the providers, there were 6 psychologists (37.5%), 5 programme administrators (31.3%), 2 case managers (12.5%), 1 counsellor (6.3%), 1 social worker (6.3%) and 1 occupational therapist (6.3%). Majority of the providers were female (n=14, 87.5%). Seven of the providers served in the public sector, 5 were in the SSAs, while the remaining 4 were in the private or charity organisations.

Owing to the small sample size of clients (n=3; female, n=2, male, n=1), the main themes were identified from the provider interviews and, if relevant, corroborated and triangulated with the client accounts. Saturation was achieved after 2 provider interviews, as new themes did not emerge, and determined after a discussion within the study team. Altogether, the responses shared by
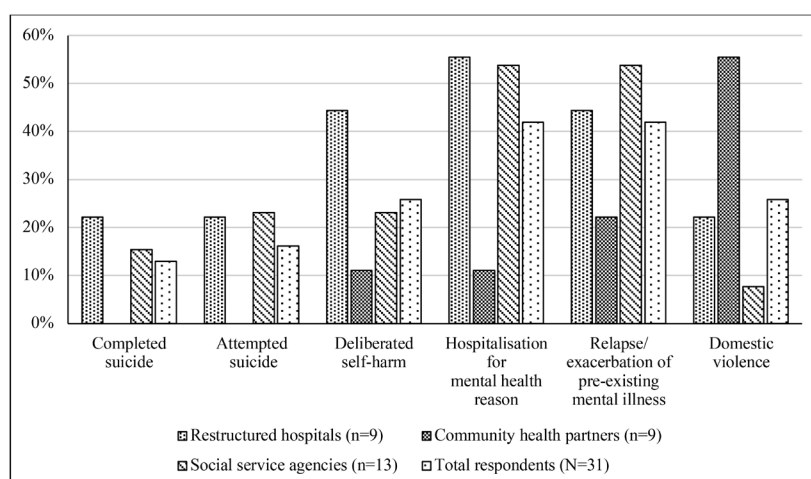

Fig. 1. Percentage of respondents reporting increase in crisis situations.
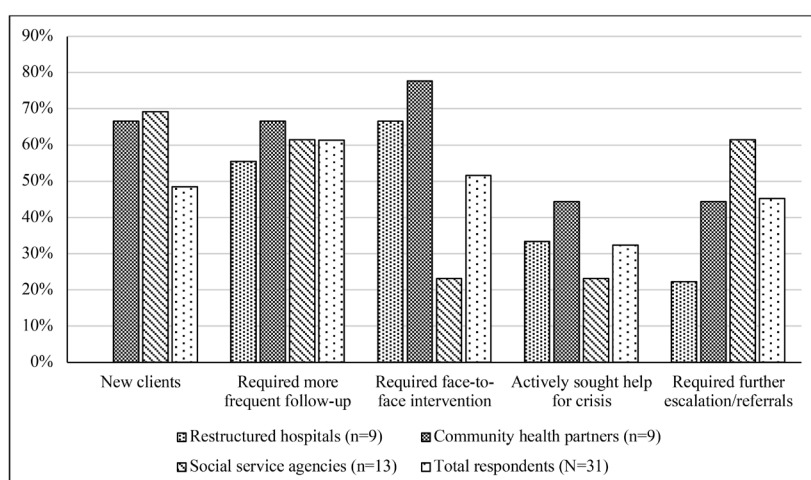

Fig. 2. Percentage of respondents reporting increased service use.

all participants showed 3 distinct themes: impact on clients, impact on service provision and impact on mental health landscape.

Impact on clients

With the challenges of COVID-19 and its associated precautionary measures, several impacts on the clients were raised. Five response subthemes were identified from the provider interviews: (1) COVID-19 restrictions bringing about more challenges to clients' mental health (2) social-related impact; (3) domestic issues; (4) caregiver impact; and (5) demonstration of social support and resilience (illustrative quotes in Table 1).

The providers shared about how COVID-19 had brought more challenges to the profiling of their clients. They noted an increase in severity of anxiety and obsessive-compulsive disorder symptoms in their clients during the initial phases of the pandemic. Some of

Table 1. Subthemes and illustrative quotes of theme 1: Impact on clients.

Subthemes	Illustrative quotes
Increased challenges with COVID-19	"when the numbers were climbing, the anxiety of having COVID themselves… the clients might feel… the anxiety of catching the illness" – Provider O; female, mental health programme coordinator, social service "I felt that I should wear two [masks], because I felt safer that way and I was afraid… Back then I was still worried, and I still kept washing my hands… I felt that phase 1 and 2 were relatively challenging for me." – Client 1; female "the situation looks like very scary also, you know, especially what—cannot sit here cannot sit there—literally you cannot go out. You know, there's a lot of restriction, I think it has an impact on some people's mental health." – Provider K; female, counsellor, social service
Social-related impact	"quite a number of elderly live on their own… there's no one there to look out for them. At least like last time there's a lot of social service agencies and day care centres that elderly can go to" – Provider B; female, caseworker, charity organisation "these centres function as a respite for caregivers, and to also stimulate the seniors so that it will delay the cognitive decline" - Provider E; female, social work associate, social service
Domestic issues	"a lot of them came in with more... domestic-related interpersonal issues"- Provider J; female, psychologist, primary care "Mental health of my current patients and the patients that I see are a bit worse by having to stay at home. Some relationships at home like the domestic violence and conflict, it's much worse" – Provider A; female, social worker, public hospital "So there were a few cases with family violence, physical as well as verbal aggression shown by either one of the spouses" – Provider M; female, clinical psychologist, private practice
Caregiver impact	"couples and parents who had to manage not just like their own needs but they also had to take care of those that were depending on them as well, so I think it might have cause a lot of conflict as well." – Provider B; female, caseworker, charity organisation "day care centre was actually quite overwhelmed during the circuit breaker because a lot of caregivers are trying to send their loved ones to day care… So they felt very frustrated that they have to manage caring for their loved ones and also work." – Provider D; female, social work associate, social service "this time (I) was really (feeling) very down and the next thing is—my husband went to the day care centre so it is—shutting down so we have to stay home… So during the pandemic I also lost my job. So like, (I feel) more tensed up." – Client 2; female, caregiver of patient with dementia
Demonstration of social support and resilience	"So for some, they have very strong familial support. That was actually a very strong protective factor for them… I think some of them also have that mental resilience, they know that this thing will eventually—they have hope that it will eventually get better." – Provider D; female, social work associate, social service "For the elderly, they pretty much gone through the whole hard-knock life… So we get elderly coming in telling us "I'm very worried but what to do, life is like that"… so growing up with this kind of mentality, could have given them that sense of resilience – Provider J; female, psychologist, primary care "I think parents of kids with extra or additional needs, even if they are not so severe, already have a resilience that we don't appreciate enough, for them sometimes just getting their child to eat, put on socks, the things that they battle through every day is a lot, so I think they already have resilience in reserve." – Provider N; female, occupational therapist, private practice

their clients shared about fear of COVID-19 exposure, excessive worrying and excessive prevention practices such as more frequent hand washing and double masking. Some providers also noted the difficulties in getting their clients who are cognitively compromised (e.g. people with dementia) to adhere to the COVID-19 measures, such as mask wearing and social distancing.

The providers also noted the social impact that their clients experienced from the COVID-19 measures. Particularly, the countrywide lockdown meant that the elderly and other residents that rely on physical venues for support (e.g. day care centres, leisure venues) lost access to these social resources, leading to increased feelings of isolation. Relating to the clients' inability to leave their homes, the providers shared about the increase in domestic issues and in caregiver burden that their clients faced during the lockdown period. Furthermore, some clients who experienced family violence still stayed with the perpetuators. Clients who were also caregivers had to care for both the elderly and their children, all while still working from home. These challenges imposed substantial mental stress on the clients, leading to more mental health issues.

The providers highlighted the importance of social support and resilience in their clients that could help alleviate the impact of the pandemic. Strong family support was reported to be a protective factor against feeling isolated. The providers also shared about the demonstration of resilience in their clients who had gone through the "whole hard-knock life" (Provider J) for the elderly, and in parents of special needs children who already had "resilience in reserve" (Provider N). The clients also demonstrated resilience by picking up new technological skills to access telehealth services, make bill payments and connect with family and friends. One client aptly shared that "there's good and there's bad" (Caregiver 2).

Impact on service provision

Guidelines from authorities were released frequently and changes had to be implemented by the providers almost immediately. These frequent changes in guidelines impacted the mental health and social service provision. Three response subthemes for the impact on service provision were noted: frequency of changes to guidelines, manpower difficulties and innovation in the online shift of services (Table 2).

The providers shared about how the organisations were not given enough time to adjust to the guidelines. As one provider shared, "within one week, certain instructions can change a few times, our work processes can change a few times" (Provider C). The numerous

rules and guidelines also led to some confusion and anxiety. Manpower issues were also reported by some providers who described an increased workload due to split-team arrangements and manpower redeployment. Consequently, motivation and morale of the team were affected owing to the increased pressure and workload.

The providers also shared about the need for their services to be delivered online to reduce the risk of exposure of their clients to the pandemic virus and shared about their experiences of learning to use the video-conferencing platforms. Some organisations started using the social media and video streaming sites to conduct workshops and engage their clients in activities. While these had been reported to be a convenient way of delivering the services, some providers doubted their effectiveness. The providers shared that, compared with face-to-face sessions, it was difficult to build rapport and look at non-verbal cues when the clients could not be seen beyond the screen. There were also doubts about clients being in a safe space without distractions during the virtual sessions, as many of them were attending the sessions from their homes, which might not be the safest space for counselling.

Impact on mental health landscape

Some providers shared that the creation of the National Care Hotline, a phone-in service for emotional and psychological support during COVID-19 by the ministries, was important in helping vulnerable individuals cope with the pandemic. Along the same vein, the providers noted a general increased awareness and recognition of the importance of mental health and its profession in the general population, with more people willing to step out to seek help. They highlighted that an overall greater awareness of mental health in the general population can reduce the impact of the pandemic (Table 3).

DISCUSSION

Integrating both quantitative and qualitative aspects of the study provided us with a more holistic understanding of the impact of the COVID-19 pandemic and its restrictions on mental health service delivery in Singapore. Two key findings are highlighted from the results of this study: (1) mental health and social services have been challenged to meet the evolving demands brought about by the pandemic; and (2) more societal attention is needed on mental health and social services.

Evolving demands due to the pandemic

First, all domains of mental health and social services have been challenged to meet the evolving demands

Table 2. Subthemes and illustrative quotes of theme 2: Impact on service provision.

Subtheme	Illustrative quotes
Frequency of changes to guidelines	"Every day there was new kind of measures and there were new things to consider or worry about… you're not allowed to sit in a park, and then the next day you can, or you must one metre distance, and suddenly you had to wear masks… So that was a bit of anxiety provoking." – Provider M; female, clinical psychologist, private practice "I think within one week, certain instructions can change a few times, our work process can change a few times." – Provider C; male, case manager, public hospital "because there were so many advisories and so many rules that were set in place, it was very confusing to follow through this whole thing." – Provider D; female, social work associate, social service
Manpower difficulties	"I think we have arranged to be 50% onsite at any point of the time… 50% will be on site then the other 50% will be working from home… we wanted to do a permanent arrangement but then the onsite teams said it's too heavy for them" – Provider C; male, case manager, public hospital "For staff, we will definitely have to reassure staff, we have to check in with them, and see whether, because if they are under split teams, they might be overworked, they might take in a bit more clients than they used to, so we have to check in on them." – Provider E; female, social worker associate, social service "We cannot do anything, if you really need to push yourself right… it is going to be a problem, it can work for a certain period of time, but I will say definitely is not sustainable… Because it's at the expense of the individual service provider. As a team, I think we can run. But as an individual, we are slowly exhausted. So then, is another question of I don't know how long this team can run. – Provider L; female, psychologist, primary care
Innovation in the workplace	"COVID-19 has taught me to be more innovative… how to improve processes… I should do something to work on the processes, so lesser for them on the administrative work." – Provider G; female, centre manager, social service "COVID-19 has taught caregivers to be more resourceful, you know like I said they were not able to do their usual activities and things like that. A lot of caregivers became more resourceful" – Provider H; female, psychologist, social service
Innovation in the online shift of services	"Online sessions are more convenient in the sense that you can do it at your own place and time, you know like, I guess it's more convenient for them in that sense… it might be a bit more challenging for counsellors to do online counselling because you, like you can't really know what they're thinking and feeling because you're not seeing them face-to-face and there might be other distractions around as well so it won't be the same as face-to-face counselling when you're in a, like you know we're in a safe space and you know you can talk your feelings out." – Provider B; female, caseworker, charity "if it's on Zoom then a lot of restrictions because I cannot see beyond the screen—I cannot see the other body movements because all the postures, all the non-verbal cues are important in my line of work… and also some assessments like IQ you cannot do it online anyway because they have to do some non-verbal tasks." – Provider P; female, psychologist, private practice "The inability to also connect, so a lot of loneliness experience because of that as well, given that your home is not the safest place… some people in the background now that we've had noise outside that's picked up that they're just very, very distracting, but there's nothing that you can do technically" – Provider M; female, clinical psychologist, private practice

Table 3. Illustrative quotes of theme 3: Impact on mental health landscape.

Subtheme	Illustrative quotes
Increased recognition of importance of mental health	"A good thing that came out of this pandemic is that there became more awareness about mental health and the importance of taking care of one's own mental health…" – Provider H; female, psychologist, social service "the government, the media… actually sort of put emphasis on mental health during this period… Actually they increased the awareness and this actually helped people to seek help… because I was also the National Care Hotline volunteer as well and because of this availability of service right… because of this—increased emphasis on mental health during this period." – Provider I; male, psychologist, primary care "Because of the COVID situation, I do have to acknowledge that the idea of psychology or profession of mental health really just was brought a bit more to the forefront… So I think the pandemic has definitely showcased that mental health or psychologists… without this kind of support, I think there would have been a lot more individuals who may have spiralled or gone a little bit more out of control, due to the lack of connection, and feeling supported in many ways." – Provider M; female, psychologist, private practice

brought about by the pandemic. Despite the study respondents coming from a wide range of professions, all have reported some degree of impact on their service provision. This impact was evident in the survey arm in that all the participants (i.e. restructured hospitals, community health partners, SSAs) indicated increased service use, and both providers and clients, in the qualitative interviews, shared on the challenges of service provision during the pandemic.

Local and international studies have shown that more people needed and were seeking more psychological help during the COVID-19 pandemic.[29,30] Owing to the reprioritisation of treatment services for COVID-19 cases, there was a rechannelling of new tertiary care clients towards primary care. Day activity centres and social support venues were closed, while service provider teams were segregated with reduced clinic sessions. The healthcare sector, especially the mental health and social services, had to find innovative solutions to provide continuity of care.[31-35] In that respect, innovations in technology and clinical processes enabled the use of online mental health service delivery, but some providers shared that these might be neither effective in nor capable of reaching out to everyone. These challenges towards digital adoption that the sector faced were also not unique to the Singapore context. A study in Hong Kong on community centres for older adults found that those centres which adopted online services faced constraints such as limited digital literacy of staff members and low digital accessibility, including lacking devices and poor internet connection, for service users.[36]

Moreover, the increase in new clients in PCHPs and SSAs in this study corroborated the issues related to the increased workload in relation to the reduction in manpower. Restrictions on home visitations during the pandemic also made matters worse. SSAs also reported an increase in clients requiring further escalation but were unable to offer face-to-face interventions. The pursuit of providing continued care for clients was an uphill task for the mental health and social services sectors during the pandemic. Indeed, the increased barriers to access mental health care will severely affect clients with pre-existing mental illness, which could result in mental relapse or further uncontrollable situations.[29]

Societal attention on mental health and social services

It is evident that more societal attention has to be given to mental health and social services. The COVID-19 pandemic and its related measures have caused an unprecedented impact on the general health of the population. People were not able to go out of their homes during periods of lockdown, resulting in increased tensions within unsupportive households and increased rates of domestic violence. Fears of contracting COVID-19 and of its disease progression have produced a general sense of anxiety in the population.

With the world facing the COVID-19 pandemic for the long term and the threat of the disease becoming less acute, attention has to be shifted to mitigate the psychosocial impact of the restrictions surrounding the pandemic. The disruptions to mental health and social service delivery have likely impacted the morale of service providers. Providers may experience compassion fatigue and burnout more often than before.[37,38] The findings from this study are concerning as respondents reported increased service use but were faced with persistent and unpredictable barriers. Mental healthcare providers and allied health professionals alike have reported worse mental health outcomes during the pandemic in many studies globally,[35,39] and some have reported resorting to using negative coping strategies such as alcohol and tobacco to cope with the stress of the pandemic.[40] Although our study did not collect data on the utilisation rates of mental health support by the providers, one study found low rates (between 1% and 22%) of allied health professionals in the United States using any form of mental health support, despite them experiencing stress.[39] Far greater emphasis and investment of resources for mental health and social services from the whole-of-society are needed to confront the "mental health tsunami".[41]

With the protracted pandemic and constant threat of new variants, public health measures should shift towards supporting people holistically. Healthcare systems should seek to empower and destigmatise people who seek help. With the increase in awareness of mental health issues, healthcare policies should adopt a proactive approach in mental health care, stepping up in their engagement with schools and outreach to the public. Systems could be in place to monitor and address the distress levels in vulnerable and at-risk populations (e.g. healthcare workers, elderly living alone, marginalised individuals).

As a result of the pandemic, the rapid push of digital solutions in mental health practice (e.g. teleconsultations) has created new opportunities to provide sustainable preventive mental health care and support. With growing adoption of online service delivery in the mental health and social service sectors, medical schools can institutionalise a curriculum on digital mental health by leveraging the experience gained from using telehealth during the pandemic to improve and upskill mental health and social service providers on delivering telehealth care to their clients effectively.

Limitations

The findings of this study should be considered along with its limitations. The data collection was conducted primarily online (i.e. online survey and interviews) to reduce physical contact, which may have excluded some providers and clients who faced barriers in accessing the internet (e.g. low technology literacy). Further, significant effort was needed in collating the administrative data for the survey, and some organisations neither responded to nor provided data for the study. These limitations can thereby reduce the generalisability of the findings. Nonetheless, a wide range of mental health and social service providers participated in this study, and a set of broad (rather than narrow) observations and vast opinions of service providers were captured through the qualitative interviews.

It was noted that only 3 clients participated in the qualitative interviews. Efforts were made to recruit more clients through repeated email outreach to the providers. However, the providers were unable to refer their clients as the sessions were mostly virtual and the providers had expressed that most of their clients were not interested to participate in the interviews. Despite this limitation, the overall mixed method design of the study through integrating the survey with the interviews reinforced the robustness of the study's overall findings. Overall, the study findings indicate a strong and necessary need for more extensive studies on COVID-19 and its impact on the mental health landscape.

CONCLUSION

At the conclusion of this study in April 2021, Singapore was going into its second circuit breaker owing to increasing COVID-19 cases driven by the Delta variant. Dining in was once again ceased, and social gatherings were prohibited. However, the health ministry had acknowledged the importance of making mental health and social service support accessible during times of crises. Mental health and social services were considered essential, and restrictions to providing such services were also lifted. The health ministry had also increased funding to population mental health programmes. This range of initiatives represented a shift in the whole-of-society's mindset in recognising that mental health is an important aspect of coping with the pandemic. It is hoped that the findings from this study contribute to the ever-growing research of the COVID-19 pandemic on the overall public health of the country and the region, and further guide the development of health guidelines for the current COVID-19 pandemic and potentially future outbreaks.

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Risk and protective factors of mental health during the COVID-19 pandemic: A cross-sectional study in Singapore

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ABSTRACT

Introduction: The main aims of the study were to: establish the average levels of psychological distress, suicidality and positive mental health (PMH); and examine their associated risk and protective factors in the population of Singapore during the early phase of the COVID-19 pandemic.

Method: Participants from a national psychiatric epidemiological study conducted in the general population of Singapore from 2016 to 2018, who had agreed to be re-contacted, were invited to participate in the study that was conducted from May 2020 to June 2021. Questionnaires assessing psychological distress, causes of stress, resilience and PMH were administered.

Results: A total of 1,129 respondents completed the study. The mean age was 47.7 (standard deviation = 16.5) years. The prevalence of stress, depression and anxiety was 7.1%, 8.0% and 8.4%, respectively. The final pathways model showed that high concerns related to possible COVID-19 infection of family members or friends were significantly associated with higher stress (β = 0.242, $P<0.001$), depression (β = 0.152, $P=0.001$) and anxiety (β = 0.280, $P<0.001$). High resilience was significantly associated with lower stress (β = -0.482, $P<0.001$), depression (β = -0.394, $P<0.001$) and anxiety (β = -0.516, $P<0.001$), and with high PMH (β = 0.498, $P<0.001$).

Conclusion: The findings highlight the negative impact of fear of COVID-19 infection, social distancing and isolation on the mental health of the population. Resilience and PMH were associated with lower psychological stress, and interventions to improve these characteristics can enhance mental health and well-being.

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Keywords: COVID-19, positive mental health, resilience, well-being

INTRODUCTION

The COVID-19 pandemic has significantly impacted people's well-being globally.[1] Individuals faced several stressors during the pandemic, including fear of contracting the disease, experiencing severe symptoms of COVID-19, losing loved ones to the disease, financial insecurity, and social isolation. Furthermore, children and youths experienced disruption to their usual routine such as schooling, and loss of developmental milestones including graduation and starting on their work life. In addition, domestic violence increased due to the close living conditions imposed by sheltering at home, and caregivers could not access respite care and other professional services.[2,3] On the other hand, the pandemic also revealed the emergence of several protective factors. These included personal and socioecological factors such as resilience, social support,[4] social participation and trust in government[5,6] that promoted mental health and well-being. However, the presence of these factors, their relative importance and their interaction would likely differ in context, time and place.

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Singapore is a multiethnic city-state with a population of about 5.5 million.[7] Following the epidemic caused by severe acute respiratory syndrome (SARS)-associated coronavirus in 2003, Singapore's healthcare and public health systems had enhanced their preparedness response. However, despite these measures, the country was challenged on several fronts by the COVID-19 pandemic, including surges of panic buying by the populace, widespread transmission among its large migrant worker population, an ageing population at higher risk of complications, and the consequent fear of overwhelming the healthcare system. A nationwide stay-at-home measure (circuit breaker) was imposed on all Singapore residents in April 2020 to control the spread of the infection in a then-unvaccinated population. In addition, public health interventions such as contact tracing, restriction of travel, enhanced surveillance using polymerase chain reaction (PCR) tests, and mandatory masking were introduced progressively to improve case detection and to reduce transmission. As a result, the country moved through several phases before entering the transition phase to COVID-19 resilience on 26 April 2022.[8]

While several studies have examined the impact of the pandemic on healthcare worker's mental well-being during the pandemic in Singapore,[9,10] few studies have examined the impact of the pandemic on the mental health of the general population. Studies from elsewhere have reported high levels of depression, anxiety and stress in the general population during the pandemic.[11,12]

A systematic review that examined the impact of COVID-19 on the general population found a high prevalence of symptoms of anxiety (6.33–50.9%), depression (14.6–48.3%), post-traumatic stress disorder (7–53.8%), and stress (8.1–81.9%) across China, Denmark, Iran, Italy, Nepal, Spain, Turkey and the US.[13] Given that risk and protective factors contributing to an individual's well-being during a pandemic differ across countries, the authors felt that it is essential to examine the mental health status and the contributory factors in Singapore's population. Such information could help inform government policy in terms of ascertaining the impact of social distancing and other restrictive measures on mental health and rationalise resource allocation.

Mental health is a complex and multidimensional construct. Current research suggests that mental distress and mental health coexist and interact. Positive emotions and relationships diminish psychological distress during periods of crisis, and maintain mental health despite the upheaval.[14] Keeping this broader perspective of mental health as the guiding principle, the main aims of our study were to: establish the average levels of psychological distress, suicidality and positive mental health (PMH); and examine their associated risk and protective factors in the population of Singapore during the early phase of the pandemic.

METHOD

Sample size estimation

To estimate the sample size of the study, we used previously estimated prevalence rates of mental disorders from a low prevalence of 1.6% (generalised anxiety disorder) to a high prevalence of 6.3% (major depressive disorder) ascertained in the Singapore Mental Health Study, which was conducted in 2016 (SMHS 2016).[15] If the margin of error of parameter estimates was assumed to be 1% across disorders, while the Type 1 error rate was controlled at 5%, the final adjusted sample size required to achieve this level of precision with an allowance of 30% incomplete data, would range from 1,269 to 1,663.[16]

Survey population and subjects

Participants from the SMHS 2016,[15] a national psychiatric epidemiological study conducted in the general population of Singapore, had agreed to be re-contacted (n=3370) for future studies. They were followed up using phone calls or emails during the acute phase of the pandemic, and face-to-face interviews in the later stages. The inclusion criteria for this study reflected the criteria of the SMHS 2016 study. Those who participated were

Singapore citizens or permanent residents, aged 21 years and above, able to speak in English, Chinese or Malay, and available for a Zoom platform (Zoom Video Communications) or face-to-face interview. All participants provided written informed consent either using online software or in person. Interviews were conducted on the Zoom platform or in person, and data was captured using QuestionPro (QuestionPro, Austin, US). A total of 1,129 participants agreed to participate in the study conducted from May 2020 to June 2021, giving a response rate of 54.8% (after excluding those whose contact details were invalid).

The ethical approval for the study was obtained from the National Healthcare Group Domain Specific Review Board. All participants provided written informed consent.

Questionnaires

General Anxiety Disorder-7 (GAD-7)

The GAD-7 was designed to identify probable cases of generalised anxiety disorder and to assess symptom severity. The items describe the most prominent diagnostic features of generalised anxiety disorder. GAD-7 scores range from 0 to 21.[17] A cut-off score of ≥10 was used to determine caseness, or case definition.

Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9 is a 9-item instrument used to identify depression and functional outcomes of participants.[18] A PHQ-9 sum score of ≥10 was used for the definition of caseness for depression. The last item of PHQ-9 was used for determining suicidality.

Stress

The Depression Anxiety and Stress Scales (DASS) was used to capture stress.[19] The stress subscale assesses tension, agitation, and negative affect. A cut-off score of ≥15 was used to determine stress.

Social support

Social support was measured by the 6-item Medical Outcomes Study Social Support Survey.[20] Respondents were asked a stem question about the level of social support they receive from various sources. Mean scores across the 6 items were calculated, with higher scores indicating greater levels of social support.

Resilience

Resilience was measured using the Brief Resilience Scale (BRS), a 6-item instrument that assesses the ability of individuals to bounce back or recover from stress.[21] Participants indicate the extent to which they agree with each statement on a 5-point scale (1 = "strongly disagree", 5 = "strongly agree").

Positive mental health (PMH)

The Rapid-Positive Mental Health Instrument (R-PMHI) is a 6-item unidimensional measure of PMH or mental well-being.[22] The R-PMHI comprises 5 positively worded items. The total PMH score is obtained by the sum of item scores divided by 6. A higher score indicates better PMH.

The study examined sources of stress, including the risk of contracting COVID-19 by self or family, employability, and financial concerns. We also examined social distancing and preventive measures employed by people to avoid infections, and other COVID-19-related factors like exposure to COVID-19 cases in their neighbourhood, and whether they had been placed under quarantine. Lastly, sociodemographic data were captured using a structured questionnaire.

Data analysis

Statistical analyses were carried out using STATA software version 15 (Stata Corporation, College Station, Texas, US) and Mplus version 8.2 Muthén & Muthén. A weighted analysis was used to ensure that the survey findings were representative of the Singapore adult population. Mean and standard errors were calculated for continuous variables, and frequencies and percentages for categorical variables. Structural Equation Modelling (SEM) with latent variables was applied to examine how sociodemo-graphic factors and COVID-19-related factors influence each other and subsequently lead to psychological distress. Fig. 1 presents the initial hypothesised pathways model of the relationship between sociodemographic factors, COVID-19-related factors, and psychological distress derived from the literature.

Before estimating the structural models, measurement models were estimated using confirmatory factor analysis followed by exploratory factor analysis if the original factor structure did not fit. In the case of a variable measured with a single item, the variable was included as an observed variable. In the structural model, the hypothesised pathways model was fitted with the adult general population sample by adding pathways from each potential sociodemographic and COVID-19-related factor to each psychological distress as a latent outcome variable. The misspecification of the model was examined using modification indices. The decision to explore and keep new pathways also followed their theoretical meaningfulness. The indirect effect was
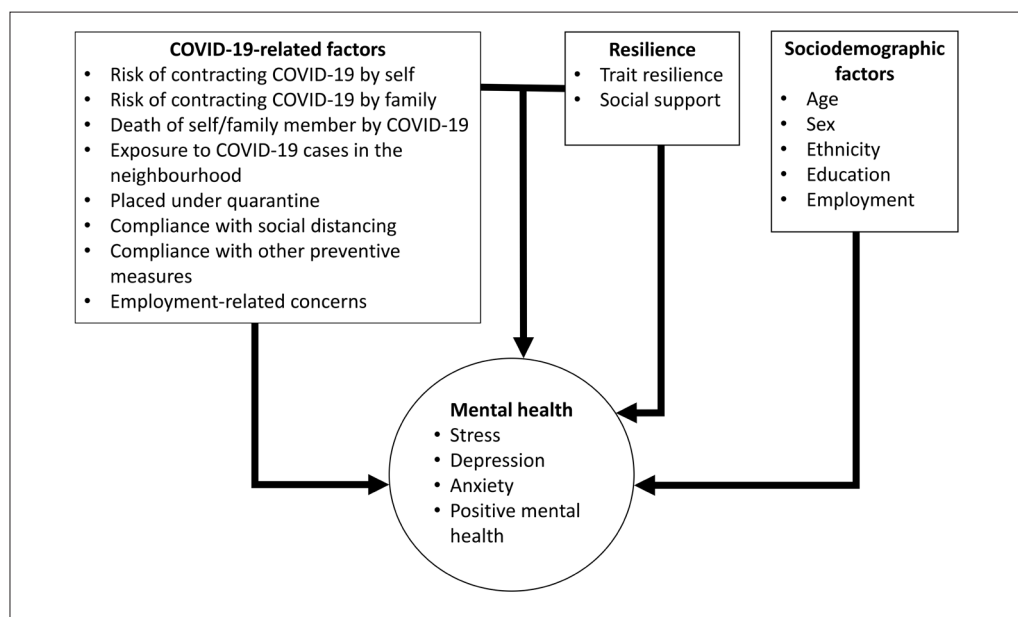
Fig. 1. Graphical representation of the effects of potential risk factors on psychological distress and direct, indirect and moderating effects of potential resilience factors.

tested using the model indirect procedure. Potential interaction effects between latent resilience, PMH and COVID-19-related factors were tested using latent moderated structural (LMS) equations with XWITH command.[23] Simple slopes were further estimated using model constraint command if a significant interaction was found between the variables. Given that LMS is computationally intensive, a series of smaller models with a single outcome, predictor, and moderator variable were tested one at a time. The robust maximum likelihood estimator with robust standard error was used. The goodness-of-fit of the SEM model was mainly evaluated using 3 indices. The root mean square error of approximation (RMSEA) incorporates a penalty function for poor model parsimony; values under 0.06 suggest close approximate (adequate) fit, whereas values above 0.10 indicate poor fit and that the model should be rejected.[24] The comparative fit index (CFI) and the Tucker-Lewis index (TLI) represent the incremental fit indices, with values >0.95 indicating adequate fit.[24]

RESULTS

Sociodemographic characteristics of the sample

A total of 1,129 respondents completed the study, with a mean age of 47.7 (standard deviation = 16.5) years. The sample comprised 50.9% female and 49.1% male respondents. The majority were of Chinese ethnicity (74.6%), and currently married (62.5%) (Table 1).

The prevalence of stress was 7.1%, while that of depression and anxiety was 8.0% and 8.4%,

respectively. The prevalence of suicidal thoughts was 4.8%. The mean scores of BRS and R-PMHI were 3.6 (0.6) and 3.7 (0.7), respectively. Prevalence of depression, anxiety, stress and suicidal ideation, mean resilience and PMH by sociodemographic factors is shown in Table 2.

Final pathways model

Fig. 2 shows significant pathways of the final model and their goodness-of-fit indices. The measures of model fit were as follows: chi-square of model fit = 2093.03 (degree of freedom = 1443), TLI = 0.953, CFI = 0.955, and RMSEA = 0.022. The indices suggest that the final model fits the data well. The final model shows that high concerns related to possible COVID-19 infection of family members or friends were significantly associated with higher stress (beta coefficient (β) = 0.242, $P<0.001$), depression (β = 0.152, $P=0.001$), and anxiety (β = 0.280, $P<0.001$). Living in a neighbourhood with COVID-19 cases was significantly associated with higher stress (β = 0.468, P =0.041), while social distancing and preventive measures were significantly associated with depression (β = 0.136, $P=0.003$). High resilience was significantly associated with lower stress (β = -0.482, $P<0.001$), depression (β = -0.394, $P<0.001$), anxiety (β = -0.516, $P<0.001$), and significantly associated with high PMH (β = 0.498, $P<0.001$). In comparison, high PMH was significantly associated with lower stress (β = -0.280, $P<0.001$), depression (β = -0.335,

Table 1. Sociodemographic characteristics of the sample.

		No.	%ᵃ	Singapore Census 2020 %ᵇ	Cohen's h effect Sizeᵇ
Age group	21–34	426	27.5	24.5	0.1
	35–49	361	26.9	28.5	0.04
	50–64	219	26.1	27.8	0.04
	65+	123	19.5	19.2	0.01
Sex	Female	527	50.9	51.7	0.02
	Male	602	49.1	48.3	0.02
Ethnicity	Chinese	398	74.6	76.1	0.03
	Malay	278	13.0	12.4	0.02
	Indian	324	9.0	8.5	0.02
	Others	129	3.3	3.0	0.02
Marital Status	Never married	363	27.4	26.9	0.01
	Married	681	62.5	62.8	0.01
	Divorced/separated/widowed	85	10.2	10.3	0.003
Education	Primary and below	51	13.8	16.3	0.1
	Secondary	151	24.6	24.3	0.01
	Post-secondary	398	28.3	27.1	0.03
	Degree and above	529	33.3	32.4	0.02
Employment	Employed	309	71.5	63.8	0.2
	Economically inactive	570	21.6	32.2	0.24
	Unemployed	235	6.9	4.0	0.13

ᵃ Weighted percentage

ᵇ Columns for Census % and Cohen's h effect sizes have been added to show the differences between the weighted sample and the Census. Cohen's h effect size = small 0.2; medium 0.5; large 0.8

Due to limited data, marital and education percentages were extracted from the Census of Population and General Household Survey in 2020 among Singapore resident population aged 20 years and above, while employment percentages were extracted from the Census of Population and General Household Survey in 2000 among Singapore resident population aged 20 years and above.

$P<0.001$), and anxiety ($\beta = -0.252$, $P<0.001$). In addition, those who were quarantined for COVID-19 were significantly associated with higher resilience ($\beta = 0.314$, $P=0.041$). Several sociodemographic and clinical factors were significantly associated with psychological distress, resilience and PMH. For example, younger age was significantly associated with higher stress ($\beta = -0.015$, $P<0.001$), depression ($\beta = -0.018$, $P<0.001$), and anxiety ($\beta = -0.013$, $P<0.001$). All significant associations are shown in Supplementary Table S1. The final model explained 42.9%, 56.3% and 48.9% of the variance in stress, depression, and anxiety levels, respectively.

Moderation and mediation effects

As shown in Table 3, most interaction effects were not significant. We found only one significant interaction between living in a neighbourhood with COVID-19 cases and resilience on stress. The effect of living in a neighbourhood with COVID-19 cases on stress was significant and positive at all values of resilience (i.e. detrimental effect). We also found that the negative association between resilience, stress, anxiety and depression was mediated by PMH. The proportion of total effect of resilience on stress, depression and anxiety levels that was mediated by PMH was 22.4%, 29.8% and 19.5%, respectively.

Table 2. Prevalence of depression, anxiety, stress and suicidal ideation; mean resilience and positive mental health by sociodemographic factors.

|		Depression		Anxiety		Stress		Suicidal thoughts		Resilience		Positive mental health	
		N	%	N	%	N	%	N	%	Mean	SD	Mean	SD
Age, years	21–34	57	12.7	55	13.1	55	12.7	26	7.8	3.02	0.36	4.52	0.91
	35–49	26	8.9	32	8.8	32	6.7	16	3.4	3.04	0.34	4.48	0.91
	50–64	10	3.7	13	4.8	11	4.7	9	3.1	3.00	0.25	4.57	0.83
	65+	5	5.8	8	6.1	4	3.0	3	4.9	3.04	0.26	4.39	0.79
Sex	Male	46	5.7	44	6.1	46	6.7	30	5.4	3.03	0.34	4.41	0.98
	Female	52	10.2	64	10.6	56	7.5	24	4.2	3.02	0.29	4.58	0.83
Ethnicity	Chinese	29	7.7	32	7.7	27	6.4	18	4.8	3.02	0.20	4.41	0.64
	Malay	35	11.0	35	11.2	31	9.1	16	5.5	3.01	0.56	4.80	0.99
	Indian	25	6.4	29	9.3	32	8.2	16	4.3	3.07	0.65	4.66	1.46
	Others	9	7.6	12	10.6	12	10.8	4	3.6	3.05	0.53	4.77	1.31
Marital status	Never married	57	14.9	50	14.8	47	12.3	25	7.1	3.00	0.32	4.40	1.00
	Married	31	4.1	51	5.7	49	5.4	25	3.7	3.04	0.31	4.53	0.90
	Divorced/separated/widowed	10	13.1	7	8.0	6	3.4	4	5.7	3.01	0.29	4.53	0.67
Education	Primary	4	12.4	2	6.2	2	6.2	3	6.9	2.96	0.22	4.04	0.67
	Secondary	11	6.2	16	7.8	10	5.4	7	5.0	3.03	0.22	4.68	0.63
	Post-secondary	49	10.2	46	11.6	42	10.0	24	6.3	3.04	0.35	4.50	0.99
	Degree and above	34	5.6	44	7.1	48	6.2	20	2.6	3.04	0.35	4.55	0.89
Employment	Employed	71	7.6	84	8.4	85	6.8	36	3.5	3.03	0.32	4.54	0.86
	Economically inactive	17	7.2	15	6.8	10	5.5	12	8.4	3.04	0.28	4.47	0.92
	Unemployed	10	14.1	9	13.4	7	15.5	6	7.1	2.94	0.29	4.12	1.06

SD: standard deviation
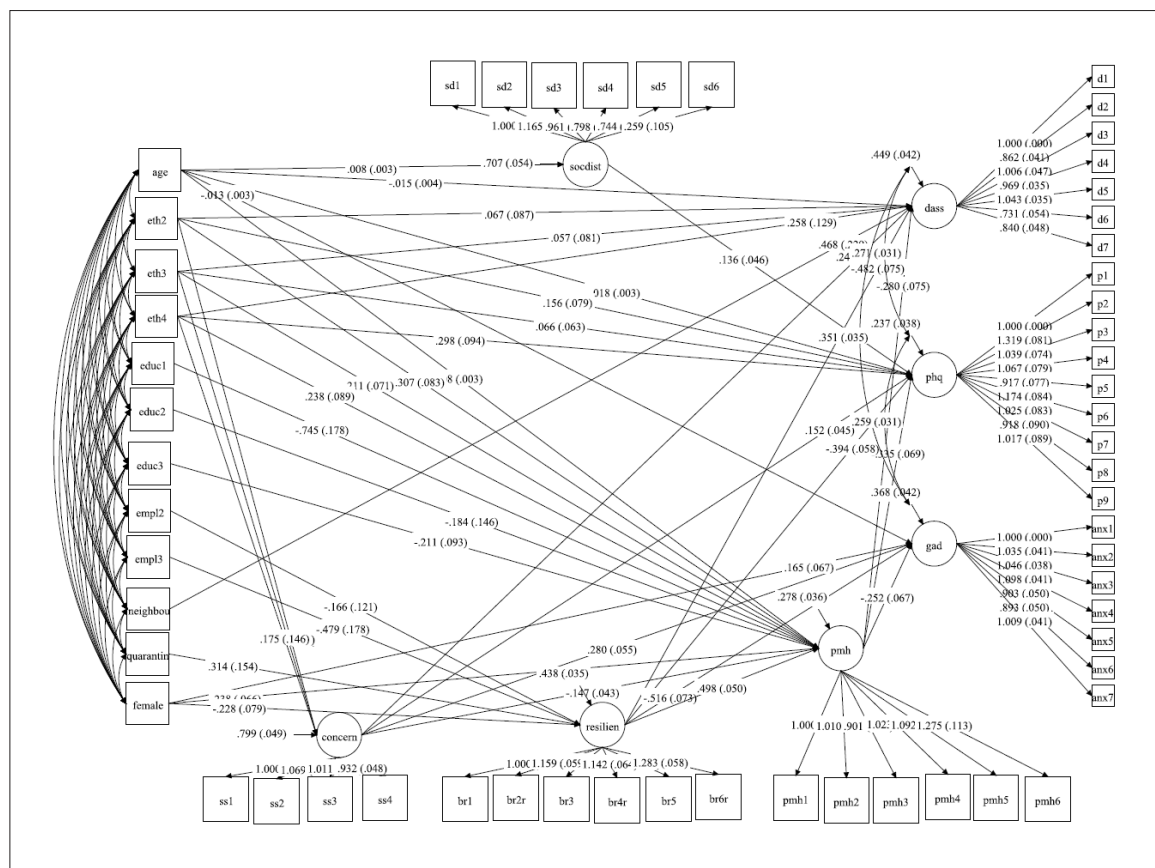
Fig. 2. Final model of the pathways between sociodemographic factors, COVID-19-related factors, resilience and psychological factors. anx1–anx7: the 7 items of GAD-7 scale; br1–br6: the items of the Brief Resilience Scale (resilience) ("r" after the item refers to reverse coding); BRS: Brief Resilience Scale; DASS: Depression, Anxiety and Stress Scale; d1–d7: the 7 items of the DASS stress subscale; educ1: primary or less; educ2: secondary; educ3: post-secondary; empl2: economically inactive; empl3: unemployed; eth2: Malay, eth3: Indian; eth4: Others; GAD-7: General Anxiety Disorder-7 scale; neighbour: exposure to COVID-19 in their neighbourhood; p1–p9: the 9 items of PHQ-9; PHQ-9: Patient Health Questionnaire-9; pmh1–pmh6: the 6 items of the R-PMHI scale; quarantine: placed under quarantine; R-PMHI: Rapid-Positive Mental Health Instrument; sd1–sd6: the items of the social distancing and preventive measures ("socdist"); ss1–ss4: the items of COVID-19- related stress/concerns

DISCUSSION

In all 15.3% (n=197) of the population of Singapore experienced depression, anxiety, stress or suicidality during the acute phase of the pandemic. The prevalence of stress was 7.1%, while that of depression and anxiety was 8.0% and 8.4%, respectively. The prevalence of psychological distress was not significantly different from that identified in other Asian studies conducted during the pandemic. For example, the Japan COVID-19 and Society Internet Survey (JACSIS), a large-scale, internet-based, self-reported questionnaire survey, was conducted between 25 August and 30 September 2020. The study found that severe psychological distress (defined as Kessler 6 Scale score ≥13) was prevalent in 10.0% of the respondents.[25] Using the same questionnaires as the current study, a web-based cross-sectional survey targeting adults in Chungnam Province, South Korea, found that 18.8%

of the participants had symptoms of depression, 10.6% had symptoms of anxiety, and 5.1% had a high level of perceived stress during the COVID-19 pandemic.[26]

Prevalence of suicidal thoughts in our study was 4.8%. The number of suicides released in Singapore's Report on Registration of Births and Deaths in 2020 was 452, which is a 13% increase from 2019.[27] Several studies have highlighted the role of COVID-19 as a risk factor for higher levels of suicidal behaviours during the pandemic.[28] A systematic review that examined the potential factors for suicidal behaviours in the context of the COVID-19 outbreak, identified significant associations with both personal and contextual factors including financial difficulties, psychological distress, social isolation, and fears related to contracting COVID-19.[29]

The mean value of resilience as determined by the BRS was 3.6. The mean resilience in a sample of

Table 3. Moderation analysis testing the interaction between selected predictor (IV) and moderator (M) on the dependent variable (DV).

	Dependent variables		
	Stress	Anxiety	Depression
IV: Concern	0.236[a]	0.336[a]	0.123[b]
M: PMH	-0.329[a]	-0.315[b]	-0.358[a]
Interaction term	0.011	-0.009	-0.006
IV: Concern	0.200[a]	0.245[a]	0.088[c]
M: Resilience	-0.472[a]	-0.557[a]	-0.462[a]
Interaction term	0.020	0.007	-0.001
IV: Neighbourhood	1.249[a]	1.306	0.554
M: PMH	-0.390[c]	-0.485	-0.342[a]
Interaction term	0.035	-0.325	-0.491
IV: Neighbourhood	1.205[b]	1.114	0.561
M: Resilience	-0.574[a]	-0.780[a]	-0.519[a]
Interaction term	0.607[c]	0.613	0.058
IV: Social distance			0.048
M: Resilience			-0.488[a]
Interaction term			-0.003

PMH: positive mental health

[a]$P<0.001$, [b]$P<0.01$, [c]$P<0.05$: not tested due to non-significant pathways presented in Fig. 2.

healthcare workers in Singapore as measured by the BRS before the pandemic was no different.[30] This suggests that the population was largely resilient and adapted well to the adverse impacts. Another protective factor may be the effective handling of the COVID-19 pandemic by the Singapore government. The steps include an effective and rapid public health response to the crises, incremental deployment of Singapore's resources, and open communication with the public.

The study also identified several potential risk factors related to lower mental health and well-being. High concerns related to possible COVID-19 infection of family members or friends were significantly associated with higher stress, depression and anxiety, while living in a neighbourhood with COVID-19 cases was significantly associated with higher stress.

Infectious diseases tend to be associated with fear. This fear is the accrual consequences of experiences and memories of prior epidemics, and to fictional accounts of such threats in popular movies or books that tend to depict apocalyptic scenarios.[31] This fear is typically widespread and acutely felt during the early stages of a pandemic wherein the infectious agent has

a rapid transmission rate, the mode of infection is not well established, where there is no effective vaccine, and the epidemic is associated with high morbidity and mortality. Extant literature shows that those who feared COVID-19 were more likely to have psychological distress.[12,32,33]

On the other hand, social distancing and preventive measures were significantly associated with depression. Social distancing and preventive measures put in place to prevent the transmission may have resulted in isolation and loneliness, especially among singles, which in turn is associated with poor mental health outcomes.[34] It is also possible that the closure of workplaces and schools as part of the social distancing measures may have led to uncertainty about employment and education progression, which could have resulted in psychological distress.[35]

Lastly, our study, like several others, identified younger age to be significantly associated with stress, depression and anxiety.[12,36] The greater disruption and uncertainty in terms of study and employment, loss of sense of belonging, disruption of structure, and loneliness have been proposed to explain this association.[37] Resilience that usually comes with life experiences, lack of exposure to prior pandemics, and a greater sense of deprivation and isolation as younger people tend to be more physically and socially active, are all likely to have contributed to psychological distress in younger adults.

Resilience and PMH were associated with lower distress. Studies have identified individual resilience as a protective factor against psychological distress during the pandemic.[38] The relationship between resilience and mental health could be explained through the "biopsychosocial model of resilience", which posits a multilevel process that protects in stressful situations and disturbances to the norms in individuals.[39] This model describes a range of individual (e.g. immune system and mental health) and group (e.g. lineage, geographical or social) level resources and mechanisms that offer protection against distress. PMH encompasses positive emotions, feelings and functioning. A study from Pakistan found that PMH mitigated the fear of COVID-19 and reduced anxiety.[40] Other elements of PMH, such as altruism and a sense of calm, may have also helped individuals with high PMH to flourish in the face of adversity and consequently have lower psychological distress.

Our study is one of the few that identified PMH as mediating the negative association between resilience and psychological distress. Previous research has similarly found PMH to be a significant mediator of the relationship between mental disorders and quality of

life,[22] indicating its likely role in reducing the impact of harmful exposures on health outcomes in individuals. Having high resilience can improve aspects of PMH such as positive affect and positive outlook towards health outcomes; and offer behavioural memory and coping efficiency to deal with adversity, which in turn reduces distress. On the other hand, research also shows that positive emotions and mental health lead to increased resilience, allowing individuals to rebound from stressful situations.[41]

This study has several limitations. One is the cross-sectional design, which does not allow for causal interpretations. Furthermore, the data collected from May 2020 to June 2021 included the lockdown period and the subsequent lowering of restrictions. This may have resulted in a mixed sample. However, analysing the data by splitting into 2 halves did not show much variation in the results. While every effort was made to contact respondents and encourage their participation in the study, there was a significant non-response rate of about 50%. The study did not collect information on whether the participants had tested positive for COVID-19 at any point before the interview. The frequency of clinically significant depression and/or severe depressive symptoms following COVID-19 infection can range from 3 to 12%; thus, infection itself could be a contributing factor of the psychological distress in the population.[42] Lastly, there may have been possible response bias by the respondents in answering the questions about psychological distress and PMH though researchers emphasised the confidential nature of the study.

On the other hand, the strengths of the study included the use of a random, representative sample interviewed by trained researchers using validated questionnaires on Zoom or face-to-face, which ensured the reliability of the data. The use of English and local languages to conduct the interview allowed the inclusion of all ethnic and age groups in the sample.

CONCLUSION

The findings of our study advance the current knowledge about the impact of the COVID-19 crisis on the Singapore population and provide insights about the risk and protective factors that influence individuals' mental health and well-being. In particular, the results highlight the negative impact of fear of COVID-19 infection, social distancing and isolation on the mental health of the population, while resilience and PMH were associated with lower psychological stress. Research has shown that resilience can be enhanced by several psychological interventions, based on

cognitive behavioural therapy[43] and mindfulness.[44] These interventions can be delivered online using interactive modes, making them more accessible and cost-effective. Thus, public health initiatives to build resilience must be considered at the community and national level as an essential component of pandemic preparedness. Furthermore, rapid identification of groups that are at high risk of developing psychological distress is important. Identification can be done through rapid epidemiological and qualitative studies, by leveraging community providers of mental health and telepsychiatry. The timely dissemination of evidence-based information on the pandemic and preventive measures that can counter the spread of the infection and mitigate psychological distress is equally important. Going forward, these methods for identification of high-risk groups and rapid dissemination of health information must be incorporated as part of Singapore's Total Defence strategy against pandemics.[45]

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Clinical efficacy of primary human papillomavirus (HPV) screening with partial genotyping for HPV-16 and HPV-18 subtypes in women from 25 years old

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ABSTRACT

Introduction: Cervical screening programmes differ in the age of women recommended for primary human papillomavirus (HPV) testing. This study aims to determine the clinical efficacy and impact of 14-high-risk HPV DNA testing for women from 25 years old.

Method: This was a retrospective analysis of data collected prospectively from women 25 years or older who attended hospital-based gynaecology clinics for cervical screening. Women with history of cervical neoplasia or abnormal cytology were excluded. High-risk HPV DNA testing with partial genotyping for HPV-16 and HPV-18 were performed on cobas 4800 System (Roche Diagnostics International AG, Rotkreuz, Switzerland). Women tested positive for the 12 other high-risk HPV subtypes (HPV-12 other) had a reflex cytology test. Positive screening included positive for HPV-16 and/or HPV-18, HPV-12 other with cytology abnormalities equal to or greater than atypical squamous cells of undetermined significance, and repeated positive HPV at 12 months. HPV detection and colposcopy referral rates, and detection of high-grade neoplasia were determined.

Results: Of 10,967 women studied, 822 (7.50%) were HPV DNA positive. The overall discharge rate to routine screening according to screening protocol was 93.1%. Colposcopy referral rate was 4.4%. The screening detected 41 cervical intraepithelial neoplasia grade 2+ (CIN2+) (0.37%) and 31 (0.28%) CIN3+. The number of colposcopies needed per case of CIN2+ was 9.5, similar for women below and above 30 years old. The number of colposcopies needed per case of CIN3+ for HPV-16 positivity was 8.5, compared to 17.0 for other categories (_P_=0.040). Colposcopy efficacy was similar for HPV-18 and HPV-12 other positivity with abnormal cytology.

Conclusion: Taking CIN2+ detection and colposcopy referral rate as endpoints, HPV testing in Singapore can be extended to include women from 25 years old.

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Keywords: Cervical cancer screening, cervical intraepithelial neoplasia, colposcopy, obstetrics and gynaecology, Pap smear

INTRODUCTION

The World Health Organization has launched a campaign to eliminate cervical cancer on the basis of effective vaccines against oncogenic human papillomavirus (HPV) subtypes, with mass screening and eradication of high-grade pre-malignant lesions, cervical intraepithelial neoplasia grade-2 (CIN2) and grade-3 (CIN3).[1,2] HPV-based screening has been shown to be sensitive in detecting high-grade lesions and is effective and suitable in mass cervical screening.[3-5] More importantly, recent evidence shows that HPV-based screening prevented development of invasive cervical carcinoma among women who screened negative.[6] HPV DNA testing is cost-effective and has been adopted by many national cervical screening programmes.[7,8]

However, HPV-based screening faces several challenges, including the low specificity of HPV-positivity for high-grade lesions.[9] The problem is exaggerated for young women who experience high prevalence of HPV infection. Some national screening programmes limit HPV-based testing to women beyond 30 years old.[10] Appropriate strategies are needed to improve the

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CLINICAL IMPACT

What is New

- Cervical screening in Singapore can be simplified to a single human papillomavirus (HPV)-based modality for all eligible women from 25 years old.

Clinical Implications

- This study identified areas that could improve the efficacy of the current cervical screening protocol in Singapore.

- Our data provided evidence that HPV-18-positive cases should also undergo cytology triage instead of the current practice of immediate referral to colposcopy.

- The persistent HPV positivity rate was 51.9% at 12-months follow-up. Additional mode of screening such as HPV-self screening should also be explored to overcome the low compliance rate for 12-month follow-up (32.2%).

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positive predictive value of HPV testing for high-grade lesions especially in women who are positive for a group of 12 oncogenic HPV subtypes: HPV-31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68—collectively HPV-12 other." When compared to HPV-16 and HPV-18, HPV-12 other" are associated with a substantially lower risk of high-grade lesions.[11,12] Among many approaches evaluated, partial genotyping for HPV-16 and HPV-18 and introduction of a cytology triage test for the HPV-12 other" positive cases emerged to be the best option today.[3,13]

In 2013, our institution started a cervical screening programme using primary HPV DNA testing with partial genotyping for HPV-16 and HPV-18, and reflex liquid-based cytology on specimens positive for HPV-12"other. Women whose reflex cytology was normal were scheduled for a repeat HPV testing at 12 months. This study was conducted to evaluate the clinical efficacy of HPV testing in this protocol-based screening programme. Data were analysed for HPV DNA detection rate, colposcopy referral rate, prevalence of high-grade lesions and number of colposcopies to detect a high-grade lesion.

METHOD

Clinical data were collected in a database prospectively from all women 25 years or older who attended hospital-based gynecology clinics in Singapore and had undertaken a routine cervical screening between November 2013 and December 2021. The data analysis was based on information from this database on primary HPV screening. Women who had previous cervical neoplasia or abnormal cytology were excluded.

One cervical scrape sample was obtained from each woman and kept in 20mL PreservCyst Solution (ThinPrep Hologic, Marlborough, US). The sample was sent to the hospital's molecular laboratory for HPV DNA analysis.

Screening was done with primary high-risk HPV DNA testing with partial genotyping for HPV-16 and HPV-18 (cobas 4800 System, Roche Diagnostics International AG, Rotkreuz, Switzerland). A reflex liquid-based cytology test was performed on the same sample as triage for cases positive for HPV-12 other."All cases positive for HPV-16 or HPV-18, and cases positive for HPV-12 "other" with reflex cytology showing atypical squamous cells of undetermined significance (ASCUS) or worse by Bethesda classification were considered abnormal. "Cases positive for HPV-12 other" in which reflex cytology showing changes less than ASCUS were scheduled for a repeat HPV testing 12 months later. These cases were then considered abnormal if repeat testing was positive for HPV DNA.

Women with normal screening results were discharged to routine screening scheduled in 5 years. Women with abnormal results were referred to colposcopy in the same hospital. Colposcopy was performed by a fixed team of trained colposcopists. Cervices with abnormal findings were biopsied for histopathology examination. The final diagnosis of CIN and invasive cancer was based on the histology of cervical biopsies (cervical punch biopsies or loop electrosurgical excision procedure), and hysterectomy specimen where applicable. The results were reviewed by gynaecologic histopathologists.

The outcome measures of the analysis were detection rate for CIN2+ and CIN3+, numbers of abnormal tests, repeat tests at 12 months, and colposcopies for each case of CIN2+ and CIN3+.

Waiver of consent was granted for this retrospective study by the hospital's ethics committee (CIRB: 2016/2385) and carried out in accordance with the 1964 Declaration of Helsinki ethical standards.

Pearson's chi-square analysis was performed using SPSS Statistics software version 21.0 (IBM Corp, Armonk, US). Statistical significance was set at $P<0.05$.

RESULTS

The database included 10,967 eligible women. Of these, 966 (8.8%) were below 30 years old and 10,001 (91.2%)

were 30 years old or more. Of the latter subgroup, the mean age was 47.8 years (95% confidence interval [CI] 47.58–48.02).

The overall prevalence of high-risk HPV DNA positivity for the entire screening cohort was 7.50% (n=822/10,967) (Table 1). The detection rates of the high-risk HPV subtypes were 1.25% for HPV-16, 0.52% for HPV-18, and 6.21% "for HPV-12 other (Table 2). Comparing women below 30 years old to older women, the odds ratio of HPV positivity was 2.43 (95% CI 2.012.95) ($P<0.0001$). Generally, the overall prevalence of HPV and its subtypes declined steadily across increasing years of age groupings (Table 2).

Table 1. Overall detection rate of at least one category of high-risk HPV DNA on first screening.

Age grouping		High-risk HPV positive		
years	n	n	%	95% CI
<30	966	145	15.0	12.67–17.66
30–39	2726	265	9.72	8.59–10.97
40–49	2988	203	6.79	5.89–7.80
50–59	2655	118	4.44	3.68–5.32
≥60	1632	91	5.58	4.49–6.85
Total	10967	822	7.50	6.99–8.03

CI: confidence interval; HPV: human papillomavirus

In all, 685 "women 'tested positive for HPV-12 other. Of these, 629 (92.4%) did not show concurrent positivity with HPV-16 and/or HPV-18. These women had a reflex liquid-based cytology evaluation (Table 3). Overall, 419 women (66.6%) were negative for intraepithelial lesions or malignancy (NILM). The frequency of NILM was similar across the age groupings ($P=0.145$). Mild cytological abnormalities (ASCUS or low-grade squamous intraepithelial lesion (LSIL)) were more often observed among women below 30 years old (35.5%) compared to older women (23.5%). High-grade lesions were seen in 0.9% of women below 30 years old, compared to 3.7% of women aged 30 years or above ($P=0.135$).

Of the 419 women assigned for repeat testing at 12 months, 284 (67.8%) defaulted. The default rate was similar across all age groupings. Of the 135 (32.2%) women who undertook the test, 65 (48.1%) cases were negative, and 70 (51.9%) cases were positive for HPV DNA (Fig. 1). All HPV positive cases had HPV-12 other, 'with concurrent HPV-16 positivity in 3 cases and HPV-18 positivity in 1 case.
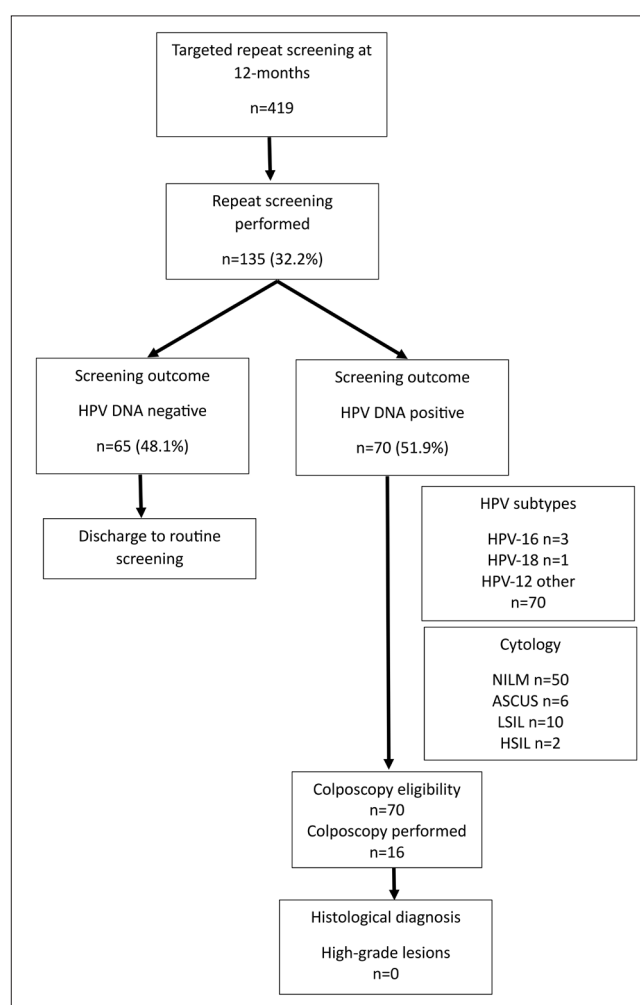

Fig. 1. Outcome of repeat screening at 12-months.
ASCUS: atypical squamous cells of undetermined significance; HPV: human papillomavirus; HSIL: high-grade intraepithelial lesions; LSIL: low-grade intraepithelial lesions; NILM: negative for intraepithelial lesions and malignancy

Of the total screened cohort, 10,210 women tested negative for HPV DNA. These included 10,145 women from the initial screening test and 65 women from repeat testing at 12-months. These women (93.1%) were discharged to routine 5-yearly screening.

The final histological diagnosis confirmed 41 cases of CIN2+ (0.37%) and 31 (0.28%) cases of CIN3+ (Table 4). The detailed breakdown showed 10 CIN2, 25 CIN3 and 6 cases of invasive carcinoma. More than half of all cases of high-grade lesions (51.2% CIN2+ and 51.3% of CIN3+) were related to HPV-16. The frequency of CIN3+ by HPV subtype category was 11.8% for HPV-16, 5.4 % for HPV-18 and 6.6% for HPV-12 other ($P=0.175$).

Excluding 284 women who defaulted repeat testing at 12 months, 4.4% of the women were recommended

Table 2. Distribution of human papillomavirus subtypes by age grouping of subjects at initial screening.

HPV subtype	Age Grouping, years														
	<30 (n=966)			30–39 (n=2726)			40–49 (n=2988)			50–59 (n=2655)			≥60 (n=1632)		
	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
HPV-16	29	3.0	2.01–4.31	42	1.54	1.11–2.08	36	1.20	0.84–1.67	14	0.53	0.29–0.88	16	0.98	0.56–1.59
HPV-18	6	0.6	0.23–1.35	14	0.51	0.28–0.86	19	0.64	0.38–0.99	10	0.38	0.18–0.69	7	0.43	0.17–0.88
HPV-12 other	126	13.0	10.87–15.53	224	8.22	7.18–9.37	163	5.46	4.65–6.36	99	3.73	3.03–4.54	73	4.47	3.50–5.62

CI: confidence interval; HPV: human papillomavirus

Table 3. Outcome of reflex cytology examination among women tested positive for HPV-12 other.

Cytology outcome	Total cohort (n=629)			Age Grouping, years									
				<30 (n=110)		30–39 (n=209)		40–49 (n=148)		50–59 (n=94)		≥60 (n=68)	
	n	%	95% CI	n	%	n	%	n	%	n	%	n	%
NILM	419	66.6	60.39–73.31	70	63.6	128	61.2	104	70.3	70	74.5	47	69.1
ASCUS	80	12.7	10.09–15.38	17	15.5	26	12.4	18	12.2	15	16.0	4	5.9
LSIL	107	17.0	13.94–20.56	22	20.0	46	22.0	23	15.5	6	6.4	10	14.7
HSIL	20	3.2	1.94–4.91	1	0.9	9	4.3	3	2.0	2	2.1	5	7.4
Others	3	0.5	0.10–1.39	0	0.0	0	0.0	0	0.0	1	1.1	2	2.9

ASCUS: atypical squamous cells of undetermined significance; HSIL: high-grade intraepithelial lesions; LSIL: low-grade intraepithelial lesions; NILM: negative for intraepithelial lesions and malignancy; Others: included unsatisfactory smears

Table 4. Histological diagnosis of overall screening.

Histology	Age Grouping (years)	Diagnosis by HPV subtypes			
		HPV-16+	HPV-18+	HPV-12 other+ and LBC+	Overall
CIN2+	<30	5	0	2	7
	30–39	6	1	8	15
	40–49	7	1	4	12
	50–59	2	1	1	4
	≥60	1	0	2	3
	Overall	21	3	17	41
CIN3+	<30	1	0	1	2
	30–39	6	1	5	12
	40–49	6	1	4	11
	50–59	2	1	1	4
	≥60	1	0	1	2
	Overall	16	3	12	31

CIN: cervical intraepithelial neoplasia; HPV: human papillomavirus; LBC: liquid-based cytology

for colposcopy (n=472/10,683) (Table 5). This prevalence amounted to 69.1% of all women tested positive for HPV DNA at the initial screening. Of these, 391 (82.8%) undertook colposcopy examination. Both the eligibility and compliance of colposcopy showed a statistically significant difference across age groupings from less than 30 years old to 60 years old and more. Most notably, 8.3% of women below 30 years old were recommended for colposcopy compared to 4.4% for the entire cohort.

There was no statistically significant difference across age groupings for detecting CIN2+ (Fig. 2). However, to detect a case of CIN3+, the number of colposcopies needed was 38.5 for women below 30 years old, compared to 10.8 for women in the older age groupings (P=0.053). Compared to the other categories of HPV subtypes collectively, HPV-16 positive group of women needed a lower number of colposcopies for each case of high-grade lesions: CIN2+ (6.5 versus 12.8, P=0.051) and CIN3+ (8.5 versus 17.0, P=0.040) (Table 5).
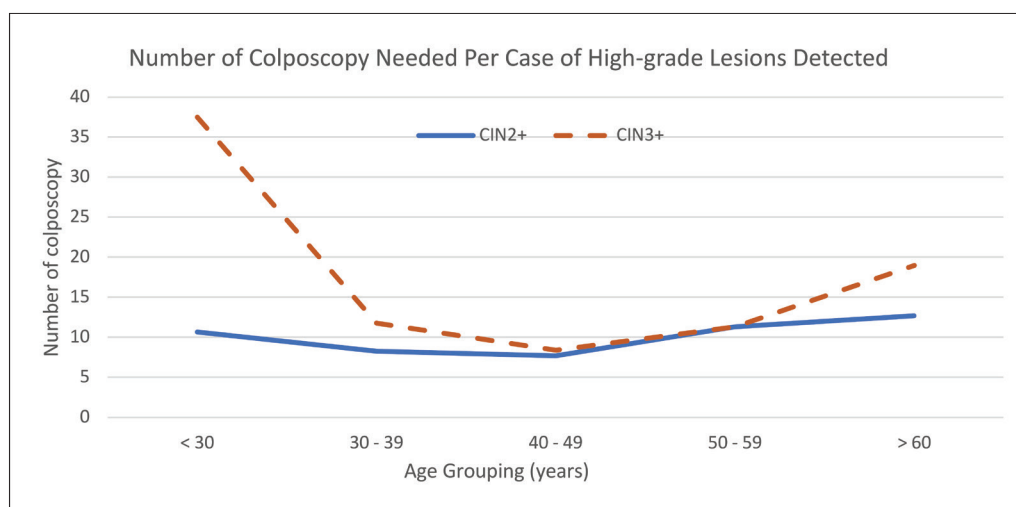

Fig. 2. Number of colposcopy needed per case of CIN2+ and CIN3+.
CIN: cervical intraepithelial neoplasia

DISCUSSION

This report presented a real-world experience of a cervical screening protocol involving primary HPV DNA testing with partial genotyping for HPV-16 and HPV-18, and reflex liquid-based cytology testing on positive HPV-12 other" cases. "In the cohort, there were 41 cases of CIN2+ (0.37%) and 31 (0.28%) cases of CIN3+, including 6 cases of invasive carcinoma. The detection rate of high-grade lesions reflected the low and steadily declining trend in the incidence rate of cervical cancer in Singapore,[14] and was similar to the rates (0.27–0.87%) reported in other studies.[15,16]

The overall prevalence of high-risk HPV DNA positivity was 7.50%. The detection rate of HPV and its subtypes were within ranges reported globally.[13,17-20] The variation in the reported HPV positivity rate between individual studies largely reflected the age of screening population. As universally observed, the prevalence of HPV infection peaks in women in their 20s and declines steadily after 30 years old. Not surprisingly, comparing women below 30 years old to older women, the odds ratio of HPV positivity in this study was 2.43 ($P<0.0001$).

The rate of returning to routine screening, an important outcome measure of a screening programme, was 93.1% in our study. This high discharge rate dispelled fears that HPV-based screening might increase the burden on clinical services. It underscores the importance of using HPV technology validated for disease endpoints. In fact, the extremely high negative predictive value of HPV testing for high-grade lesions and invasive cancers—over a long interval of 5 years or more—contributes to a favourable cost-effectiveness of the screening programme.[8,21,22]

It has been long recognised that HPV testing has a very high sensitivity and is significantly superior to cytology in detecting high-grade lesions. However, it is important to note that, based on our management protocol of partial genotyping for HPV-16 and HPV-18, and reflex cytology for HPV-12 other," 69.1% "of women who had detected HPV DNA at the initial screening were referred to colposcopy. The referral rate for colposcopy and number of colposcopies needed for detecting a case of high-grade lesion are well accepted measures for assessing the performance of a cervical screening programme. In our study, the colposcopy referral rate of 4.4% was consistent with published data of 3–4.1%.[9,18-20] However, detailed analysis of referral rate by age groupings showed a significant trend of higher rates among young women ($P<0.0001$). The referral rate was almost double (8.3%) for women below 30 years old (Table 5). Overall, the attendance rate for colposcopy was 82.8%. A higher attendance rate in the younger women group was observed ($P=0.0016$).

The number of colposcopies performed for detecting a case of high-grade lesion was 9.5 for CIN2+ and 12.6 for CIN3+ (Table 5). These numbers can be translated to a colposcopy detection rate of 10.5% for CIN2+ and 7.9% for CIN3+. These rates are generally accepted and justified the current referral criteria for colposcopy.[11,23] Despite the high colposcopy referral rate for younger women, the relatively high prevalence of CIN2 lesions among them resulted in an overall comparable colposcopy efficacy between all age groupings.

Our observations carry 3 significant implications on managing HPV-based cervical screening. Firstly, the detection rate for CIN2+ and CIN3+ was most significant for HPV-16 positivity ($P=0.040$) compared to other subtypes of HPV. HPV-16 positivity alone accounted for more than half of all cases of CIN2+ (51.1%) and CIN3+ (51.3%) in this study. HPV-16 genotyping in HPV-based screening is clearly beneficial. However, the number of colposcopies needed for a case of CIN2+ or CIN3+ was similar for women referred by HPV-18 positivity "or "by HPV-12 other-and-cytology positivity. Similar findings have also been reported.[24] These data support the suggestion that HPV-18 positivity may be managed with a reflex cytology triage test as with HPV-12 other positivity.

Secondly, women younger than 30 years old contributed 17% of all CIN2+ cases in this study. Others have reported that women between 25 and 29 years old contributed a large number of CIN2+ in screening populations.[25] The number of colposcopies needed for a case of CIN2+ in this age grouping was 11, which is similar to the older age groupings ($P=0.8062$). It seems logical that primary HPV-based cervical screening should be extended to women between 25 and 29 years old.

Thirdly, it was important to note that the observed compliance rate of 32% for repeat testing was unacceptably low. This rate was lower than the reported rate of exceeding 80% in some reports.[24] The low rate mirrored the participation rate of women attending recommended regular cytology screening at 3-yearly intervals in the previous national screening programme, a phenomenon that appeared to be obstinately constant in Singapore.[26] The low compliance rate could not be ignored as HPV positivity was found in more than half of the women who attended the repeat testing. In fact, 4 (3%) women acquired additional HPV subtypes: 3 were positive for HPV-16 and one for HPV-18, in addition to being positive for HPV-12 other." The prevalence of HPV-16 among these women was more than doubled that found in the initial screening cohort (1.25%). Although

Table 5. Summary of overall colposcopy outcome: eligibility, compliance and efficacy from cumulative data from round-1 screening and repeat testing on subgroup of women tested positive for HPV-12 other at 12 months.

	Age Grouping, years						HPV typing			
	<30	30-39	40-49	50-59	≥60	Total	HPV-16	HPV-18	HPV-12 other	Total
Overall (n)[a]	913	2642	2918	2612	1598	10683	136	56	491	683
Colposcopy recommended (cumulative number including repeat test at 12 months)										
No. of cases	80	156	117	59	60	472	136	56	280	472
%	8.8	5.9	3.0	2.3	3.8	4.4	100	100	57.1	69.1
Difference between groups	$P<0.00001$[b]						Not applicable			
Colposcopy performed										
No. of cases	77	128	95	49	42	391	136	56	199	391
%	96.3	82.1	81.2	83.1	70	82.8	100	100	71.1	82.8
Difference between groups	$P=0.0016$[b]						Not applicable			
No. of colposcopy per CIN2+ case										
	11	18.5	7.9	12.3	14	9.5	6.5	18.7	11.7	9.5
Difference between groups	$P=0.8062$[b]						$P=0.051$[b]			
No. of colposcopy per CIN3+ case										
	38.5	10.7	8.6	12.3	21	12.6	8.5	18.7	16.6	12.6
Difference between groups	$P=0.2244$[b]						$P=0.1205$[b]			
Difference between subgroups	$P=0.053$[b] Subgroup: age <30 years versus ≥30 years						$P=0.040$[b] Subgroup: HPV-16 versus Other HPVs			

[a] Overall number excluded 284 women who defaulted repeat HPV DNA testing at 12-months follow-up.
[b] χ^2-test

no high-grade lesions were detected in this small group of women in the present analysis, the poor compliance rate for a recommended management protocol is worrisome for a large population in a nationwide programme. It is important for national programmes to consider including alternative sampling methods such as self-sampling, which improves participation in screening.[27] Emerging evidence confirmed that the sensitivity of HPV testing between physician-collected samples and women self-collected samples was comparable.[28,29]

It is reasonable to question if the findings of a retrospective institutional study of this nature can be extended to community-based national screening. We overcome this limitation by including only women attending the health service for primary screening. Women on clinical management of abnormal screening tests were actively excluded. The low prevalence of high-grade lesions observed in this analysis was indicative of the primary screening nature of the studied cohort, reflecting similar prevalence as the general population.

We examined the potential impact of low compliance rate of repeat HPV testing at 12 months on detection rate of high-grade lesions among the defaulters. There was no difference in the default rate between age groupings to suggest potential bias between compliant and non-compliant women. Of those who undertook repeat tests, HPV positive rate was 51.9%. However, there were no high-grade lesions detected. The potential contribution of CIN2+ cases from defaulters, if any, to the overall pool of high-grade lesions was likely to be small and would not have altered the overall conclusions.

The strengths of this study include its prospective nature of clinical data collection from a single institution, which ensured the accuracy and completeness of clinical information in the database. In addition, single institutional practice ensured consistency in the execution of screening management protocol, standard of colposcopy, cytopathology and histopathology examination and reporting. These characteristics increased the robustness of the data analysed.

Distinct from HPV DNA technological studies, this report focused on the outcome of a screening protocol. The analysis on 10,967 women carried a large sample size. The inference from the observations was of clinical significance.

CONCLUSION

Our findings indicated that the current cervical screening protocol was efficacious with a discharge rate of 93.1% of women to routine screening. The overall HPV DNA positive rate was 7.5%. The colposcopy referral rate was 4.4%. The number of colposcopies performed to detect a case of high-grade lesion was 9.5 for CIN2+ and 12.6 for CIN3+. Comparable colposcopy efficacy between different age groupings of women suggests that primary HPV screening should be extended to women between 25 and 29 years old. The impact of introducing cytology triage testing for HPV-18 positive cases, instead of immediate referral to colposcopy, warrants further evaluation to reduce the colposcopy referral rate. Sample collection alternative to routine clinic collection should be explored to increase the compliance rate of follow-up repeat testing.

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LETTER TO THE EDITOR

Healthcare worker job burnout, anxiety and depression: A one-year comparison during COVID-19 in Singapore

Dear Editor,

The mental health of our healthcare workforce has never been as scrutinised as it has the last three years since the COVID-19 pandemic. Worldwide, appreciation of healthcare workers (HCWs) as the first line of defence during the pandemic soared, even as studies of HCW mental wellness increased exponentially.[1,2] Our prior study in March 2020 found that 33%, 13% and 24% of HCWs in Singapore experienced elevated symptoms of perceived stress, anxiety and job burnout, respectively, and in six months saw a 1.0% increase in stress and 1.2% increase in job burnout.[3]

But what of the longer-term effects? There are few long-term studies that have quantified the effects of the protracted pandemic on HCWs' mental well-being, which is what we sought to do. We measured changes in the proportion of HCWs reporting job burnout, anxiety and depression from mid-2020 to mid-2021 during the COVID-19 pandemic in Singapore. We also examined the extent to which job factors, HCW-perceived work conditions, demographic factors and vaccination status predicted the psychological outcomes of interest controlling for baseline functioning.

The study data consisted of a subset of HCWs who completed the one-year follow-up electronic survey (n=634), drawn from a convenience sample of doctors, nurses and allied health professionals in 4 Singapore tertiary hospitals. We used ultra-short screeners comprising the one-item job burnout question from the Physician Work Life Scale, the Generalized Anxiety Disorder-7 (GAD-7) scale and the Patient Health Questionnaire-2 (PHQ-2) to measure depression symptoms. We compared changes in outcomes and factors of interest from 2020 to 2021 of the same group of HCWs using conditional logistic regressions with time as the independent variable. In order to identify predictors of burnout, anxiety and depression in 2021, we utilised logistic regressions that simultaneously examined current job factors (occupation, contact with COVID-19 cases, work night shifts) and HCW-perceived work conditions (job risk, work longer than usual hours, clarity of work protocols, teamwork, feeling appreciated at work), controlling for burnout, anxiety and depression in 2020. We were particularly interested in whether job factors and perceived work condition that were recently changed versus a sustained condition had different effects on outcomes of interest. For example, we

distinguished those who reported working longer hours in both 2020 and 2021 (sustained) from those who reported working longer hours in 2021 but not 2020 (recent increase).

We found that job burnout, anxiety and depression were reported by 39%, 18% and 16% in 2021, which increased from 25% (P<0.01), 14% (P=0.02) and 12% (P=0.03) in 2020. The rate of job burnout had a distinct increase (by 14 percentage points [pp]) compared to anxiety and depression (4pp each). These increases are likely due to the protracted pandemic. See Fig. 1A–C.

Furthermore, burnout was predicted by recently increased and sustained levels of longer working hours (OR= 2.52, 95% CI [1.40–4.52] and 2.60 [1.55–4.40], respectively). Anxiety was predicted by sustained longer working hours (2.60 [1.47–4.60]) and depression was predicted by sustained night shift work (2.15 [1.06–4.39]). Perceiving good teamwork (0.38 [0.17–0.84], 0.30 [0.18–0.51]) and feeling appreciated at work (0.37 [0.17–0.81], 0.26 [0.15–0.44]) that is recent or sustained decreased the odds of job burnout. Sustained feeling of appreciation decreased the odds of anxiety (0.46 [0.24–0.87]) and depression (0.30 [0.15–0.57]). Put together, recent and sustained change in work conditions were associated with job burnout, while only sustained changes (i.e. HCWs reported them in both 2020 and 2021) were associated with anxiety and depression; our findings suggest a lower threshold for effects on job burnout compared to anxiety and depression. This may explain the greater increase in job burnout as compared to anxiety and depression within a year.

It is worth highlighting that working longer-than-usual hours (a more practical, logistical aspect of work) and feeling appreciated at work and perceiving teamwork (work culture aspects) were associated with HCW outcomes. Feeling appreciated at work emerged as an important protective factor; it decreased the odds of job burnout, anxiety and depression by 2-4 folds. Despite the majority of HCWs reporting that they felt appreciated at work, we saw a decrease in the proportion over time, perhaps reflecting the challenge of sustaining these feelings in a protracted pandemic. Interestingly, feeling appreciated only had a significant effect on anxiety or depression when sustained (so, no "quick fixes"). Our findings highlight the need to inculcate and maintain a work culture of appreciation for HCW

(A) Burnout
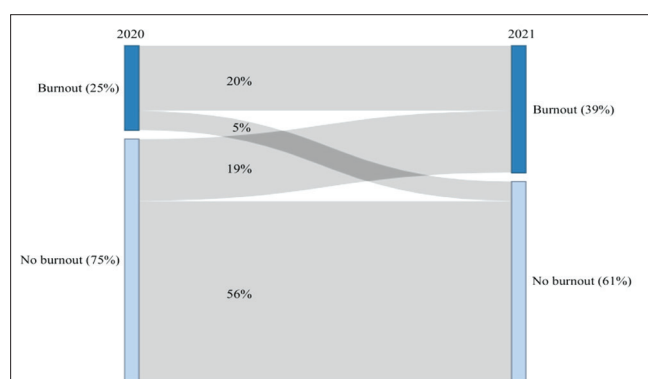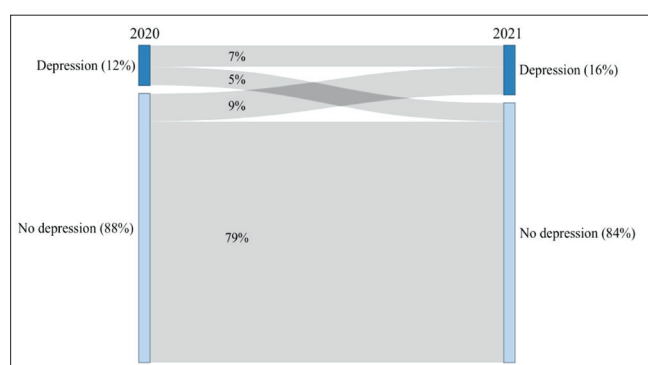
(B) Anxiety
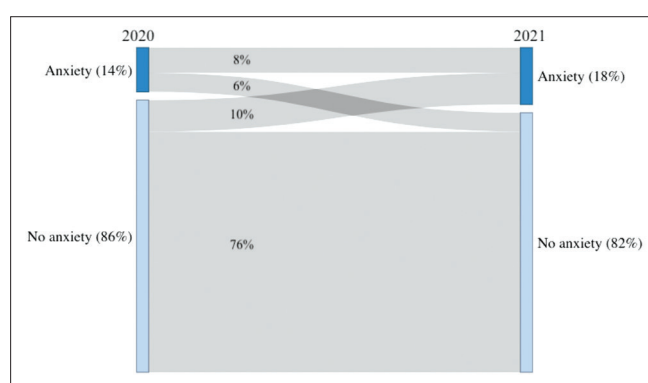
(C) Depression

Fig. 1 (A to C). Changes in burnout, anxiety and depression rates from 2020 to 2021, in our study sample of doctors, nurses and allied health professionals.

well-being.

Another protective factor that decreased the odds of job burnout was the perception of good teamwork. Being able to trust one's team, having aligned goals and engaging in open and constructive communication undoubtedly makes a HCW's job easier during a pandemic where there are higher volumes of patients to attend to and additional safety protocols.[4] However, we also saw that HCWs reported a significant decrease in teamwork in the last year, potentially reflecting the policies in place to minimise social interactions among HCWs for safety purposes.

Neglecting HCW well-being can lead to workforce attrition, with trickle-down effects that impact patient outcomes and quality of patient care.[5] Our previous qualitative examination of HCW unmet needs indicate multifaceted suggestions that begin at addressing manpower, workload and rest.[6] Additionally, giving HCWs more control over their working hours and flexibility in taking leave, could provide a sense of self-agency and mitigate the perception of working longer hours than usual.

The pandemic has challenged how we can provide support to HCWs. Nonetheless, there are various ways to harness technology to enable meaningful interpersonal connections. A supportive work environment may be cultivated through online platforms where HCWs can seek support and social connectivity (e.g. training peer supporters, team-based debriefing, self-help resources) or encouragement of self-care (e.g. through mindfulness practice or use of apps to reduce mental exhaustion and improve emotional regulation).[9-10]

Our one-year comparison offers a unique perspective of psychological well-being of HCWs during an unprecedented pandemic. We hope that our findings continue to spur the monitoring and care of HCW mental health even as we exit the pandemic.

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Poor survival rate of pregnancy-associated breast cancer in Asian countries

Dear Editor,

Asia has a lower incidence of breast cancer than North America, Oceania, and Western Europe. However, breast cancer rates have been rising fast in recent decades.[1] Breast cancer cases in Asian countries now constitute 40% of all cases diagnosed globally, and mortality due to breast cancer has similarly risen among Asian women.[1] With an estimated age-standardised rate of 29.1 per 100,000, the rate of breast cancer incidence in Asia is projected to range from one-fourth to one-third of those in high-risk regions.[2] Due to the increase in the prevalence of breast cancer along with delayed childbirth and low parity, pregnancy-associated breast cancer (PABC) cases are subject to rise in Asian countries. This article aims to raise awareness on PABC, which is rare but increasingly common.

Breast cancer that develops during or within a year after pregnancy is known as PABC, and it poses a diagnostic and treatment challenge. PABC can be described as breast cancer occurring during pregnancy or within 1 year of childbirth.[3] It can also involve cases of breast cancer identified within 2 years of delivery[4] or 5 years after childbirth.[5] The definition of PABC varies, which could lead to different conclusions about the relationship between pregnancy, postpartum stage and breast cancer.

PABC patients in Asian populations studied had a lower survival rate than their non-pregnant counterparts.[6,7,8,9,10] A study on Japanese women observed poorer prognoses in breast cancer patients with recent childbirth, than in individuals who had given birth less recently or were nulliparous. The 5-year survival rate of Japanese women with less than 2 years of pregnancy and PABC was 64.3% compared to 90.6% in non-PABC women.[6] In a Korean population, survival was significantly shorter in PABC patients with a 5-year survival rate of 80.11%, compared to non-PABC patients at 95.99%; similarly, 5-year survival rate was lower in patients with postpartum breast cancer at 77.15% compared to non-PABC group at 95.97%.[7] In a Taiwanese population, the 5-year survival rate in the antepartum PABC group was 65.7% while that in the postpartum group was 81.8%; and in the non-PABC group was 90.5%. No significant differences were observed in overall survival among the 3 groups (P=0.15).[8] In a retrospective study of 110 women with breast cancer in Saudi Arabia, 33 patients in the pregnant group died. The 5-year survival rate of PABC

was 65% and 82% in non-PABC patients (P=0.002). Disease-free survival of PABC was 47.5% compared with 65.4% in the non-PABC group.[9] In a nationwide population-based study, 30,230 breast cancer patients from 2002 to 2014 were identified from the cancer registry in Taiwan. Among them, 90 cases were antepartum, 347 were identified within 1 year after delivery, and 1,993 were identified from 1 to 5 years after delivery. In the study, a total of 2,920 patients died from breast cancer by the end of 2014, and breast cancer was the leading cause of mortality in 89% of the patients.[10] Among breast cancer patients in India, the 3-year overall survival rate in the antepartum group was 74.2% (95% confidence interval [CI] 58.3–94.4) and in the postpartum group was 62.8% (95% CI 47.9–82.3).[11]

Women who had breast cancer and recent previous pregnancies less than 2 years were 2.9 times more likely to die than non-PABC women (hazard ratio [HR] 2.9, 95% CI 1.05–4.56; P=0.036).[6] Postpartum breast cancer in Korean women was related to a worse survival rate (HR=1.57, 95% CI 0.82–2.99; P=0.1708).[7] On the other hand, breast cancer during pregnancy was not related to a lower risk of survival, with a multivariable HR of 1.09 (95% CI 0.15–7.91; P=0.9355).[7] In a Taiwanese study, all postpartum breast cancer patients had a greater mortality rate compared to those without a pregnancy history. Antepartum PABC cases had an HR of 1.9 (95% CI 1.17–3.12), and postpartum PABC cases had an HR of 1.92 (95% CI 1.48–2.48).[10]
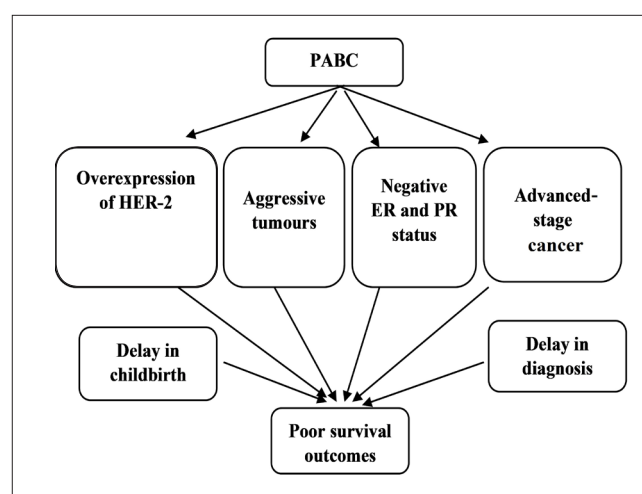

Fig 1. Factors contributing to poor survival in PABC.
ER: estrogen; receptor; HER-2: human epidermal growth factor receptor 2; PABC: pregnancy-associated breast cancer; PR: progesterone receptor

Fig. 1 shows possible factors for poor survival observed in PABC women. The factors include aggressive tumours, advanced-stage cancer, and overexpression of human epidermal growth factor receptor 2 (HER-2) along with the negative status of estrogen receptor (ER) and progesterone receptor (PR).[12] These factors, combined with a delay in diagnosis and childbirth, can lead to poor survival outcomes, as observed in several studies. Aggressive tumour features in young breast cancer patients who had just given birth were noted in a study conducted on Japanese women.[6] Tumours of >5cm size were more common in the pregnant (21.1%) and postpartum groups (18.4%) than in non-pregnant women (7.9%).[10] Similarly, a higher proportion of negative ER and PR status has been found in the PABC group.[7,9,10] Advanced-stage cancer was more common in PABC women than in the non-PABC group in a study on Saudi women. This was significant (P=0.01) in 55.7% of patients with advanced-stage cancer in the PABC group compared with 36.7% in the non-PABC group.[9] In Taiwanese women studied, advanced-stage cancer was more prevalent in those with a breast cancer diagnosis during gestation (16.7%) and within 1 year of childbirth (18.4%) than those without any record of pregnancy (9.7).[10] PABC patients who delivered within 2 years had a significantly more advanced stage, larger size, more axillary lymph node involvement, higher histological grade, and more progesterone receptor negative, HER2 positive, and triple negative tumours than those who had given birth less recently or women who never gave birth.[6] Overexpression of HER-2 has also been common in PABC cases. A retrospective study from a tertiary medical centre in Taiwan reported overexpression of HER-2 in the PABC group (47.6%) than in their non-pregnant counterparts (19.7%).[8] Similarly, overexpression of HER-2 was noted in the PABC group in the Saudi population[9] and the Chinese population.[13] Another study on Taiwanese women also reported higher expression of HER-2 in 36.36% of pregnant women and 26.5% of postpartum cases compared to 24.57% of those without a recent pregnancy record. Overexpression was also common in 32% of patients with >1 to ≤2 years postpartum PABC and 29.56% of those with >2 to ≤5 years postpartum PABC.[10]

In conclusion, a low survival rate for PABC was prevalent in different populations across Asia. However, most PABCs had favourable maternal and fetal outcomes and delivered healthy infants.[11,13] For any comparison for survival between PABC and non-PABC patients, staging is the main prognostic factor that should be adjusted or matched. We would like to highlight the importance of understanding the behaviour of PABC in Asian women and developing required treatment plans.

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Eosinophilic esophagitis and immunoglobulin E-mediated food allergy

Dear Editor,

Food allergy (FA) is an adverse reaction to a specific food antigen—normally harmless to the healthy population—which is mediated by immunological mechanisms and arises in an individual susceptible to that particular allergen.[1] FA is a public health problem affecting children and adults, and its prevalence has been increasing over the past decades.[2,3] In addition to immunoglobulin E (IgE)Ig-mediated FA (IgE-FA), there is growing recognition of cell-mediated disorders such as eosinophilic esophagitis (EoE).[3] EoE is characterised by symptoms of esophageal dysfunction in children and adults. However, in children, the symptoms are similar to those of gastroesophageal reflux or swallowing disorders. Additionally, EoE in children and adults present at least 15 eosinophils/high-power field (eos/HPF) on esophageal biopsies, in the absence of other causes of esophageal eosinophilia.[4]

It has recently been described that the syndrome of food-induced immediate response of the esophagus (FIRE) in adult patients with EoE consists of severe pain for several hours, together with unpleasant retrosternal pressure, just after contact of food with the esophageal mucosa.[5,6]

Pollen food allergy syndrome (PFAS) consists of IgE-FA to pollen and multiple foods that cross-react. PFAS starts in seconds or 1–2 minutes after food intake with oropharyngeal pruritus, tight throat, difficulty swallowing, dysphonia, and nasal and ear itching.[7]

In EoE, PFAS has yet to be evaluated. To our knowledge, no study has assessed the presence of FIRE or both FIRE and PFAS in children or patients with esophageal diseases without EoE. This paper's objectives are to study patients with EoE: (1) the prevalence of FIRE, PFAS, and both FIRE and PFAS; (2) the differences between patients with FIRE with and without EoE; and (3) the presence of FIRE in esophageal diseases other than EoE.

This is a prospective observational and analytical study that included patients evaluated from 2007–2020 in the Allergology Service of a university hospital located in the mid-south of Spain.

Following current consensus guidelines, patients were diagnosed with EoE and FIRE in our study. We performed skin prick tests in all patients, with aeroallergens battery (mites, pollens, fungi and epithelium of cats and dog), and food battery (milk, egg, wheat, lentil, nuts and fish/seafood), with the food implicated.

Patients were diagnosed with IgE-FA when allergic symptoms occurred "immediately" after ingestion of a relevant food allergen, and they were sensitised to the same item.

Variables and features of patients studied included epidemiological data (prevalence of FIRE, PFAS and both), demographics, symptoms, comorbidities, sensitisation to allergens, endoscopic phenotype, histological study (eos/HPF) and adherence and response to treatment.

We obtained informed consent in writing from the patients/guardians. The Clinical Research Committee of our hospital approved this study.

The SPSS Statistics software version 26 (IBM Corp, Armonk, US) was used. Categorical variables were described with percentages; 2 groups were compared using the chi-square test for categorical variables and Mann Whitney test for continuous variables. Confidence intervals of 95% were estimated.

A total of 386 patients were diagnosed with EoE from 2007 to 2020. The mean age was 35 years; 11% were <14 years. Most (75%) were male. Of the patients, 83.5% were atopic, 82% had a respiratory allergy, 11% atopic dermatitis and 29% a food allergy. The time of evolution of the symptoms until the diagnosis was 6 years and 8 months. Eighty seven percent had dysphagia, 27% had impactions, and 12.5% had other signs of esophageal dysfunction. Of 122 patients with EoE and FA, about 25% were sensitised to profilin and 25% to lipid transporting lipoprotein (LTP). The prevalence of PFAS in patients with EoE and FA was about 16%, and of FIRE was 36% We detected 3 patients with FIRE without EoE who were 9, 10 and 12 years old, and 4 patients with esophageal disease in EoE (3 patients with gastroesophageal reflux disease and 1 patient with Schatzki ring) (Fig. 1). Overall, we did not find significant differences in multiple features studied between the patients with EoE (with or without FIRE) (Fig. 1).

Discussion. One evidence that EoE is a food-mediated allergic disease is that almost all patients responded to an elemental diet. Many reacted to a diet in which dairy, wheat, eggs, and soy were eliminated; food-specific IgE and Th2 cells are consistent with a loss of tolerance to trigger foods. Many patients have concomitant IgE-
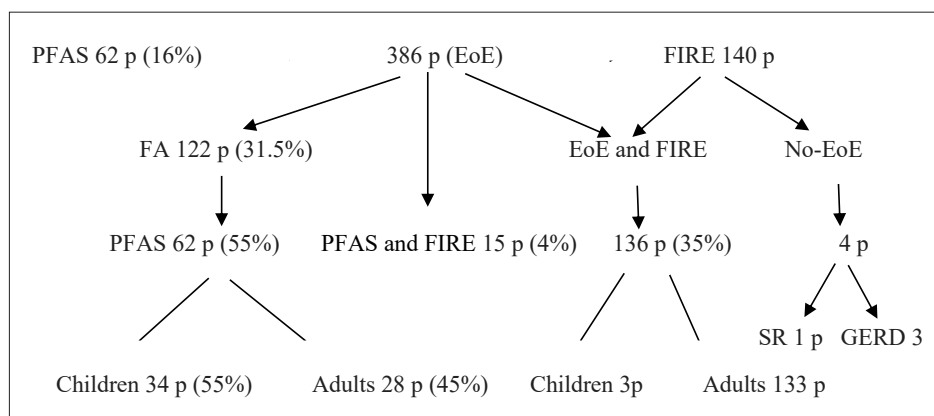
Fig. 1. Patients with EoE and PFAS, with FA and EoE, with EoE and FIRE, with EoE, FIRE, and PFAS, and with FIRE without EoE.
EoE: eosinophilic esophagitis; FA: food allergy; FIRE: food-induced immediate response of the esophagus; GERD: gastroesophageal reflux disease; p: patients; PFAS: pollen food allergy syndrome; SR: Schatzki ring

mediated food allergy and other allergic comorbidities in our series of patients.[8] The prevalence of IgE-FA and EoE is 31.5%; however, in one study, only the paediatric population amounted to 56.9%.[9]

In this study, the prevalence of PFAS is lower (16%) than that found by other researchers (26%),[10] which could be explained by different aerobiology in the regions where the study was carried out. About a quarter of the patients were sensitised to panallergens such as profilin and LTP. Also, the prevalence of FIRE in our patients (children and adults) is lower (36%) than that reported by other studies on only adult patients. It has yet to be studied if FIRE is exclusive to EoE and adult patients.[5] In our study, the concurrence of FIRE and PFAS is low (4%) in patients with EoE. We detected FIRE in 3 atopic children >8 years. They needed to go to the emergency room due to intense pressure in the chest that prevented them from breathing normally 5 minutes after the start of eating (melon and pineapple). The Allergology Service ruled out IgE-FA alertness, and they were later diagnosed with EoE. We have also evaluated patients with non-EoE esophageal pathology but with FIRE. We have not found significant differences between the patients with EoE (with and without FIRE) in multiple features studied. Therefore, the patients with EoE (with or without FIRE) are similar.

FIRE and PFAS are 2 types of local FA with symptoms at the esophagus and oropharynx, but different mechanisms trigger them.

In conclusion, in EoE, one-third of patients can have FIRE; one-fifth can have PFAS, but the concurrence of PFAS and FIRE is low. For the first time, we can say that FIRE is a response of the esophagus not exclusive to EoE or adult patients. The presence or absence of FIRE does not influence EoE.

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LETTER TO THE EDITOR

Investigating the stressors and coping mechanisms of students in medical school: A qualitative study

Dear Editor,

Medical school can be a stressful experience for students, with burnout being increasingly common.[1] Stressors in medical education include a heavy academic workload, pressure of good academic performance, and comparison with peers of high aptitude.[2] Stress can be either beneficial or detrimental to development, depending on personal regulation and coping mechanisms.[3] Consequences of poor coping include mental disorders, substance abuse, dropping out of school, and self-harm.[4] Furthermore, poor coping in medical school often carries into working life as a junior doctor, with the risk of physician suicide being higher than the general population.[5]

Most studies on coping in medical school focus on the quantitative causes rather than qualitative journey of students. Our study fills this gap by holistically characterising the perspectives and lived experiences of students in a medical school in Singapore, investigating stressors along with cognitive, affective, and behavioral coping mechanisms.

Eleven in-depth interviews were conducted with participants from the Yong Loo Lin School of Medicine, National University of Singapore through recruitment by purposive sampling. Recruitment proceeded until content saturation was reached when no further themes emerged from the interviews.[6,7] Open-ended questions were asked and revolved around participants' academic, social and personal experiences in medical school, their coping with stress, and the effects of stress on their lives (Supplementary Materials, Appendix A). The interviews were transcribed and analysed by 4 independent authors using an interpretative phenomenological approach, where inquiry was grounded in the tacit knowledge of participants who constructed meaning from their experiences.

"It's an information dump, and there's always the question of: do I really need to know this?" (Participant 9)

In pre-clinical years, participants grappled with a heavy academic workload and a lack of knowledge boundaries. Despite being academically excellent, participants felt overwhelmed and insecure about their academic abilities. The ambiguity of the extent and scope of the curriculum resulted in participants being unable to identify what is important, and over-compensating by studying as much as they could. The Pass/Fail system implemented to reduce fixation on grades paradoxically caused even more stress due to uncertainty over academic standing.

Participants struggled to form supportive and dependable relationships in medical school as structured social systems were randomly allocated, often being "luck of the draw". Those who did not come from predominant junior colleges were disadvantaged and took more time to fit into the new community. Participants kept their struggles to themselves, with a few admitting to not coping well in school. There was the pressure to appear invulnerable to be socially accepted; hence they were not proactive in seeking help. Authority figures like the faculty or the school's Student Affairs were avoided as they were perceived to be bureaucratic and impersonal.

In clinical years, a surge in demand was placed on the medical knowledge of participants, who felt unprepared to step up as future doctors. The metaphor of a "shortened runway" was used to describe the limited time participants had to master all the knowledge and skills required before graduation, given restrictions imposed by COVID-19. Many felt burnt out by long hours of clinical training and studying, leaving little time to spend with family or explore passions outside of medicine.

"Once adapted, I have to adapt again." (Participant 4)

Participants had to adjust from campus-based to hospital-based learning in clinical years, where they attended ward rounds, observed surgeries, and sat in for clinics. However, many felt like they did not know their "place" in different hospital settings and within the medical team. The frequent changes in clinical postings to different departments in different hospitals resulted in the need to constantly adapt. Moreover, participants grappled to adjust their learning style from information acquisition in pre-clinical years to information integration in clinical years, where they had to apply theoretical knowledge on real-life clinical scenarios on patients.

Both positive and negative role models were pivotal in shaping the clinical experience of participants. Doctors who ignored or failed to engage made participants feel
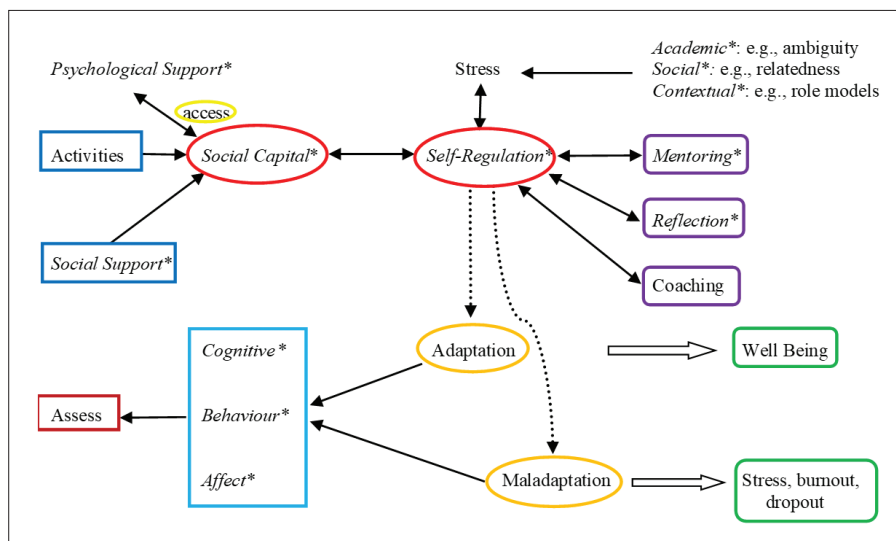
Fig. 1. Schema encapsulating key issues surrounding the stress that student participants faced, and their self-regulation and adaptation.
* Indicates areas where the students can be helped.

demoralised and invisible, while doctors who showed them the ropes and were patient made them feel inspired and driven. Nearly all participants expressed a deep desire to be mentored. However, this was unable to fulfilled due to the faculty's busy schedule. In addition, mentorships were perceived to be academic and professional in nature, with few participants approaching mentors for personal issues.

"...I felt like a parasite feeding off patients' suffering." (Participant 6)

While patient interaction taught participants empathy and gave fulfilment, many were affected by the trauma they witnessed, as they did not know how to deal with difficult emotions that arose—some of these included helplessness, isolation and guilt as participants felt responsible yet unable to alleviate the suffering of patients. Participants were not guided to reflect on these experiences, resulting in missed opportunities for self-development and professional identity formation.

Participants responded to stressors via various cognitive, affective and behavioral adaptations modulated by their intrinsic dispositions. Cognitive strategies included reframing negative thoughts into positive ones, reconnecting to one's sense of purpose, metacognitively reflecting on their difficult experiences and journalling. Affective strategies included motivating themselves to stay hopeful and optimistic. Behavioral strategies include voicing out struggles and reaching out to seek psychiatric help, counselling or sharing their struggles on social media. Participants who were able to tap on negative experiences to help others or continued to engage in hobbies coped better. All of these contribute to social capital. A framework linking the sources of stress, self-regulation and social capital was proposed (Fig. 1). Adaptation to stress requires self-regulated thoughts alongside planned feelings and behaviors cyclically adapted with reflective practice. Mentors play a key role in this process through guidance and positive role modelling.

As educators, it is vital to understand the medical school journey, its concomitant challenges and students' coping mechanisms to guide students through their formative years of medical education. The end-goal of medical school is to nurture students into competent doctors who possess resilient minds and a strong sense of purpose. It is hoped that the insights gleaned from studying stressors in medical school and identifying positive adaptive behaviors can benefit future students in navigating their own medical school journeys. Future direction for supporting students through medical school may focus on professional identity formation and fostering more effective student-mentor relationships.

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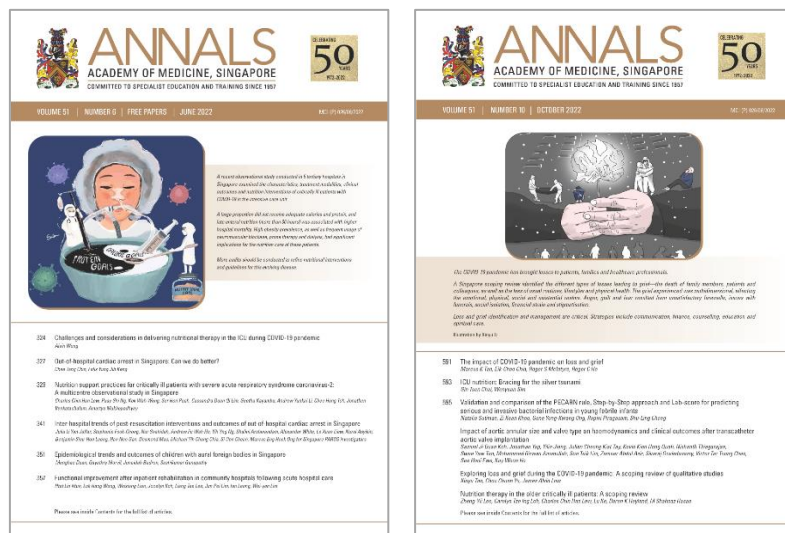
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