



*"An unfree mind is just like a windmill inside the bell jar!"*

**Mehmet Murat Ildan (1965)**

Turkish playwright and novelist

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### EDITORIAL

- 215 The AAMS, Your Journal  
*Erle CH Lim*

### ORIGINAL ARTICLES

- 217 Comparison of the Proportion and Healthcare Utilisation of Adult Patients with Uncontrolled Severe Asthma versus Non-Severe Asthma Seen in a Southeast Asian Hospital-Based Respiratory Specialist Clinic  
*Tunn Ren Tay, Hang Siang Wong, Rosna Ihsan, Hsiao Peng Toh, Xuening Choo, Augustine KH Tee*
- 229 An Ecologic Study of Trends in the Prevalence of Myopia in Chinese Adults in Singapore Born from the 1920s to 1980s  
*Sonoko Sensaki, Charumathi Sabanayagam, Pavan K Verkicharla, Adeola Awodele, Kok Hian Tan, Audrey Chia, Seang Mei Saw*
- 237 Predicting Pneumonia in Acute Ischaemic Stroke: Comparison of Five Prediction Scoring Models  
*Tian Ming Tu, Sheena SH Phua, Sanchalika Acharyya, Wai May Ng, Daniel CT Oh*

### COMMENTARY

- 245 Return to Work is an Important Therapeutic Goal  
*Brian See, Sin Eng Chia, Kee Seng Chia*

Please see inside Contents for the full list of articles.

# Professional Medical Congress Organisation for Professionals....



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## The AAMS, Your Journal

Erle CH Lim,<sup>1,2</sup> *MBBS, MMed (Int Med), FRCPS (Glasgow)*

I have had the pleasure of serving on the Editorial Board of the Annals, Academy of Medicine, Singapore (AAMS), under 2 indefatigable, dedicated and farsighted editors – Vernon Oh and EK Tan, and now take up the mantle of Editor-in-Chief with anticipation, yet mindful of the big shoes I have to fill. Under the leadership of both these editors, the AAMS has risen from an obscure, largely local journal, to one that now receives submissions from all over the world.

In the last decade, we have seen the AAMS breaking the 1.0 Journal Citation Reports impact factor (IF) barrier in 2008 (no mean feat, considering we did not have one before the year 2000). Whilst the Editorial Board of the Annals has not obsessed with “chasing the numbers”, we have been mindful that having a decent IF has meant that we have been able to attract meaningful and impactful papers from researchers around the world. This has meant, of course, that the AAMS became more relevant to our readership. The journal has, perhaps, been denied a further rise in its IF (and indeed, the IF has fallen slightly in this last year) because of the general nature of the journal. Catering to general practitioners, surgeons, physicians, subspecialists and scientists has allowed the AAMS to proffer to its readership a cornucopia of interesting articles. At the same time, however, it has suffered from being “too general”, and offering “simplistic” articles.

In our efforts to be relevant and relatable to the local and international community, we of the AAMS have steadfastly maintained that the journal must be provided gratis to the medical community. We have been fortunate in having our parent organisation, the Academy of Medicine, Singapore, allow us to give hard copies of the journal to all Fellows of the Academy, whilst also providing pdf copies free of charge, via our website. Unfortunately, what is freely given is often also under-appreciated.

I have heard colleagues making disparaging remarks about the journal, maintaining that its offerings are not of high standard; yet others have felt chagrined that their articles

have not been accepted for publication, complaining that “local journals should publish local articles”. This, then, is a double-edged sword. The AAMS is a journal for the medical community and must be the flag-bearer for local researchers, and yet it must maintain its standards.

The Editorial Board of the AAMS is proud to report that, since 1990, all submitted articles are anonymised to reviewers and indeed, to the Editorial Board, when deciding on their suitability for publication. We have also made it a policy to send articles to suitable, well published reviewers in the field, to assess the scripts for scientific rigour, relevance, and clinical importance. We will continue to do so, whilst remaining mindful of our charge to promote local research endeavours. To that end, we have tried our best to provide useful and constructive comments, in addition to those of our reviewers, in helping worthy articles get published in the journal.

We have increased the number of sections in the journal, to make the journal more interesting and relevant to our readership – e.g. we now publish images in medicine, commentaries, basic science, and medical education articles. We will also introduce Academy Matters, a supplementary newsletter to accompany the journal, featuring speeches, abstracts, *materia non medica*, and other articles that may not be suitable for publication in the journal proper, but are relevant and useful nonetheless.

One of the criticisms levied against the journal is that we have been tardy in returning decisions on papers. This is partly true. We have tried to make first-cut decisions on whether articles merit being sent for review, and have, I think, improved in getting rejection notices to unsuccessful authors within a fortnight, if not within a week. Where we have failed is in getting good quality reviews (and suggestions for improvement) out within a suitably short time – but again, this, we have addressed, and will continue to try to improve on. Moving forward, we will set up a schema to ensure that all articles will be processed within 3 months of submission, if not sooner. Within the next 3

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months, we will create, on our AAMS website, a survey for the readership of the AAMS to inform us of your needs, complaints and suggestions, which we will take seriously and try to address.

To end, I would like to thank you for your support of the AAMS. I would like to convey my thanks to our past

members of the Editorial Board, who have served the journal faithfully and well, and to express the excitement I feel in working with the new Editorial Board, I will strive to serve the academic needs of the medical community, and increase the international profile of the journal. Your Academy Matters, and so does the journal!

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# Comparison of the Proportion and Healthcare Utilisation of Adult Patients with Uncontrolled Severe Asthma versus Non-Severe Asthma Seen in a Southeast Asian Hospital-Based Respiratory Specialist Clinic

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## Abstract

**Introduction:** Understanding the burden of uncontrolled severe asthma is essential for disease-targeted healthcare planning. There is a scarcity of data regarding the proportion, healthcare utilisation and costs of patients with uncontrolled severe asthma in Asia. This study aimed to plug the knowledge gap in this area. **Materials and Methods:** Consecutive patients with asthma managed in our respiratory specialist clinic were evaluated prospectively. Healthcare utilisation comprising unscheduled asthma-related primary care visits, emergency department (ED) visits and hospital admissions were obtained from the national health records system. We defined uncontrolled severe asthma as poor symptom control (Asthma Control Test score <20); 2 or more asthma exacerbations requiring  $\geq 3$  days of systemic corticosteroids in the previous year; 1 or more serious asthma exacerbation requiring hospitalisation in the previous year; or airflow limitation with pre-bronchodilator forced expiratory volume in 1 second (FEV<sub>1</sub>) <80% predicted despite high dose inhaled corticosteroids and another controller medication. **Results:** Of the 423 study participants, 49 (11.6%) had uncontrolled severe asthma. Compared to non-severe asthma, patients with uncontrolled severe asthma were older and more likely to be female and obese. They had a median of 2 (interquartile range: 0 to 3) exacerbations a year, with 51% having  $\geq 2$  exacerbations in the past 12 months. They were responsible for 43.9% of the hospital admissions experienced by the whole study cohort. Mean annual direct asthma costs per patient was S\$2952  $\pm$  S\$4225 in uncontrolled severe asthma vs S\$841  $\pm$  S\$815 in non-severe asthma. **Conclusion:** Approximately 12% of patients with asthma managed in a hospital-based respiratory specialist clinic in Singapore have uncontrolled severe asthma. They account for a disproportionate amount of healthcare utilisation and costs. Healthcare strategies targeting these patients are urgently needed.

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**Key words:** Cost, Exacerbations, Singapore

## Introduction

Patients with severe asthma have poorly controlled asthma despite high intensity asthma medication,<sup>1</sup> and historically have been thought to represent about 5% of the asthma population.<sup>2</sup> A more recent study conducted in the Netherlands estimated that 3.6% of the adult asthma population have uncontrolled severe asthma.<sup>3</sup> Although these patients constitute a minority of all patients with asthma, they have a high burden of disease

and are responsible for a disproportionate amount of healthcare utilisation and costs.<sup>4-7</sup> It is therefore essential to understand the magnitude of the problem and appreciate the characteristics of this group of patients in order to optimise healthcare delivery.

Large cohort studies of patients with asthma and severe asthma have been carried out in Europe<sup>8,9</sup> and the United States,<sup>10</sup> providing invaluable insight into patient characteristics and asthma phenotypes. There is

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comparatively less data in non-Western populations. Apart from ethnic differences in asthma prevalence,<sup>11</sup> ethnic differences in asthma phenotypes,<sup>12</sup> asthma morbidity and healthcare utilisation<sup>13</sup> have also been observed in various populations. Therefore, findings in Western countries may not be globally representative, especially in Asia.

Four distinct asthma phenotypes have been described in 2 Korean adult asthma cohorts<sup>14</sup> but the proportion of patients with severe asthma was not reflected in this particular study. Asthma-related healthcare utilisation in Singapore has been reported previously<sup>15,16</sup> but the subgroup of uncontrolled severe asthma was not examined. To our knowledge, the prevalence and healthcare utilisation of uncontrolled severe asthma patients in Singapore (and Asia) have not been described before.

The recent 2014 European Respiratory Society/American Thoracic Society (ERS/ATS) guideline<sup>1</sup> defined patients with severe asthma as those with uncontrolled asthma despite being on high intensity asthma medication (Global Initiative for Asthma [GINA] treatment Step 4 or 5). Uncontrolled asthma is defined as 1 or more of the following: poor symptom control with Asthma Control Test (ACT) score <20; 2 or more asthma exacerbations requiring  $\geq 3$  days of systemic corticosteroids in the previous year; 1 or more serious asthma exacerbation requiring hospitalisation in the previous year; or airflow limitation with pre-bronchodilator forced expiratory volume in 1 second (FEV<sub>1</sub>) <80% predicted.

This study aimed to determine the proportion of asthma patients who fulfilled the 2014 ERS/ATS criteria for uncontrolled severe asthma<sup>1</sup> in a respiratory specialist clinic in Singapore and describe their healthcare utilisation and direct asthma costs. We hope that this will better inform health practitioners about the burden of uncontrolled severe asthma in our local setting.

## Materials and Methods

This was a cross-sectional observational study of consecutive patients with physician-diagnosed asthma seen at the respiratory specialist clinic of a restructured government hospital serving the eastern and north-eastern region of Singapore. About 35% of the country's population reside in the eastern and north-eastern region.<sup>17</sup> Our respiratory specialist clinic receives asthma referrals from primary care clinics, inpatient ward discharges, as well as interdepartmental referrals. Over a period of 1 year from 1 January 2015 to 31 December 2015, patients aged  $\geq 18$  years with asthma were invited to participate in the study. Patients were included only if alternative diagnoses were excluded and the managing respiratory specialists indicated that asthma was the most likely diagnosis. This study

was approved by the SingHealth Centralised Institutional Review Board (Reference 2014/835/C). Verbal consent for questionnaire administration was obtained from all participants.

For patients with multiple visits to the respiratory clinic during the study period, inclusion into the study and data collection was performed only at the earliest clinic visit during the study period, irrespective of whether it was the subject's first consultation in the respiratory clinic. Demographic characteristics and asthma history were collected using a standardised questionnaire administered in clinic (Appendix 1). Comorbidities were based on patient report and supplemented by review of all available medical records. Medication adherence was assessed based on patient self-report. The most recent results, including but not limited to spirometric parameters and peripheral blood eosinophil counts, were used for analysis. All study participants were reviewed by asthma nurses to reinforce medication adherence and correct inhaler techniques.

Asthma-related symptoms were assessed using the ACT.<sup>18</sup> The ACT score is the sum of responses to the 5 items relating to asthma symptoms and asthma reliever use over the last 4 weeks. The ACT score ranges from 5 to 25, with a higher score reflecting better asthma control. A score less than 20 indicates poor control. Asthma exacerbation was defined by the requirement for 3 or more days of systemic corticosteroids. Healthcare utilisation comprising primary care visits, emergency department (ED) visits and hospital admissions for asthma exacerbations in the previous 12 months were based on a review of the National Electronic Health Records (NEHR) system. All visits to and medication prescriptions at government primary care clinics (polyclinics) and government hospitals in Singapore are reflected on the NEHR.

A conservative estimation of the direct costs of asthma was calculated based on the costs of maintenance of asthma drugs, unscheduled asthma-related primary care consultations, ED visits and asthma-related hospital admissions. Drug costs were based on unsubsidised retail pricing at our hospital's pharmacy, excluding the 7% Goods and Services Tax (GST). The unit cost per primary care consultation was the non-resident rate of S\$44.60 at SingHealth polyclinics.<sup>19</sup> The unit cost per ED visit was our hospital's ED attendance fee of S\$115. The cost of each hospitalised day was based on our hospital's unsubsidised private rate of S\$430. Our cost calculation for primary care visits, ED visits and hospital stay did not include additional costs incurred for investigations and medications. Unsubsidised drug, medical consultation and hospitalisation costs were used to better reflect actual costs and provide uniformity of cost calculation across patient groups with varying subsidy levels. We did not have available data to

calculate the indirect asthma costs in our cohort.

Patients were considered to have uncontrolled severe asthma if they fulfilled the 2014 ERS/ATS criteria.<sup>1</sup> They had to have uncontrolled asthma defined as 1 or more of the following: poor symptom control with ACT <20; 2 or more asthma exacerbations requiring  $\geq 3$  days of systemic corticosteroids in the previous year; 1 or more serious asthma exacerbation requiring hospitalisation in the previous year; or airflow limitation with pre-bronchodilator FEV<sub>1</sub> <80% predicted, despite being on GINA treatment Step 4 or 5. In addition, these patients must have been managed in our clinic for at least 6 months to ensure asthma medication and comorbidities have been optimised.

Data were analysed using SPSS version 22. Estimates using categorical variables were expressed as number (proportions) and continuous variables were expressed as either median (interquartile range [IQR]) or mean (standard deviation [SD]). Comparisons between groups were performed using chi-square test, Mann-Whitney U test or Student's t-test as appropriate. A *P* value <0.05 was taken to be statistically significant.

## Results

### Demographics

During the study period, 528 patients with physician-diagnosed asthma were managed in our respiratory clinic, of which 423 (80.1%) agreed to participate in the study. The baseline characteristics of the 423 patients are shown in Table 1. Patients who declined to participate in the study (*n* = 105) were older (median age 59 [45 to 71] years vs 54 [34 to 65] years, *P* = 0.01) and were more likely to be female (61% vs 52.7%, *P* = 0.012).

Although females were older than males in our cohort (median age 59 [44 to 67] years vs 48 [22 to 62] years, respectively, *P* <0.001), the median age of asthma onset in females was also older than males (37 [15 to 50] years vs 18 [7 to 48] years, respectively, *P* <0.001). Consequently, there was no difference in the duration of asthma between males and females.

Although there were disproportionately fewer Chinese and more Malay patients (Table 1) with asthma seen in our clinic cohort as compared to the national population census,<sup>20</sup> there was no difference in ethnic composition between patients who participated in the study and those who declined participation (*P* = 0.418).

### Uncontrolled Severe Asthma

Forty-nine patients (11.6%) fulfilled the criteria for uncontrolled severe asthma. Compared to patients with non-severe asthma, patients with uncontrolled severe

Table 1. Baseline Characteristics of Patients

Baseline Characteristics	Values
Age, median (IQR)	54 (34 – 65)
Female, n (%)	200 (52.7)
Race, n (%)	
Chinese	217 (51.3)
Malay	149 (35.2)
Indian	39 (9.2)
Others	18 (4.3)
Smoking, n (%)	
Never smoker	294 (69.5)
Ex-smoker	58 (13.7)
Current smoker	64 (15.1)
Missing data	7 (1.7)
Smoking pack-years, median (IQR)	13 (2 – 23)
Age of onset, median (IQR)	29 (10 – 49)
Early onset <18 years, n (%)	175 (41.4)
Duration of asthma, median (IQR)	17 (7 – 33)
Family history of asthma (first degree relatives), n (%)	194 (45.9)
Presenting symptoms, n (%)	
Dyspnoea	256 (60.5)
Wheeze	286 (67.6)
Cough	293 (36.4)
Chest tightness	154 (36.4)
Self-reported asthma triggers, n (%)	
Dust mite	246 (58.2)
Animal dander	38 (9)
Pollen	3 (0.7)
Irritants	219 (51.8)
Viral infection	207 (48.9)
Exercise	66 (15.6)
Temperature change	160 (37.8)
NSAIDs	1 (0.2)
Work-related symptoms, n (%)	65 (15.4)
History of near-fatal asthma, n (%)	33 (7.8)
Asthma-related comorbidities, n (%)	
Sinonasal disease	134 (31.7)
Gastroesophageal reflux	65 (15.4)
Obesity (BMI >30 kg/m <sup>2</sup> )	145 (34.3)
Non-asthma related comorbidities, n (%)	
Hypertension	132 (31.2)
Diabetes mellitus	63 (14.9)
Ischaemic heart disease	37 (8.7)
Self-reported medication adherence, n (%)	312 (73.8)

BMI: Body mass index; ED: Emergency department; FEV<sub>1</sub>: Forced expiratory volume in 1 second; ICS: Inhaled corticosteroid; IQR: Interquartile range; LABA: Long-acting beta-agonist; NSAID: Non-steroidal anti-inflammatory drug

Table 1. Baseline Characteristics of Patients (Cont'd)

Baseline Characteristics	Values
Skin prick testing, n (%)	
Positive	57 (13.5)
Negative	6 (1.4)
Not performed	360 (85.1)
Sensitising allergens in patients with positive skin prick testing, n (%)	
Dermatophagoides pteronyssinus	44 (78.6)
Dermatophagoides farinae	42 (75)
Blomia tropicalis	43 (76.8)
Cockroach	12 (21.4)
Cat	19 (33.9)
Dog	13 (23.2)
Aspergillus	6 (10.9)
Asthma preventers, n (%)	
ICS only	79 (18.7)
ICS LABA combination	343 (81.1)
Oral corticosteroids	6 (1.4)
Leukotriene receptor antagonist	62 (14.7)
Theophylline	16 (3.8)
Tiotropium	6 (1.4)
ICS dose (beclomethasone dipropionate dose equivalent), n (%)	
Low dose 200 – 500 ug/d	146 (34.5)
Medium >500 – 1000 ug/d	187 (44.2)
High >1000 ug/d	87 (20.6)
Asthma Control Test score, median (IQR)	21 (18 – 23)
Number of exacerbations, median (IQR)	0 (0 – 1)
Patients with frequent exacerbations $\geq 2$ per year, n (%)	101 (23.9)
Primary care visits, median (IQR)	1 (1 – 2)
ED visits, median (IQR)	1 (1 – 2)
Hospital admissions, median (IQR)	1 (1 – 2)
Pre-bronchodilator FEV <sub>1</sub> , L/min, median (IQR)	1.9 (1.37 – 2.53)
Pre-bronchodilator FEV <sub>1</sub> , percentage predicted, median (IQR)	76 (64 – 90)

BMI: Body mass index; ED: Emergency department; FEV<sub>1</sub>: Forced expiratory volume in 1 second; ICS: Inhaled corticosteroid; IQR: Interquartile range; LABA: Long-acting beta-agonist; NSAID: Non-steroidal anti-inflammatory drug

asthma were older, had a longer duration of asthma and were more likely to be female (Table 2). Other differences between patients with uncontrolled severe asthma and those with non-severe asthma are shown in Table 2. We did not observe any ethnic differences between the 2 groups.

As shown in Table 2, patients with uncontrolled severe asthma had poorer lung function and were more likely to be on high dose inhaled corticosteroids than those with

non-severe asthma. In patients with uncontrolled severe asthma, 6.1%, 49% and 3.8% were on add-on tiotropium, leukotriene receptor antagonist and theophylline, respectively. Only 2 patients (4.1%) with uncontrolled severe asthma were on maintenance oral corticosteroids. None were on biologic agents for asthma.

Patients with uncontrolled severe asthma had a median of 2 (0 to 3) exacerbations a year; 51% were considered to be frequent exacerbators with  $\geq 2$  exacerbations the past 1 year. In patients with uncontrolled severe asthma, there was no significant difference between the frequent and non-frequent exacerbators in terms of peripheral blood eosinophils levels or comorbidities. A greater proportion of patients with uncontrolled severe asthma had at least 1 primary care visit, ED visit and hospital admission compared to patients with non-severe asthma (Table 2). There was no significant difference in the median hospital length of stay between the 2 groups.

Although patients with uncontrolled severe asthma made up 11.6% of the study cohort, they were responsible for 23.3% of the primary care visits, 23.4% of the ED visits and 43.9% of the hospital admissions. The annual total direct costs for asthma in the entire study cohort was S\$459,023, with patients having uncontrolled severe asthma accounting for 31.5% of the total costs. The mean annual total direct asthma costs per person was S\$2952  $\pm$  S\$4225 for uncontrolled severe asthma and S\$841  $\pm$  S\$815 for non-severe asthma. Details of costs breakdown are described in Table 3.

## Discussion

Our study is the first to examine the proportion of uncontrolled severe asthma in a restructured hospital in Singapore. We showed that 11.6% of asthma patients in our hospital's respiratory specialist clinic had uncontrolled severe asthma. This figure is comparable to results from a tertiary care hospital in Melbourne, Australia, where 13.3% of asthma patients seen in a respiratory specialist clinic were thought to be challenging to manage.<sup>21</sup>

Patients seen in the respiratory clinic are unlikely to reflect the general asthma population as most of the patients with milder asthma would have been managed at the primary care level. Only the difficult-to-manage cases would be referred on to specialist care.<sup>22</sup> Local data for the proportion of asthma patients managed by respiratory physicians in hospital-based clinics is not available, and we are therefore unable to extrapolate our data to determine the magnitude of uncontrolled severe asthma in Singapore. However, a population study conducted in Asian countries reported that 4.1% of asthmatics in the general population had severe asthma.<sup>23</sup>



Table 2. Comparison of Uncontrolled Severe vs Non-Severe Asthma

	Uncontrolled Severe Asthma (n = 49)	Non-Severe Asthma (n = 374)	P Value
Age, median (IQR)	59 (47 – 70)	54 (32 – 65)	0.012
Female, n (%)	33 (67.3)	164 (44.7)	0.003
Race, n (%)			0.199
Chinese	19 (38.8)	198 (52.9)	
Malay	21 (42.9)	128 (34.2)	
Indian	5 (10.2)	34 (9.1)	
Others	4 (8.2)	14 (3.7)	
Smoking, n (%)			0.155
Never smoker	39 (79.6)	255 (68.2)	
Ex-smoker	7 (14.3)	51 (13.6)	
Current smoker	3 (6.1)	61 (16.3)	
Missing data	0	7 (1.9)	
Smoking pack-years, median (IQR)	5 (2 – 5)	13 (2 – 21)	0.788
Age of asthma onset, median (IQR)	35 (12 – 49)	28 (9 – 50)	0.347
Early onset <18 years, n (%)	17 (34.7)	158 (42.2)	0.313
Duration of asthma, median (IQR)	22 (12 – 37)	17 (6 – 32)	0.05
Work-related symptoms, n (%)	10 (20.4%)	55 (14.7%)	0.298
History of near-fatal asthma, n (%)	5 (10.2%)	28 (7.5%)	0.512
Asthma-related comorbidities, n (%)			
Sinonasal disease	16 (32.7)	118 (31.6)	0.886
Gastroesophageal reflux	9 (18.4)	56 (15)	0.536
Obesity (BMI >30 kg/m <sup>2</sup> )	23 (46.9)	122 (32.6)	0.047
Non-asthma-related comorbidities, n (%)			
Hypertension	20 (40.8)	112 (29.9)	0.123
Diabetes mellitus	13 (26.5)	50 (13.4)	0.015
Ischaemic heart disease	5 (10.2)	32 (8.6)	0.701
High dose ICS (beclomethasone dipropionate >1000 ug/d), n (%)	47 (95.9)	40 (10.7)	<0.001
Asthma Control Test score, median (IQR)	18 (12 – 21)	21 (19 – 24)	<0.001
Patients with frequent exacerbations ≥2 per year, n (%)	25 (51)	76 (20.3)	<0.001
At least 1 primary care visit, n (%)	21 (42.9)	63 (16.8)	<0.001
At least 1 ED visit, n (%)	19 (38.8)	83 (22.2)	0.033
At least 1 hospital admission, n (%)	17 (34.7)	45 (12)	<0.001
Number of primary care visits, median (IQR)	1 (1 – 2)	1 (1 – 2)	0.892
Number of ED visits, median (IQR)	2 (1 – 3)	1 (1 – 2)	0.453
Number of hospital admissions, median (IQR)	1 (1 – 3)	1 (1 – 1)	0.02
Duration of hospital stay, median (IQR)	4 (3 – 8)	3 (2 – 5)	0.213
Pre-bronchodilator FEV <sub>1</sub> , L/min, median (IQR)	1.44 (1.01 – 2.19)	1.96 (1.47 – 2.64)	<0.001
Pre-bronchodilator FEV <sub>1</sub> , percentage predicted, median (IQR)	68 (57 – 87)	77 (65 – 91)	0.018
Patients with peripheral blood eosinophil ≥0.3 × 10 <sup>9</sup> /L, n (%)	18 (39.1)	144 (50.3)	0.158

BMI: Body mass index; ED: Emergency department; FEV<sub>1</sub>: Forced expiratory volume in 1 second; ICS: Inhaled corticosteroid; IQR: Interquartile range

Despite making up about 12% of the patients with asthma seen in our respiratory outpatient clinic, those with uncontrolled severe asthma accounted for nearly half of the total hospital admissions. Furthermore, half of the

patients with severe asthma had frequent exacerbations and were more likely to have had at least 1 asthma-related healthcare visit in the past year. Our results are not surprising since increasing asthma severity has been associated with

Table 3. Annual Direct Costs\* Per Patient of Asthma

	All Patients (n = 423)	Uncontrolled Severe Asthma (n = 49)	Non-Severe Asthma (n = 374)
Hospital admission costs, mean (SD)	346 ± 1460	1509 ± 3842	193 ± 573
ED visit costs, mean (SD)	57 ± 144	115 ± 228	49 ± 127
Primary care visit costs, mean (SD)	16 ± 49	32 ± 49	14 ± 45
Maintenance asthma drug costs, mean (SD)	667 ± 433	1296 ± 354	585 ± 370

ED: Emergency department; SD: Standard deviation

\*In Singapore dollars.

greater healthcare use.<sup>5,6</sup> More than half of the asthmatics in a population study conducted in Asia<sup>23</sup> had at least 1 hospital emergency room or unscheduled emergency visit for asthma in a 12-month period. Pooled analysis of data from various severe asthma clinics in the United Kingdom found that more than 80% of patients had at least 1 ED or primary care visit, and almost half had at least 1 hospital admission for asthma in the past year.<sup>24</sup>

Yi et al recently described a cohort of patients with severe asthma in Singapore although the proportion of patients seen in their institution with severe asthma was not reported.<sup>25</sup> Similar to our findings, they reported high healthcare utilisation in their cohort. About 50% of their patients had an ED visit in the past 2 years, and 20% of the patients had a hospital admission for asthma in the past 2 years.

Increased healthcare utilisation has been shown to translate into direct asthma costs.<sup>26,27</sup> Patients with uncontrolled severe asthma had direct asthma costs that was more than 3 times higher than non-severe asthma in our cohort, largely attributable to the higher hospital admission costs. The Asthma Insights and Reality in Asia-Pacific (AIRIAP) study conducted in general asthma patients showed that urgent asthma care, as compared to maintenance care, accounted for a higher proportion of total care costs in many Asian countries, including China and Hong Kong.<sup>28</sup> The same study also showed that poor asthma control was responsible for significantly increasing urgent care costs.

Although not examined in our study, asthma morbidity resulting in loss of work productivity also contributes to asthma costs indirectly. A study conducted in the United Kingdom found that indirect asthma costs, estimated using the Disability Living Allowance, made up 13.2% of asthma costs.<sup>26</sup> Indirect asthma costs may even account for the majority of total asthma costs in certain populations.<sup>29</sup> A survey conducted in Singapore by Ng et al found a significant association between absence from work and acute healthcare resource use.<sup>15</sup> Therefore, apart from adversely impacting patient health outcomes, severe

uncontrolled asthma has substantial economic and societal ramifications as well.

Our study and that of others<sup>21</sup> showed that a substantial proportion of patients with asthma who were managed by specialists would continue to have uncontrolled severe asthma. This was likely due to the complexity and heterogeneity of severe asthma. Some patients who may have truly treatment-resistant asthma would benefit from phenotype-targeted immunotherapy.<sup>30-32</sup> Others may have additional diagnoses or comorbidities contributing to poor asthma control.<sup>33</sup> There is increasing evidence to show that dedicated severe asthma clinics, through systematic evaluation, can improve asthma outcomes even in patients already managed by specialists.<sup>24,34</sup>

### Limitations

We recognise certain limitations in our study. Firstly, a relatively large proportion of patients (19.9%) declined to participate in the study. We were unable to ascertain the study impact of differences between participants and non-participants. Secondly, we established healthcare utilisation based on visits recorded in the NEHR system. This would have missed healthcare visits to private clinics and hospitals which may result in an underestimation of asthma-related primary care visits as the majority of primary healthcare services are provided by private practitioners.<sup>35</sup> However, the reverse is true of hospital-related healthcare and we would have included most of the ED visits and hospital admissions. Thirdly, asthma was diagnosed based on clinician impression and not all patients had objective evidence of variable airflow obstruction. As this was an observational study, including only patients with objective evidence of variable airflow obstruction would lead to under-representation of a large proportion of our asthma cohort. Fourthly, medication adherence was based on patient report, which is notoriously inaccurate.<sup>36</sup> However, we did not have access to objective methods of adherence measurements, such as electronic dose monitors and pharmacy prescription refills. Lastly, we were unable to calculate the indirect asthma costs in our cohort due to

unavailability of relevant data. Tan et al recently described the direct and indirect asthma costs in a cohort of asthma patients seen at primary care clinics in Singapore.<sup>37</sup> In that study, indirect costs was about 12% of the direct costs. This figure is likely to be higher in uncontrolled severe asthma due to the higher frequency of exacerbations.

## Conclusion

Patients with severe asthma make up about 12% of patients with asthma seen in the respiratory specialist clinic. Although representing a minority of the general asthma population, they account for a disproportionate amount of healthcare utilisation. Further understanding of the relevant mechanistic pathways driving poorer outcomes in severe asthma in our local context, as well as strategies to better manage this group of patients, are needed.

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## Appendix 1

**Patient initials:**

**Patient number:**

**Date:**

**Weight:** \_\_\_\_\_

**Height:** \_\_\_\_\_

**BMI:** \_\_\_\_\_

### (i) Demographics

**Occupation:** \_\_\_\_\_

#### **Smoking**

☐ Yes: Number of pack-years: \_\_\_\_\_

☐ No

☐ Ex-smoker (quit for  $\geq 6$  months)

### (ii) Asthma history

**Age of onset (symptoms):** \_\_\_\_\_

**If age of onset >12 yr old, any wheeze present in childhood ( $\leq 12$  years):** ☐ Yes ☐ No

#### **Symptoms at presentation (check all that apply)**

☐ SOB

☐ Cough

☐ Wheeze

☐ Chest tightness

#### **Triggers of symptoms (check all that apply)**

☐ Environment:

☐ Dust mites

☐ Animal fur

☐ Pollen

☐ Viral infection

☐ Medications

☐ NSAID

☐ B blockers

☐ Irritants

☐ Smoke

☐ Chemicals

☐ Strong odors

☐ Strong emotions

☐ Hormonal

☐ Menstrual cycle

☐ Pregnancy

☐ HRT/OCP

☐ Temperature change

☐ Exercise

☐ Others: Specify \_\_\_\_\_

#### **Continued exposed to any of the identified triggers (excluding temperature, exercise, emotions)?**

☐ Yes

☐ No

#### **Symptoms related to workplace (worse at work, better during weekends or holidays)**

☐ Yes

☐ No

☐ NA

#### **History of near fatal asthma (needing invasive or non-invasive mechanical ventilation)**

☐ Yes

☐ No

**Family history of asthma:** ☐ Yes ☐ No

If yes, specify:

☐ Parents

☐ Siblings

**(iii) Comorbidities**

☐ Rhinosinus disease

Treatment: ☐ Yes ☐ No

☐ GERD

Treatment: ☐ Yes ☐ No

☐ Eczema

Treatment: ☐ Yes ☐ No

**Skin prick test:** ☐ Done ☐ Not done

Date: \_\_\_\_\_

☐ Positive:

☐ D Pteronyssinus

☐ D Farinae

☐ Blomia

☐ Cockroach

☐ Cat

☐ Dog

☐ Peanut

☐ Aspergillus

☐ Negative

**(iv) Current medication**

On controllers: ☐ Yes ☐ No

Compliance: ☐ Yes ☐ No

Type of controllers

☐ ICS

Specify: ☐ Beclomethasone

☐ Budesonide

☐ Others

☐ ICS + LABA

Specify: ☐ Seretide

☐ Symbicort

☐ Zenhale

☐ Others

☐ Leukotriene antagonist eg montelukast

☐ Theophylline

☐ Tiotropium

☐ Long term oral steroids (prednisolone)

**Dose of ICS**

	Low dose (ug/d)	Medium dose (ug/d)	High dose (ug/d)
<b>Beclomethasone dipropionate</b>	<input type="checkbox"/> 200-500	<input type="checkbox"/> >500-1000	<input type="checkbox"/> >1000
<b>Budesonide</b>	<input type="checkbox"/> 200-400	<input type="checkbox"/> >400-800	<input type="checkbox"/> >800
<b>Fluticasone</b>	<input type="checkbox"/> 100-250	<input type="checkbox"/> >250-500	<input type="checkbox"/> >500
<b>Mometasone</b>	<input type="checkbox"/> 200	<input type="checkbox"/> ≥400	<input type="checkbox"/> ≥800
<b>Others</b>	Specify:		

**(v) Asthma control**

ACT score: \_\_\_\_\_

**Written asthma action plan:**

☐ Yes

☐ No

**SECTION D**

Date of first respiratory clinic consult: \_\_\_\_\_

Age: \_\_\_\_\_

Gender: ☐ Male ☐ FemaleRace: ☐ Chinese ☐ Malay ☐ Indian ☐ Others**(i) Health care use past 12 months (requiring  $\geq 3$  days of steroid bursts)****Primary care visits**☐ Yes: Number of visits \_\_\_\_\_ ☐ No**A&E visits**☐ Yes: Number of visits \_\_\_\_\_ ☐ No**Hospital admissions**☐ Yes: Number of admissions \_\_\_\_\_ ☐ NoICU admissions: ☐ Yes ☐ No**(ii) Other comorbidities**☐ Hypertension☐ DM☐ IHD☐ OSA☐ Psychiatric illness☐ Anxiety ☐ Depression ☐ Others \_\_\_\_\_**(iii) Medications (past 6 months)**Antihistamines: ☐ Yes ☐ NoNasal steroids: ☐ Yes ☐ NoGERD medication: ☐ Yes ☐ NoAspirin: ☐ Yes ☐ NoNSAIDs: ☐ Yes ☐ NoACE-I: ☐ Yes ☐ NoARB: ☐ Yes ☐ NoB1 specific blockers: ☐ Yes ☐ NoNon selective B blockers: ☐ Yes ☐ No**(iv) Lung function:**☐ Done: Date \_\_\_\_\_ ☐ Not done

	Pre	% Predicted	Post	% predicted	%change
FEV1 (L)					
FVC (L)					
FEV1/FVC (%)					
FEF25-75 (L/sec)					

**Methacholine challenge test**☐ Done: Date: \_\_\_\_\_ PC20 (mg/ml) \_\_\_\_\_☐ Not done**CXR/CT**☐ Not done☐ Normal☐ Hyperinflated☐ Other abnormalities: Specify \_\_\_\_\_**Investigations available****Blood eosinophil count:** ☐ Done ☐ Not done

Date: \_\_\_\_\_

Absolute: \_\_\_\_\_

Percentage: \_\_\_\_\_

**Blood neutrophil:** ☐ Done ☐ Not done

Date: \_\_\_\_\_

Absolute: \_\_\_\_\_

Percentage \_\_\_\_\_

**Serum IgE:** ☐ Done ☐ Not done

Date: \_\_\_\_\_

Value: \_\_\_\_\_

**FeNO:** ☐ Done ☐ Not done

Date: \_\_\_\_\_

Value: \_\_\_\_\_

**(v) Asthma diagnosis**☐ Objective asthma diagnosis ☐ Clinical diagnosis☐ FEV1 or FVC BDR  $\geq 20\%$  +  $\geq 200\text{ml}$ ☐ MCT positive (PC20  $< 16\text{mg/ml}$ )**(vi) Meets GINA criteria for severe asthma:** ☐ Yes ☐ No

Step 4 or 5 of GINA treatment

GINA symptoms 'uncontrolled' or ACT score  $< 20$



## An Ecologic Study of Trends in the Prevalence of Myopia in Chinese Adults in Singapore Born from the 1920s to 1980s

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### Abstract

**Introduction:** This study aimed to investigate secular trends in the prevalence of myopia over 6 decades (from the 1920s to 1980s) in Chinese adults in Singapore. **Materials and Methods:** Parental myopia prevalence was estimated using a parent-completed questionnaire in paediatric cohorts that included: 1) The Singapore Cohort Of Risk factors for Myopia (SCORM), 2) The Strabismus, Amblyopia and Refractive Error in Singaporean Children (STARS), and 3) The Growing Up in Singapore Towards healthy Outcomes (GUSTO). Published estimates for myopia prevalence from 5 adult studies in Singapore were reviewed. Secular trends in the prevalence of myopia were correlated with changes in the education system. **Results:** The prevalence of parental myopia in SCORM (n = 2943), STARS (n = 4938), and GUSTO (n = 1072) was 47.8%, 53.4%, and 73.4%, respectively; corresponding calendar years these parents might have started schooling were 1966, 1973, and 1983 (born in 1960, 1967, and 1977), respectively. Mean age of parents was 41.3, 40.1, and 33.4 years, respectively. Prevalence of myopia in adult studies in persons who started elementary school in 1928, 1934, 1938, 1939, 1942, 1948, 1952, 1958, 1962, 1972, 1982, and 1995 were 36.4%, 39.7%, 30.0%, 31.5%, 33.0%, 26.4%, 32.5%, 48.7%, 39.4%, 52.0%, 82.2%, and 85.9%, respectively. **Conclusion:** During the past few decades, the prevalence of myopia increased rapidly, especially in persons who started elementary school after the 1980s (born after 1970). The education system was expanded after Singapore's independence in 1965, and the new education system was introduced in 1978. These changes, together with increasing intensive schooling, may have contributed to the increase in myopia prevalence.

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**Key words:** Education, Refractive error, Secular trend

### Introduction

Myopia is a significant public health problem. The prevalence of myopia is increasing substantially worldwide, particularly in east and southeast Asian urban areas,<sup>1</sup> where 80% to 90% of school leavers have myopia and 10% to 20% have high myopia.<sup>2,3</sup> This is of concern because myopia is associated with ocular complications leading to substantial visual loss.<sup>4-6</sup> In addition, the economic burden of myopia is also high, with the total estimated costs towards annual visits and optical purchases for myopia (excluding

presbyopic lenses and sunglasses) of approximately SGD 959 (USD 755) million per year in Singapore.<sup>7</sup> Although myopiogenesis is known to interplay between genetic and/or environmental factors with the debated “nature versus nurture” effect, the steep increase in prevalence in the last few decades could possibly indicate a strong influence of the environment on myopia development.<sup>2-5</sup>

Previous studies have investigated trends in myopia prevalence and it is evident that the epidemic of myopia in several countries has gradually increased over

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generations.<sup>8-12</sup> Cross-sectional surveys (National Health and Nutrition Examination Survey [NHANES]) conducted between 1971 to 1972 and 1999 to 2004 on the United States' population have shown significantly higher prevalence of myopia in persons aged 12 to 54 years in the latter cohort (41.6%) than the earlier one (25%).<sup>8</sup> An Israeli study reported an increase in the prevalence of myopia from 20.3% in 1990 to 28.3% in 2002 among candidates for security service aged 16 to 22 years.<sup>9</sup> In Singapore, serial surveys involving military conscripts showed an increasing trend in myopia prevalence in young adults aged 16 to 25 years, from 26% in 1974 to 1984, 44% in 1987 to 1991, 77% in 1996 to 1997, and 81% in 2009 to 2010, respectively.<sup>3,10-12</sup> However, they were limited by reporting changes over shorter periods of 10 to 30 years or including selective populations such as military conscripts.

We aimed to investigate the secular trends in myopia prevalence in Chinese adults using individual-level questionnaire data of parents from 3 paediatric cohorts,<sup>13-18</sup> and published estimates from 5 adult studies in Singapore.

## Materials and Methods

### Study Populations

#### Paediatric Cohorts

We assessed the prevalence of myopia in parents (born in 1959 to 1975) of children from 3 paediatric cohorts: the Singapore Cohort Of Risk factors for Myopia (SCORM), the Strabismus, Amblyopia and Refractive Error in Singaporean Children (STARS), and the Growing Up in Singapore Towards healthy Outcomes (GUSTO). SCORM is the first myopia cohort study in Asia involving 1979 children aged 7 to 9 years who were recruited from 3 schools in

Singapore during the years 1999 to 2001 and were followed up annually until 2006.<sup>13,14</sup> STARS is a population-based study of 3009 children aged 6 to 72 months conducted by door-to-door recruitment between 2006 and 2008.<sup>15,16</sup> GUSTO is a mother-offspring cohort of 1176 babies who were recruited at 2 major public maternity units between 2009 and 2010, and are followed up to the present.<sup>17,18</sup> The refractive state (myope/emmetrope) of parents was determined based on a self-reported questionnaire by asking, "Is your child's mother/father myopic?" with "yes/no" in SCORM, "history of wearing glasses or contact lens for short-sighted" in STARS, and "current spectacles wear/contact lens" for distance vision with "yes/no" answer (spectacle prescription was also checked wherever possible) in GUSTO. The refraction data was available on 2943 parents (1479 fathers and 1464 mothers) in SCORM, 4938 (2469 fathers and 2469 mothers) in STARS and 1074 (535 fathers and 539 mothers) in GUSTO, all of Chinese ethnicity, whose mean year in which elementary school began were 1966, 1973 and 1983 (born in 1960, 1967, and 1975), respectively.

#### Adult Studies

We reviewed published estimates from 5 adult studies in Singapore with myopia data: the Tanjong Pagar Study (TPS, 1997-1998),<sup>19</sup> the Singapore Longitudinal Aging Study (SLAS, 2003-2011),<sup>20</sup> the Singapore Chinese Eye Study (SCES, 2009-2011),<sup>21</sup> and 2 military conscripts surveys (1996-1997; 2009-2010).<sup>10</sup> Myopia was defined as a spherical equivalent of at least -0.5 diopters by non-cycloplegic auto-refraction. Details of these studies are presented in Table 1.

Table 1. Evidence-based Survey of Myopia Prevalence in Chinese Adult Cohorts in Singapore

Author	Study	Year	Age at Recruitment (Years)	Birth Year	n (Men/Women)	Myopia Definition
Wong et al (2000)*	TPS	1997 – 1998	40 – 81	1922 – 1952	1113 (500/613)	Auto-refraction SE <-0.5D
Tan et al (2011)†	SLAS	2003 – 2011	55 – 85	1918 – 1948	1835 (670/1165)	Auto-refraction SE <-0.5D
Pan et al (2013)‡	SCES	2009 – 2011	40 – 80	1936 – 1966	3251 (1605/1646)	Auto-refraction SE <-0.5D
Koh et al (2014)§	Military conscripts	1996 – 1997	16 – 25	1971 – 1981	12,370 (12370/0)	Auto-refraction SE <-0.5D
Koh et al (2014)§	Military conscripts	2009 – 2010	17 – 29	1981 – 1993	20,004 (20004/0)	Auto-refraction SE <-0.5D

SCES: Singapore Chinese Eye Study; SE: Spherical equivalent; SLAS: Singapore Longitudinal Ageing Study; TPS: Tanjong Pagar Study

\*Wong TY, Foster PJ, Hee J, Ng TP, Tielsch JM, Chew SJ, et al. Prevalence and risk factors for refractive errors in adult Chinese in Singapore. *Invest Ophthalmol Vis Sci* 2000;41:2486-94.

†Tan CS, Chan YH, Wong TY, Gazzard G, Niti M, Ng TP, et al. Prevalence and risk factors for refractive errors and ocular biometry parameters in an elderly Asian population: the Singapore Longitudinal Aging Study (SLAS). *Eye* 2011;25:1294-301.

‡Pan CW, Zheng YF, Anuar AR, Chew M, Gazzard G, Aung T, et al. Prevalence of refractive errors in a multiethnic Asian population: the Singapore epidemiology of eye disease study. *Invest. Ophthalmol Vis Sci* 2013;54:2590-8.

§Koh V, Yang A, Saw SM, Chan YH, Lin ST, Tan MM, et al. Differences in prevalence of refractive errors in young Asian males in Singapore between 1996-1997 and 2009-2010. *Ophthalmic Epidemiol* 2014;21:247-55.

Table 2. Secular Trend of Self-Reported Myopia Prevalence in Chinese Adults in Singapore

	SCORM*	STARS†	GUSTO‡
<b>Fathers</b>			
Year started in elementary school (mean)	1965	1974	1981
No. of years since Singapore's independence	0	+9§	+16§
Year of birth (mean)	1959	1968	1975
Age (mean)	43.0	37.7	34.8
Total sample size (n)	1479	2469	535
Total prevalence (%)	40.8	48.6	73.4
<b>Mothers</b>			
Year started in elementary school (mean)			
No. of years since Singapore's independence	+3§	+6§	+20§
Year of birth (mean)	1962	1965	1979
Age (mean)	39.6	42.4	32.1
Total sample size (n)	1464	2469	537
Total prevalence (%)	54.8	58.2	75.0
<b>Overall</b>			
Year started in elementary school (mean)			
No. of years since independence	+1§	+8§	+18§
Year of birth (mean)	1960	1967	1977
Age (mean)	41.3	40.1	33.4
Total sample size (n)	2943	4938	1074
Total prevalence (%)	47.8	53.4	75.3

SCORM: Singapore Cohort of Risk factors for Myopia; STARS: Strabismus, Amblyopia and Refractive Error in Singaporean Children; GUSTO: Growing Up in Singapore Towards Healthy Outcomes

\*Saw SM, Tong L, Chua WH, Chia KS, Koh D, Tan DT, et al. Incidence and progression of myopia in Singaporean school children. *Invest. Ophthalmol Vis Sci* 2005;46:51-7. Samarawickrama C, Mitchell P, Tong L, Gazzard G, Lim L, Wong TY, et al. Myopia-related optic disc and retinal changes in adolescent children from Singapore. *Ophthalmology* 2011;118:2050-7.

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§'+ ' indicates years after independence.

### Statistical Analyses

The prevalence of myopia was calculated separately in males and females. Based on the assumption that people start their elementary school education from 6 years of age in Singapore (on average), the year parents commenced elementary school was calculated using their year of birth. The prevalence of myopia according to the year participants started elementary school was calculated and the statistical significance of the trend was examined using the chi-square test. Statistical analysis was conducted using Stata version 14 (StataCorp LP, TX, USA).

### Results

The prevalence of parental myopia in SCORM, STARS, and GUSTO and other related details are shown in Table 2. The prevalence of parental myopia peaked over time with estimates of 47.8%, 53.4% and 75.3% in parents whose elementary school began in year 1966 in SCORM, 1973 in STARS, and 1983 in GUSTO (born in 1960, 1967, and 1975), respectively. The mean age of these parents at the time of data collection was  $41.3 \pm 5.3$ ,  $40.1 \pm 3.2$ , and  $33.4 \pm 5.5$  years. The prevalence of myopia in parents who started/attended school before the 1980s was significantly lower (47.8% in 1966 in SCORM, 53.4% in 1973 in STARS), compared to those who attended school later (75.3% in 1983 in GUSTO).

Table 3 shows an evidence-based survey of myopia prevalence in Chinese adults who were born during the 1920s to 1990s. The myopia prevalence of Chinese adults (aged 40 to 81 years) from the TPS whose elementary school began from the year 1928 to 1958 (born in 1922 to 1952) were 36.4% in those who began school in year 1928, 30.0% in 1938, 26.4% in 1948, 48.7% in 1958. The myopia prevalence in Chinese adults (aged 65 to 80 years) from SLAS were 39.4% in those who began elementary school in year 1934 (born in 1928) and 31.5% in year 1939 (born in 1933). The prevalence of myopia in Chinese adults (aged 40 to 80 years) from the SCES whose elementary school began from the years 1942 to 1972 (born in 1936 to 1966) were 33% in those who began school in year 1942, 32.5% in 1946, 39.4% in 1962, and 52% in 1972, showing a gradual increase over time. Their mean age at the time of data collection was 75.2, 64.4, 54.7, and 47.6 years, respectively. The prevalence of myopia in women was, 30.6% in those who began school in year 1942 and 28.8% in 1952; till 1962, prevalence of myopia in females was lower than men (34.7% in 1942 and 35.9% in 1962). After 1962, prevalence of myopia in females was 40.8% in 1962 and 56.3% in 1972, higher than the prevalence in men with 37.6% in those who began school in year 1962 and 47.5% in 1972 in SCES. Prevalence of myopia in Chinese teens and enrolled young adult military conscripts adults (aged

Table 3. Evidence-based Survey of Myopia Prevalence<sup>1</sup> in Chinese Adults in Singapore

Study	TPS*	SLAS*	TPS*	SLAS*	SCES*	TPS*	SCES*	TPS*	SCES*	SCES*	Military Conscripts Study <sup>s</sup>	
Men												
Year started in elementary school (mean)	1928	-	1938	-	1942	1948	1952	1958	1962	1972	1982	1995
No. of years since independence <sup>§</sup>	-37	-	-27	-	-23	-17	-13	-7	-3	+7	+17	+30
Birth year (mean)	1922	-	1932	-	1936	1942	1946	1952	1956	1966	1976	1989
Age at recruitment (range/mean)	70-	-	60 – 69	-	70- (74.9)	50 – 59	60 – 69 (64.3)	40 – 49	50 – 59 (54.8)	40 – 49 (47.6)	16 – 25 (19.5)	17 – 29 (19.8)
Total sample size (n)	104	-	157	-	310	115	454	124	495	346	12,370	20,004
Total prevalence (%)	31.7	-	29.2	-	34.7	25.2	35.9	45.2	37.6	47.5	82.2	85.9
Women												
Year started in elementary school (mean)	1928	-	1938	-	1942	1948	1952	1958	1962	1972	-	-
No. of years since independence <sup>§</sup>	-37	-	-27	-	-23	-27	-13	-7	-3	+7	-	-
Birth year (mean)	1922	-	1932	-	1936	1942	1946	1952	1956	1966	-	-
Age (range/mean)	70-	-	60 – 69	-	70- (75.6)	60 – 69	60 – 69 (64.5)	40 – 49	50 – 59 (54.7)	40 – 49 (47.6)	-	-
Total sample size (n)	124	-	150	-	279	188	409	151	598	360	-	-
Total prevalence (%)	40.3	-	30.0	-	30.6	27.1	28.8	51.7	40.8	56.3	-	-
Overall												
Year started in elementary school (mean)	1928	1934	1938	1939	1942	1948	1952	1958	1962	1972	-	-
No. of years since independence <sup>§</sup>	-37	-31	-27	-26	-23	-27	-13	-7	-3	+7	-	-
Birth year (mean)	1922	1928	1932	1933	1936	1942	1946	1952	1956	1966	-	-
Age (range/mean)	70-	75-	60 – 69	65 – 75	70- (75.2)	50 – 59	60 – 69 (64.4)	40 – 49	50 – 59 (54.7)	40 – 9 (47.6)	-	-
Total sample size (n)	228	-	307	-	589	303	863	275	1093	706	-	-
Total prevalence (%)	36.4	39.7	30.0	31.5	33.0	26.4	32.5	48.7	39.4	52.0	-	-

SCES: Singapore Chinese Eye Study; SLAS: Singapore Longitudinal Aging Study; TPS: Tanjong Pagar Study

\*Wong TY, Foster PJ, Hee J, Ng TP, Tielsch JM, Chew SJ, et al. Prevalence and risk factors for refractive errors in adult Chinese in Singapore. *Invest. Ophthalmol Vis Sci* 2000;41:2486-94.†Tan CS, Chan YH, Wong TY, Gazzard G, Niti M, Ng TP, et al. Prevalence and risk factors for refractive errors and ocular biometry parameters in an elderly Asian population: the Singapore Longitudinal Aging Study (SLAS). *Eye* 2011;25:1294-301.‡Pan CW, Zheng YF, Anuar AR, Chew M, Gazzard G, Aung T, et al. Prevalence of refractive errors in a multiethnic Asian population: the Singapore epidemiology of eye disease study. *Invest. Ophthalmol Vis Sci* 2013;54:2590-8.§Koh V, Yang A, Saw SM, Chan YH, Lin ST, Tan MM, et al. Differences in prevalence of refractive errors in young Asian males in Singapore between 1996-1997 and 2009-2010. *Ophthalmic Epidemiol* 2014;21:247-55.

¶Methods of diagnosis of myopia: non-cycloplegic auto-refraction (spherical equivalent &lt;-0.5 D).

\*‘-’ indicates years before independence and ‘+’ indicates years after independence.



16 to 29 years) whose elementary school began in 1982 to 1995 (born in 1976 to 1989) were over 80%, roughly twice as high as participants who started schooling before the 1980s in SCES and TPS. The prevalence of myopia further increased slightly from 82.2% ( $n = 12,370$ ) in 1982 to 85.9% in 1995 ( $n = 20,004$ ). The mean age of the participants at the time of data collection was  $19.5 \pm 1.4$  years and  $19.8 \pm 1.2$  years, respectively.

Figure 1 shows the change in myopia prevalence in Chinese male adults as a function of “mean year elementary school begins” from 5 population-based cohorts (TPS, SCES, SCORM, STARS, and GUSTO) and military conscripts. Myopia prevalence data from females was excluded from the figure for better meaningful comparisons with other studies that has only men (like military conscripts). The graph indicates a continuous upward trend over the whole range of years from the 1940s to the 1990s. It shows a gradual increase in myopia prevalence from 30% to 50% during the first 30 years, then an exponential rise in individuals who started schooling after the 1980s (born after 1970), jumping to a high prevalence of over 80% ( $P$  for trend  $< 0.001$ ). The major changes in the education system in Singapore are illustrated chronologically to explore its relationship with the myopia prevalence.<sup>22</sup> The education system was expanded after independence in 1965, and enhanced its competitiveness rapidly after the introduction of the New Education System (NES) in 1978.

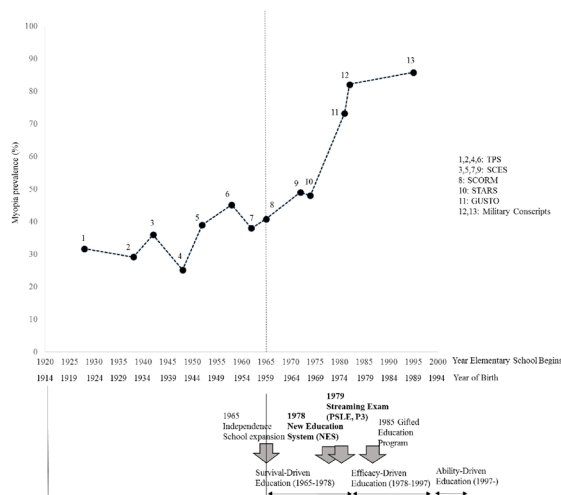


Fig. 1. Myopia prevalence as a function of year elementary school begins for Chinese males from SCES, SCORM, STARS, GUSTO and military conscripts, and education system changes in Singapore (statistical significance of trend;  $X^2 = 2528.672$ ,  $P < 0.001$ ). Survival-driven education (1965-1978): Focus on quantity, expanding schools and aim of higher enrolment rate into educational institutions. Efficacy-driven education (1978-1997): Focus on quality efficacy, streaming students into different levels of classes for their ability by examination (New Education System). Ability-driven education (1997-ongoing): Focus on students' ability, expanding variations and flexible choices according to students' differences in ability.

## Discussion

This ecologic study shows that prevalence of myopia may be increasing in Singapore in persons who started schooling from 1928 to 1995 (year of birth 1922 to 1989), with a secular upward trend and a rapid increase in persons who began schooling after the 1980s (year of birth after 1970). Ecologic studies may provide interesting observational trend data of both exposure and disease. This ecologic study may confirm findings from prior cohort studies of the environmental risk factors for myopia and the effect of the environment on secular trends.

Similar to this study's result, an upward secular trend has been seen in other countries. In the United States' national survey NHANES, myopia prevalence in persons aged 12 to 54 years was significantly higher in 1999 to 2004 (41.6%,  $n = 9609$ ) than in 1971 to 1972 (25%,  $n = 5282$ ).<sup>8</sup> In the Israeli study that examined 919,929 security service candidates aged 16 to 22 years, myopia prevalence rose from 20.3% in 1990 to 28.3% in 2002.<sup>9</sup> In other observational studies, the rapid increase of myopia prevalence in the 20<sup>th</sup> century was first noted in Eskimos in North America as the population moved into settlements. While no cases of myopia were recorded in 1947, 4.7% of adults and 16.6% of children had myopia in 1962 in Eskimos.<sup>23</sup> In Singapore, all the major races (Chinese, Indians, and Malays) experienced dramatic growth in myopia prevalence roughly in parallel with approximately 50% to 85%, 30% to 75%, 25% to 70%, respectively, between 1987 and 2010.<sup>24,25</sup> In the Chinese population, a Taiwanese study examined 300 randomly selected students for each age group from 7 to 18 years between 1983 and 2000, and found the dramatic upward trend in myopia prevalence, from 5.8% to 21% among 7 year olds, from 36.7% to 61% among 12 year olds, and from 64.2% to 81% among 15 year olds.<sup>2</sup> The Beijing Childhood Eye Study examined 15,066 children aged from 7 to 18 years in 2008 and found that prevalence of myopia of  $< -1.00$  D increased from 9.7% in 7 year olds to 74.2% in 17-18 year olds. The latter figure was already higher than the prevalence in elderly Beijing Eye study population 10 years before, which indicates an ongoing myopic shift in the young generation and prognosticates an increase in myopia prevalence in the future adult population in mainland China.<sup>26</sup> In other meta-analysis, the study including 50 population-based studies with 215,672 subjects aged 0 to 96 years reporting the prevalence of myopia from 16 Asian countries found that the upward trend for both age and year of birth, 28.2% with 60 to 69 years old to 47.3% with 20 to 29 years old, 23% with people born in 1960 to 1969 to 39.9% born in 1920 to 1929.<sup>27</sup> The meta-analysis including 145 studies covering 2.1 million people from all over the world estimated significant increase in prevalence globally, from 22.9% in 2000 to 49.8% in 2050.<sup>28</sup>

Worldwide myopia prevalence is increasing, which should be related to environmental factors. The environmental factors for myopia are near-work and lack of outdoor time.<sup>29-32</sup> In adult studies of myopia, it is difficult to obtain near-work activity prior to the onset of childhood myopia and often the final level of education attained is the best surrogate.<sup>33</sup> The increased myopia prevalence in the 20<sup>th</sup> century might be associated with increasing intensive education, mediated by more near-work and lifestyle changes with reduced outdoor time.<sup>29-32</sup>

Several studies investigated increasing myopia prevalence and the relationship between myopia prevalence and education systems. For instance, the Chinese study examined 8267 children aged 3 to 10 in 2013 in Shanghai, and found that myopia prevalence increased from 1.78% in 3-year-olds to 52.2% in 10-year-olds, which was statistically associated with attending elite “high-level” school.<sup>34</sup> The Korean National Health and Nutrition Examination Survey 2008-2011 examined 23,392 people aged 20+ years by auto-refraction, and found that myopia prevalence in the younger generation (78.9% in 20 to 29 years old, 60.7% in 40 to 49 years old) was much higher than the older generation (16.1% in 60 to 69 years old), which was associated with an increased education level. The change may be related to the rapid economic development of Korea, and with the accompanying transformation in education, high level of education (high school or university graduate) increased sharply from 16.2% to 96.9% over 40 years.<sup>35</sup> The Tajimi study that examined a random sample of 3021 Japanese aged 40 years or older found that the prevalence of myopia decreased with increasing age from 70.3% in 40 years to 13.5% in 80 years, and suggested that the decrease may reflect a rapid economic development and education expansion after the end of the Second World War in 1945.<sup>36</sup>

In Singapore, between 1819 and 1963, the education system was modelled after the British system. Immediately following independence in 1965, major reforms—the so-called “Survival-Driven Education”—focusing on quantity of education were implemented. The NES was introduced in 1978 to allow pupils to study at their pace, more suited for their ability. The Primary School Leaving Examination at 12 years and primary streaming exam for Primary 3 students, were used to channel students into different level of classes, and had begun in 1978 and 1979, respectively. In addition, in 1984, the ‘Gifted Education Programme’ commenced, in which very highly performing students were channelled into a special programme with extra enrichment classes. A large proportion of students are engaged in extra academic lessons called “tuition”. The change in the education system with more intensive schooling since 1978, may have led to the increasing prevalence of myopia in Singapore.<sup>21</sup>

The strength of the current study is that the results

presented here are based on population-based data with large sample sizes and reasonable response rates (SCORM, STARS and GUSTO),<sup>13-18</sup> which include over 7 decades of data of persons who entered schools in different calendar years. All participants were of the same race (Chinese) which is advantageous in avoiding ethnic variation.

There were also some limitations. The most important limitation is that this is an ecologic study with only observation of myopia over time and changes in the schooling system over time.

In addition, as this study is an ecological study, ecological fallacy may be considered. The correlation of exposure and disease was shown only at the group level but not at the individual level. Causality cannot be inferred. Education and myopia development should have various confounders. In addition to changes in education system, many other environmental factors such as changes in socioeconomic status, changes in reduced outdoor life style, increased near-work with electronic gadgets such as handphones and computers, or increased crowded urban spaces may also have contributed to this increase.

Second, the heterogeneity between the studies should be noted. The method of myopia assessment is different between studies in that it is based on self-report in STARS, SCORM and GUSTO, and based on non-cycloplegic auto-refraction in the others. Self-reporting may have biased the results as participants may be mistaken or misremember the information. According to the validity of self-reporting myopia prevalence in previous studies, accuracy is different between the asking methods. The direct asking method of “Are you myopic?” (like SCORM) showed the sensitivity and specificity with 0.54 and 0.83, while the indirect method using a series of questions on the use of eyeglasses and age at first dispensing (like STARS and GUSTO) showed with 0.76 and 0.74.<sup>37</sup> Examining prescribed distance glasses like GUSTO showed a good sensitivity (80%) and specificity (89%).<sup>38</sup> The Singapore Malay Eye Study (population-based, cross-sectional study), examined 2912 adults aged 40 to 80 years, and found that people with uncorrected myopia who do not wear spectacles was 4.5%.<sup>39</sup> We project that the rates of self-reported myopia in our study may be underestimated by approximately 4% and thus the true myopia rates are slightly higher. Parents who participated in the study might be more concerned about myopia, more affluent, or closer to the clinical sites, which may also have introduced a selection bias. The enrolment strategy of children’s study, such as 3 school-based (2 ordinary schools from eastern and 1 from northern provinces) design for SCORM, 2 hospital-based (maternity units) for GUSTO, and door-to-door recruitment from southwest provinces for STARS, may not have provided a true representation of the entire population and may have led to either an over- or

underestimation of prevalence.

Age is a well known factor affecting the prevalence of refractive errors. While parental age of paediatric cohorts were approximately the same, age in the adult cohorts varied greatly from the teens in military conscripts to 40 to 80 years in SCES and TPS cohorts. Since myopia may progress till 25 years, some of the young military conscripts may still become myopic after 16 years. Nuclear cataracts which is age-related may cause index myopia in later life, as increasing nuclear sclerosis of the lens with age leads to a myopic shift in refractive status.<sup>40</sup> Thus, myopia prevalence in these conscripts may even be higher than the published estimates, compared with older adults in SCES and TPS. This may be especially so given the exponential rise in myopia prevalence in persons who began schooling after the 1980s (born after the 1970s).

## Conclusion

This ecologic study showed a secular upward trend in myopia prevalence in Chinese adults who started elementary school from 1928 to 1995 (born in 1922-1989), in particular, an exponential rise in prevalence in persons who started elementary school after the 1980s (born after 1970), which may be related to increasing education after independence and specifically to the enhanced competition introduced by NES in 1978. Further population-based cohort studies will be required to identify the association at the individual level since this ecological study shows the association only at a group level. From the perspective of public health policies to prevent myopia, children should not be given excessive schooling demands. Policymakers, parents, and education experts should be aware of the associations of intensive schooling with myopia.

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## Predicting Pneumonia in Acute Ischaemic Stroke: Comparison of Five Prediction Scoring Models

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### Abstract

**Introduction:** Although pneumonia is a major complication after acute ischaemic stroke (AIS), pneumonia prediction scores have not been extensively validated. This study aimed to compare the discrimination performance of 5 pneumonia prediction scores in AIS patients. **Materials and Methods:** We retrospectively reviewed all consecutive adult AIS patients whom presented to our emergency department within 4.5 hours of symptom-onset between January 2012 and February 2015. Diagnosis had to be made by a neurologist and infarcts confirmed by neuroimaging. We excluded patients with pneumonia on presentation. Pneumonia predictors were based on the 5 prediction scoring models: Kwon's score, Chumbler's score, Acute Ischaemic Stroke-Associated Pneumonia Score (AIS-APS), A<sup>2</sup>DS<sup>2</sup> score and ISAN score. The definition of stroke-associated pneumonia was based on the criteria by the Pneumonia in Stroke Consensus Group. Analysis using area under receiver operating characteristics curve (AUROC) was performed. **Results:** Forty (5.5%) out of 731 patients analysed had stroke-associated pneumonia (SAP). A<sup>2</sup>DS<sup>2</sup> score had the highest discrimination capacity (AUROC 0.88; 95% CI, 0.84 to 0.92), followed by AIS-APS (AUROC 0.87; 95% CI, 0.83 to 0.91), Kwon's score (AUROC 0.86; 95% CI, 0.82 to 0.92), Prestroke Independence, Sex, Age and National Institutes of Health Stroke Scale (ISAN) score (AUROC 0.85; 95% CI, 0.80 to 0.90) and Chumbler's score (AUROC 0.79; 95% CI, 0.74 to 0.84). However, there was no statistical difference of discrimination capacity among A<sup>2</sup>DS<sup>2</sup> score, AIS-APS and Kwon's score. **Conclusion:** A<sup>2</sup>DS<sup>2</sup>, AIS-APS and Kwon's scores performed comparably in discriminating SAP in AIS patients.

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**Key words:** Prognosis, Epidemiology, Retrospective studies, Validation, Singapore, Brain ischaemia/complications

### Introduction

Pneumonia is a major cause of mortality, prolonged hospital stay and poor functional outcome when occurring immediately after acute ischaemic stroke (AIS).<sup>1-3</sup> Pneumonia is also common poststroke, with incidence ranging between 9% to 56%.<sup>3-5</sup> Although some pharmacological and novel non-pharmacological interventions have been shown to reduce the incidence of pneumonia in post-AIS patients,<sup>6-12</sup> universal implementation of preventive measures in all AIS patients has not consistently improved neurological outcome or mortality.<sup>13</sup> A postulated reason for the failure of pneumonia prevention intervention was that the majority

of stroke patients recruited in studies were at low risk of developing pneumonia.<sup>13,14</sup> Therefore, a reliable clinical prediction tool to identify patients at increased risk of developing pneumonia after AIS is needed in order to optimise selection of patients for early pneumonia preventive interventions.

Various different clinical factors have been shown to be associated with pneumonia after AIS.<sup>15-19</sup> Six pneumonia prediction scores have also been derived from different post-AIS populations. One score was exclusively derived from neurological intensive care patients<sup>20</sup> and was considered not applicable to our study population. The 5 pneumonia

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prediction scores evaluated in this study were Kwon's score,<sup>21</sup> Chumbler's score,<sup>22</sup> A<sup>2</sup>DS<sup>2</sup> score,<sup>23</sup> Acute Ischaemic Stroke-Associated Pneumonia Score (AIS-APS)<sup>24</sup> and the Prestroke Independence, Sex, Age and National Institutes of Health Stroke Scale (ISAN) score.<sup>25</sup> Although these scores have been previously separately validated,<sup>24,26,27</sup> they have not been subjected to head-to-head comparison within a single patient population, hence it is still uncertain which score is ideal at identifying patients at high risk of developing pneumonia. Moreover, the newly developed ISAN score<sup>25</sup> has never been externally validated in an Asian population.

The definition of stroke-associated pneumonia (SAP) used in the derivation of the pneumonia prediction scores has been inconsistent,<sup>4</sup> resulting in variability of the predictive capability of these scores. To standardise the diagnostic criteria for pneumonia complicating stroke, a new operational definition of SAP was published by the Pneumonia in Stroke Consensus (PISCES) Group.<sup>28</sup> Recommendations for the definitions of hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) were also made.<sup>28</sup> In view of the changes in pneumonia definitions, there is a need to validate the predictive capabilities of existing pneumonia prediction scores with the new criteria.

The primary aim of this study was to determine the pneumonia prediction score with the highest discrimination capacity for SAP in AIS patients, using the new operational criteria of SAP recommended by PISCES. The secondary aim was to evaluate the incidence of SAP, HAP and VAP using the new definitions.

## Materials and Methods

### *Participants*

This study was performed in adults, 21 years or older, at a single acute tertiary care teaching hospital (Tan Tock Seng Hospital) in Singapore. Our hospital consists of 1200-beds and has 400 emergency attendances per day.<sup>29</sup> Our hospital is also Joint Commission International-accredited and houses a comprehensive stroke unit with a 24 hours in-house Neurology stroke service.

Participants for this study were obtained from an AIS registry between January 2012 and February 2015. The hospital prospectively maintains a registry of all consecutive AIS patients who present to the emergency department (ED) and whom required emergent evaluation by Neurology stroke service for suitability of thrombolysis. In clinical practice, patients who present beyond 4.5 hours were considered as "late" as they no longer qualify for intravenous thrombolysis. Hence, we used the 4.5 hours time cutoff in this study to ensure that the pneumonia occurring was

a direct consequence of AIS. In addition, patients in the registry had to have radiological evidence of infarction<sup>30</sup> during the course of their hospitalisation, either by computed tomography (CT) of the head or magnetic resonance imaging (MRI). Patients with haemorrhagic strokes, as diagnosed via CT scan of the head performed in the ED as part of the hospital stroke protocol, were excluded from the registry. In addition, patients who were diagnosed with a stroke mimic, who suffered AIS while in hospital for other reasons, or who presented to the ED more than 4.5 hours from onset of symptoms were also excluded from the registry.

### *Prediction Risk Scores Variables*

Medical records at presentation to ED were reviewed to collect the clinical parameters required for scoring each pneumonia prediction score (Table 1).<sup>21-24</sup> The variables of atrial fibrillation (AF), dysphagia status and mechanical ventilation status were retrieved from medical records during the course of hospitalisation. AF status was based on electrocardiographs or continuous cardiac monitoring (telemetry or Holter) reports obtained prior to the diagnosis of pneumonia. Dysphagia status was recorded by a trained nursing staff from the stroke unit or by a speech therapist as part of the hospital stroke protocol. Mechanical ventilation status during hospitalisation was considered only up to the point of diagnosis of pneumonia. Mechanical ventilation is considered as a separate independent variable in this study and was not considered as a dysphagia risk factor.

### *Outcome Measures*

We used "definite" SAP<sup>28</sup> as the primary outcome measure of our study. "Definite" SAP required all modified Communicable Diseases Centre (CDC) criteria to be met and diagnostic chest X-ray (CXR) changes on at least 1 CXR (Table 2).<sup>28</sup> The secondary outcomes of HAP and VAP were also based on recommendations by PISCES Group.<sup>28</sup> All clinical notes, laboratory investigations and chest radiographs were reviewed to determine if the diagnostic criteria for each of the subtypes of pneumonias were fulfilled. This was conducted blinded to the clinical predictors by a single investigator (S Phua). Only the first episode of pneumonia in the course of hospitalisation was included in this analysis.

We excluded patients who were already diagnosed with pneumonia on presentation at the ED. This was because it was uncertain if the pneumonia preceded the onset of stroke and these patients could not have had their pneumonia prevented anyway. We did not exclude any patients who were intubated for neurologic reasons. Our hospital institutional review board approved this study and waiver of informed consent was approved in view of the retrospective nature of the study.

Table 1. Clinical Variables and Point Allocations of Each Scoring Algorithm

Scoring Algorithm	Clinical Variable	Assigned Points
Kwon's score	NIHSS $\geq 11$	1
	Age $\geq 65$ years	1
	Male	1
	Presence of mechanical ventilation	1
	Presence of dysphagia	1
Chumbler's score	Age $> 70$ years	1
	Abnormal swallowing test	1
	Admission NIHSS Score $\geq 2$	1
	Found down at symptom onset	1
A <sup>2</sup> DS <sup>2</sup> score	Past medical history of pneumonia	1
	Age $\geq 75$ years	1
	Atrial fibrillation	1
	Dysphagia	2
	Male	1
AIS-APS	NIHSS	
	0 – 4	0
	5 – 15	3
	$\geq 16$	5
	Age in years	
	$\leq 59$	0
	60 – 69	2
	70 – 79	5
	$\geq 80$	7
	Medical history/comorbidity	
	Atrial fibrillation	1
	Congestive heart failure	3
	Chronic obstructive pulmonary disease	3
	Current smoking	1
	Prestroke dependence (mRS $\geq 3$ )	2
	Admission NIHSS	
	0 – 4	0
	5 – 9	2
	10 – 15	5
	$\geq 16$	8
	Admission GCS score	
	9 – 15	0
	3 – 8	3
	Dysphagia	3

AIS-APS: Acute ischaemic stroke-associated pneumonia score; GCS: Glasgow Coma Scale; ISAN: Prestroke Independence, Sex, Age and National Institutes of Health Stroke Scale; mRS: Modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; OCSP: Oxfordshire Community Stroke Project

Table 1. Clinical Variables and Point Allocations of Each Scoring Algorithm (Cont'd)

Scoring Algorithm	Clinical Variable	Assigned Points
AIS-APS	OCSP subtype	
	Lacunar infarction	0
	Partial anterior circulation infarction	0
	Total anterior circulation infarction	2
	Posterior circulation infarction	2
	Admission glucose level $\geq 11.1$ mmol/L	2
ISAN score	Age in years	
	$< 60$	0
	60 – 69	3
	70 – 79	4
	80 – 89	6
	90 and above	8
	Sex	
	Female	0
	Male	1
	NIHSS on admission	
	0 – 4	0
	5 – 15	4
	16 – 20	8
	21 and above	10
	Prestroke mRS	
	Independent (0 – 1)	0
	Not independent (2 – 5)	2

AIS-APS: Acute ischaemic stroke-associated pneumonia score; GCS: Glasgow Coma Scale; ISAN: Prestroke Independence, Sex, Age and National Institutes of Health Stroke Scale; mRS: Modified Rankin Scale; NIHSS: National Institutes of Health Stroke Scale; OCSP: Oxfordshire Community Stroke Project

### Statistical Analysis

Demographic and clinical characteristics of the study population were summarised using appropriate descriptive statistics. Risk scores and the predicted probability of pneumonia for each patient were calculated according to the 5 risk prediction models. To assess the predictive performance of each risk prediction model, a univariate logistic regression model on pneumonia were fitted by entering each risk score as a continuous variable. The model fit was checked using Hosmer-Lemeshow goodness-of-fit statistics and non-parametric calibration curves were estimated using 1000 bootstrap resampling scheme. Receiver operating characteristics (ROC) analysis was done for performance comparison. Discrimination was assessed with the area under the ROC curve (AUROC) for each prediction model; 95% confidence intervals around these AUROCs were estimated. These AUROCs were then compared pair-wise with each other using DeLong's

non-parametric test to compare 2 correlated ROC curves. No formal correction was made for multiple comparisons.

In a one-sided test comparing the AUROC of a reference test to a proposed test for discrete response data using a z-test approximation, a sample size of 40 cases and a sample size of 600 controls achieves 80% power at the 5% significance level, when the AUROC for both models under the null hypothesis is 0.75 (hypothesised from Chumber's score<sup>22</sup>) and the AUROC of the proposed model under the alternative hypothesis is 0.85 (hypothesised from A<sup>2</sup>DS<sup>2</sup> score<sup>23</sup>). This assumed that the correlation between the model scores for cases is 0.9 and the correlation between controls is 0.6. Because a study population of approximately 640 patients was required, we estimated that a review of 3 years duration of our stroke registry was needed.

The optimal cutoff for each scoring algorithm was

Table 2. Definitions of Poststroke Pneumonia

Criteria	Definition
Pneumonia*	At least 1 of the following: -Fever (>38°C) with no other recognised cause -Leukopaenia (<4000 WBC/mm <sup>3</sup> ) or leukocytosis (>12,000 WBC/mm <sup>3</sup> ) -For adults ≥70 years old, altered mental status with no other recognised cause And at least 2 of the following: -New onset of purulent sputum, or change in character of sputum over a 24 hour period, or increased respiratory secretions, or increased suctioning requirements -New onset or worsening cough, or dyspnea, or tachypnea (respiratory rate >25/min) -Rales, crackles, or bronchial breath sounds -Worsening gas exchange (eg, O <sub>2</sub> desaturation [eg, PaO <sub>2</sub> /FiO <sub>2</sub> ≤240], increased oxygen requirements) And ≥2 serial chest radiographs with at least 1 of the following: -New or progressive and persistent infiltrate, consolidation, or cavitation
SAP	Fulfills the above definition of pneumonia And occurs within and including the first 7 days after onset of stroke in non-ventilated patients
HAP	Fulfills the above definition of pneumonia And occurs after 7 days after onset of stroke in non-ventilated patients
VAP	Fulfills the above definition of pneumonia And occurs more than 48 hours after initiation of mechanical ventilation

CXR: Chest X-ray; FiO<sub>2</sub>: Fraction of inspired oxygen; HAP: Hospital-acquired pneumonia; PaO<sub>2</sub>: Partial pressure oxygen; SAP: Stroke-associated pneumonia; VAP: Ventilator-associated pneumonia; WBC: White blood cell

\*In patients without underlying pulmonary or cardiac disease, 1 definitive chest radiograph is acceptable.

estimated from the ROC curves and was defined as the point with the maximum sum of sensitivity and specificity. For these cutoffs of each scoring algorithm, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were estimated with their corresponding 95% confidence intervals (CI). The same analyses were done separately for the all pneumonia cases and different subtypes of pneumonia. All statistical analyses were performed in R version 3.1.2. Tests were two-sided and statistical significance was set at 5% level.

## Results

A total of 746 patients were identified from our AIS registry between the period of January 2012 and February 2015. Fifteen patients were diagnosed with pneumonia on presentation, hence 731 patients were included in the final

Table 3. Baseline Characteristics of Participants on Admission

	Study Cohort (n = 731)
Demographics	
Age group, n (%), year	
<60	215 (29.4)
60 – 69	182 (24.9)
70 – 79	192 (26.3)
≥80	142 (19.4)
Male sex, n (%)	442 (60.5)
Vascular risk factors, n (%)	
Current smokers	237 (32.4)
Atrial fibrillation	229 (31.3)
Congestive cardiac failure	61 (8.3)
Admission NIHSS score, median (IQR)	6 (2 – 16)
Admission Glasgow Coma Scale score, n (%)	
13 – 15	551 (75.4)
9 – 12	150 (20.5)
3 – 8	30 (4.1)
Admission glucose ≥11.1, n (%)	129 (17.6)
Symptom of dysphagia, n (%)	344 (47.1)
Mechanical ventilation during admission, n (%)	44 (6.0)
OCSF subtype, n (%)	
Partial anterior circulation infarct	392 (53.6)
Total anterior circulation infarct	32 (4.4)
Lacunar infarction	218 (29.8)
Posterior circulation infarct	89 (12.2)
Pneumonia classification, n (%)	
Stroke-associated pneumonia	40 (5.5)
Hospital-acquired pneumonia	29 (3.9)
Ventilator-associated pneumonia	10 (1.4)

IQR: Interquartile range; NIHSS: National Institutes of Health Stroke Scale; OCSF: Oxfordshire Community Stroke Project



Table 4. Clinical Criteria Fulfilled by Stroke-Associated Pneumonia Patients (n = 40)

	No. of Patients (% of SAP Patients)*
At least 1 of the following:	
-Fever ( $>38^{\circ}\text{C}$ ) with no other recognised cause	34 (85.0%)
-Leukopaenia ( $<4000\text{ WBC/mm}^3$ ) or leukocytosis ( $>12\,000\text{ WBC/mm}^3$ )	27 (67.5%)
-For adults $\geq 70$ years old, altered mental status with no other recognised cause	3 (7.5%)
And at least 2 of the following:	
-New onset of purulent sputum, or change in character of sputum over a 24 hour period, or increased respiratory secretions, or increased suctioning requirements	29 (72.5%)
-New onset or worsening cough, or dyspnea, or tachypnea (respiratory rate $>25/\text{min}$ )	28 (70.0%)
-Rales, crackles, or bronchial breath sounds	9 (22.5%)
-Worsening gas exchange	17 (42.5%)
And $\geq 2$ serial chest radiographs† with at least 1 of the following:	
-New or progressive and persistent infiltrate, consolidation, or cavitation	40 (100%)

SAP: Stroke-associated pneumonia; WBC: White blood cells

\*The number of SAP patients  $\geq 70$  years old = 30 (75% of SAP patients).

†In patients without underlying pulmonary or cardiac disease, 1 definitive chest radiograph is acceptable.

analysis. Characteristics of included patients are summarised in Table 3. Using the PISCES definition, 40 (5.5%) patients were diagnosed with SAP, and 29 (3.9%) with HAP and 10 (1.4%) with VAP. A total of 79 (10.8%) patients were diagnosed with any form of pneumonia. The median onset of SAP was on day 4. A summary of the clinical criteria fulfilled by SAP patients is shown in Table 4.

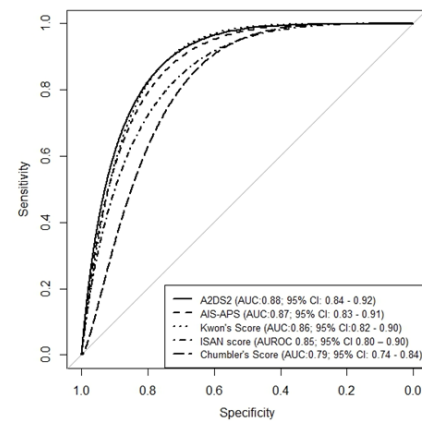


Fig. 1. Receiver operating characteristics curve for stroke-associated pneumonia. The plot of sensitivity (y-axis) versus decremental specificity (x-axis) demonstrates A<sup>2</sup>DS<sup>2</sup> with maximal area under curve. AIS-APS indicates acute ischaemic stroke-associated pneumonia score. AUC: Area under curve; CI: Confidence interval; ISAN: Prestroke Independence, Sex, Age and National Institutes of Health Stroke Scale; ROC: Receiver operating characteristics.

A<sup>2</sup>DS<sup>2</sup> score had the highest discrimination capacity for SAP (AUROC 0.88; 95% CI, 0.84 to 0.92), followed by AIS-APS (AUROC 0.87; 95% CI, 0.83 to 0.91), Kwon's score (AUROC 0.86; 95% CI, 0.82 to 0.92), ISAN score (AUROC 0.85; 95% CI, 0.80 to 0.90), and Chumbler's score (AUROC 0.79; 95% CI, 0.74 to 0.84) (Fig. 1) in decreasing order. A<sup>2</sup>DS<sup>2</sup> score also had the highest discrimination for HAP (AUROC 0.86; 95% CI, 0.80 to 0.93) and any form of pneumonia (AUROC 0.86; 95% CI, 0.82 to 0.90) (Fig. 2) compared to the rest. Although there were only 10 VAP patients, Kwon's score provided the best discrimination for VAP (AUROC 0.94; 95% CI, 0.89 to 0.98) (Fig. 2). However, despite A<sup>2</sup>DS<sup>2</sup> outperforming the other scores, there was no statistical difference of discriminating capacity for SAP among A<sup>2</sup>DS<sup>2</sup> score, AIS-APS and Kwon's score (Table 5).

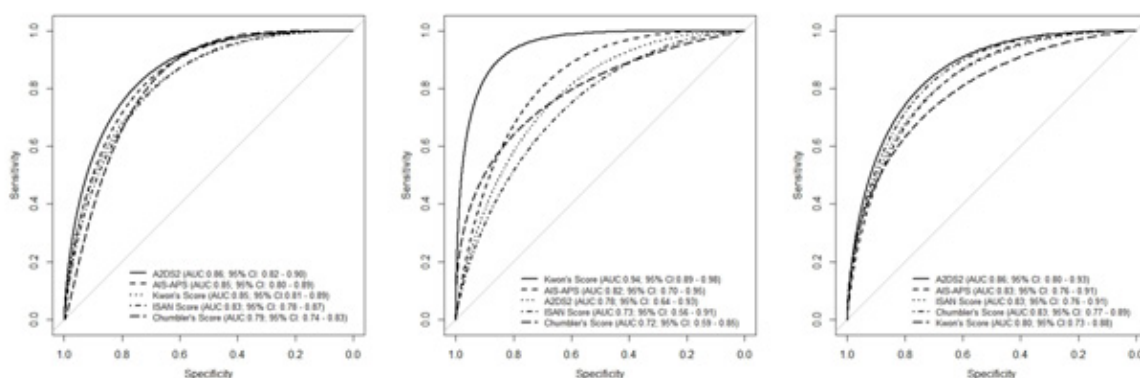


Fig. 2. Receiver operating characteristics curves for all forms of pneumonia (left), ventilator-associated pneumonia (centre) and hospital-acquired pneumonia (right). The plots of sensitivity (y-axis) versus decremental specificity (x-axis) demonstrating maximal area under curve for A<sup>2</sup>DS<sup>2</sup> score for any form of pneumonia (left) and hospital-acquired pneumonia (right). Kwon's score had the maximal area under curve for ventilator-associated pneumonia (centre). AIS-APS: Acute ischaemic stroke-associated pneumonia score; AUC: Area under curve; CI: Confidence interval; ISAN: Prestroke Independence, Sex, Age and National Institutes of Health Stroke Scale; ROC: Receiver operating characteristics.

Table 5. Pair-Wise Comparison of Discrimination Capacity for Stroke-Associated Pneumonia

	$\Delta$ AUROC*	P Value†	$\Delta$ AUROC*	P Value†	$\Delta$ AUROC*	P Value†	$\Delta$ AUROC*	P Value†
Stroke associated pneumonia (n = 40)								
A <sup>2</sup> DS <sup>2</sup> score	Ref.							
AIS-APS	0.011	0.493	Ref.					
Kwon's score	0.025	0.216	0.015	0.526	0.526			
ISAN score	0.033	0.045	0.023	0.173	0.173	0.779	Ref.	
Chumbler's score	0.091	<0.001	0.081	<0.001	<0.001	0.015	0.058	0.049

AIS-APS: Acute ischaemic stroke-associated pneumonia score; AUROC: Area under the receiver operating characteristic curve; ISAN: Prestroke Independence, Sex, Age and National Institutes of Health Stroke Scale

\* $\Delta$ AUROC denotes the difference in AUROC between the reference algorithm indicated and the algorithm listed in each row.

†P values are from DeLong's test for 2 correlated ROC curves.

All scores had similarly high NPV (98% to 100%) but relatively low PPV (9% to 20%). The optimal cutoff scores for SAP, with the maximum sum of sensitivity and specificity, for A<sup>2</sup>DS<sup>2</sup> was 7. The estimated risk from all 4 models showed acceptable agreement with the observed rate of SAP (all non-significant *P* values for Hosmer-Lemeshow test), and A<sup>2</sup>DS<sup>2</sup> provided the best agreement. The calibration curves matched well with AUROC measures for other pneumonia subtypes, Kwon's score being the best risk prediction model for VAP and all 3 other models providing good calibration for HAP (Table 6).

## Discussion

The present study is the first to compare 5 pneumonia scoring models using an AIS patient cohort. A<sup>2</sup>DS<sup>2</sup> score was able to predict SAP with the highest discrimination capacity among all scoring algorithms assessed and also had the best agreement between the predicted and observed rate of SAP. A<sup>2</sup>DS<sup>2</sup> also performed similarly well for HAP and any form of pneumonia, albeit at a different cutoff score. Despite the above, it must be noted that there was no statistical difference of discrimination capacity for SAP among A<sup>2</sup>DS<sup>2</sup> score, AIS-APS and Kwon's score. This

implies that although A<sup>2</sup>DS<sup>2</sup> performed best in our cohort, the differences of discrimination capacity among AIS-APS and Kwon's score were small. Therefore, the choice of which prediction algorithm to use clinically will depend greatly on its ease of use. Among the above 3 similarly performing predictions models, both A<sup>2</sup>DS<sup>2</sup> and Kwon's scores requires only 5 clinical variables while AIS-APS requires 8, therefore possibly favouring the former 2 over the latter in terms of practical utility.

Chumbler's score had the lowest discrimination capacity and was significantly lower compared to all other scores evaluated. The lower discrimination capacity and difference in cutoffs<sup>24</sup> may be due to different methodology used for scoring the risk factors as we used the number of risk factors present instead of the odds ratio of risk factors.<sup>22</sup> ISAN score only performed marginally poorer to A<sup>2</sup>DS<sup>2</sup> score (*P* = 0.045) and was equivalent to AIS-APS and Kwon's score. This is most likely because ISAN score only required 4 variables<sup>25</sup> in its algorithm, less than the other scoring models, contributing to its lower discrimination capacity. In addition, our study provides the first report that ISAN score may not perform as well in an Asian cohort compared to other populations.<sup>27</sup>

Table 6. Performance Statistics for Stroke-Associated Pneumonia

Prediction Model	Cutoff	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)	No. of Cases of SAP Above Cutoff	No. of Patients Above Cutoff	Percentage of Patients Below Cutoff	Hosmer-Lemeshow Statistic (P Value), No. of Groups
A <sup>2</sup> DS <sup>2</sup> score	7	90 (80–97)	75 (71–78)	18 (16–21)	99 (98–100)	36	231	68.4	0.75 (0.999), 10
AIS-APS	11	95 (87–100)	66 (62–69)	15 (13–16)	99 (98–100)	38	294	59.8	5.03 (0.169), 5
Kwon's score	3	92 (82–100)	71 (68–75)	17 (15–19)	99 (98–100)	37	256	65.0	8.60 (0.072), 6
ISAN score	11	83 (70–92)	80 (77–83)	20 (17–23)	98 (97–99)	33	191	73.9	2.39 (0.303), 4
Chumbler's score	2	100 (100–100)	38 (34–41)	9 (8–10)	100 (100–100)	40	484	33.8	3.52 (0.061), 3

AIS-APS: Acute ischaemic stroke-associated pneumonia score; CI: Confidence interval; ISAN: Prestroke Independence, Sex, Age and National Institutes of Health Stroke Scale; PPV: Positive predictive value; NPV: Negative predictive value; SAP: Stroke-associated pneumonia

All scoring algorithms had low PPV for SAP at their respective optimal cutoff scores, indicating that all these scores do not perform well if used to select an at-risk population. For the purpose of identifying high-risk patients, a higher PPV will be required, thereby requiring a higher, but less optimal, cutoff for each score. Despite adjusting the cutoffs to the highest risk group, the highest PPV remains a modest 29.1% (7 out of 24 patients for A<sup>2</sup>DS<sup>2</sup> score at the cutoff of 10). Interestingly, all 4 scoring algorithms had very high NPV (range, 98 to 100%), suggesting that all these scores are better utilised to exclude patients unlikely to develop SAP, rather than to include them. By excluding patients below the optimal cutoff scores, a reduction of approximately 60% to 68% of patients at low risk of pneumonia (using A<sup>2</sup>DS<sup>2</sup> score, AIS-APS or Kwon's score) may be achieved without significantly compromising the number of SAP detected (Table 6). This is very helpful to reduce unnecessary patient recruitment for pneumonia prevention trials.

The discrimination capacity for SAP was higher in our study population compared to previously published data on the same scores.<sup>22-24,31</sup> Possible reasons for higher AUROC results include stricter definition of pneumonia used resulting in less variance in the outcome, different cutoffs for each of the scores used from those previously published,<sup>24</sup> and a more homogenous population studied due to early presentation at the ED.

The low incidence of SAP (5.5%) is an important consideration for future researchers using the new SAP definition. If we included the 15 patients excluded from our study due to the diagnosis of pneumonia on presentation, the incidence of SAP would only be 7.5%. It is to be noted that we used the stricter “definite” SAP definition and not the “probable” SAP as an endpoint in our study as we wanted radiological evidence as proof of pneumonia. The use of the more lenient “probable” SAP may increase the incidence of pneumonia and warrants further investigation. Moreover, the diagnosis of pneumonia before stroke is likely underestimated in a retrospective design, hence the true SAP rates may be higher than 7.5%. Nevertheless, the incidence of any form of pneumonia in our study (10.8%) was comparable to other study cohorts,<sup>3</sup> hence the incidence of “definite” SAP would likely be similar in other populations.

The stroke severity of our study population (median National Institutes of Health Stroke Scale [NIHSS] = 6) was similar to the stroke severity of all reference prediction scores (median NIHSS 4-7).<sup>22-25</sup> This suggests that our study population was representative of a general stroke population and all the prediction scores could be applied to our study cohort. Nevertheless, the stroke severity in our study population was relatively mild, hence the inference of our results in severe strokes is unclear and deserves further evaluation.

The main limitation of our study was the retrospective design. Completeness of chart records and inter-observer variations of the clinical variables could not be ascertained. Incomplete symptomatology clinical records may have underestimated the pneumonia rates. Nevertheless, dysphagia assessment records, temperature records and investigations (blood and radiological) were complete for all patients. Inherent to a retrospective study, judgement error and systematic bias during data retrieval by a single blinded observer may be introduced due to the absence of a second blinded independent observer. However, we attempted to reduce this reporting bias by using objective data when interpreting clinical information as often as possible, such as an independent chest radiograph report. We did not correct for differences in management prior to the diagnosis of pneumonia that could have possibly influenced the development of pneumonia. These potentially included nursing techniques,<sup>6</sup> antibiotics or other medication use.<sup>10,11,32</sup> We also did not collect information with regard to the aetiology of the stroke which may have influenced the incidence of SAP. However, the aim of the study was to use clinical information available on presentation to predict pneumonia development during hospitalisation, hence these clinical factors were not collected. Lastly, as we only included patients who presented within 4.5 hours from onset of stroke to the ED for this study, therefore possibly limiting the generalisability of our results. In the general stroke population, less than half of AIS patients arrive within 4.5 hours from onset of their symptoms to the ED.<sup>33</sup> Therefore, the discrimination capacity of these algorithms in patients who presents late to the hospital remains uncertain.

The main strength of our study was our direct, unbiased and independent comparison of 5 published prediction scores. We only included patients with a short duration from the onset of AIS symptoms ensuring that the occurrence of SAP was a direct consequence of the AIS and not due to other inciting factors, such as prehospital delay for example. We ensured that the diagnosis of SAP for every patient was in accordance to the objective modified criteria established by CDC and recommended by PISCES<sup>28</sup> rather than via documentation of the diagnosis pneumonia in the medical notes. This reduced ambiguity of the diagnosis of SAP, which has been a subject of criticism.<sup>4</sup> We also attempted to reduce biases during our data collection by ensuring that the determination of the status of pneumonia was independent from the retrieval of the clinical predictors.

## Conclusion

In summary, our study demonstrated that A<sup>2</sup>DS<sup>2</sup>, AIS-APS and Kwon's score had comparable discrimination capacity for SAP using the new operational definition in

AIS patients. These scores performed well in excluding AIS patients who are unlikely to develop SAP, hence using these scores may improve patient selection for future pneumonia prevention trials.

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## Return to Work is an Important Therapeutic Goal

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### Introduction

Sickness absence within the Singapore workforce has risen over the past decade. The proportion of employees who took outpatient sick leave rose from 49.3% in 2005 to 60% in 2015, and the proportion that went on hospitalisation leave increased from 4.1% to 6% over the same period.<sup>1,2</sup> Some plausible causes for this upward trend could be our ageing population coupled with an upward shift in the effective retirement age to 65; changing societal and workplace norms for work attendance;<sup>3</sup> and possibly, poor awareness that work is generally beneficial to health as well as recovery from illness or injury.

### Work is Good for Health

There is strong evidence that most work is good for an individual's physical and mental health.<sup>4</sup> It is the usual means for obtaining economic resources to maintain well-being, meets psychosocial needs in our modern society where employment is the norm, and is central to an individual's identity and social worth. A cross-sectional study of the self-reported impact of long-term sickness absence found that it had a negative influence on the financial situation of 81% of respondents, and that more than 60% experienced negative effects on their leisure activities, sleep and psychological well-being.<sup>5</sup> Conversely, there is evidence that job insecurity and unemployment have adverse effects on health, particularly mental health.<sup>6,7</sup>

Sickness absence is associated with increased job loss and unemployment, with a cohort study of 60,000 Finnish workers finding that a high rate of sickness absence increased the odds of job loss among female temporary workers, as well as older permanent workers of both sexes.<sup>8</sup> Another study of over 50,000 Swedish workers showed that the risk of subsequent unemployment increased with both the number of spells and the mean duration of sickness absence.<sup>9</sup> In Singapore, a recent study by the Workplace Safety and Health Institute (WSHI) found that 83.4% of workers who sustained work injuries took more than a month of sick leave, with 24% of them becoming unemployed.<sup>10</sup>

### Preventing Iatrogenic Disability

'Primum non nocere' – first, do no harm. While it is certainly inappropriate for doctors to issue medical certificates (MCs) of durations that are too short for serious illnesses or injuries, we should be equally prudent in not providing longer than necessary medical certification based on a misguided belief that work impedes recovery. On the contrary, over-prescription of time off work may be harmful and could increase a patient's risk of long-term disability. For example, a cohort study of over 7000 French workers observed that the odds of future depression rose as the number of spells of medically certified sickness absence in excess of 7 days increased.<sup>11</sup> In the case of common musculoskeletal conditions, the probability of a worker with back pain ever returning to work diminishes as the duration of sickness absence increases, with a third to half of those still off work at 6 months remaining so at the 1-year mark.<sup>12,13</sup> While some might argue that these reflect a natural sorting according to severity, there is evidence that long periods of withdrawal from work leads to both physical deconditioning and a reduced ability to cope psychosocially.<sup>14</sup>

### Providing Work-Focused Healthcare

Doctors play a key role in helping their patients remain in or return to work, and their advice can have an impact on whether individuals go on medical leave, for how long, and if steps are taken to expedite their return to work. Yet, this does not seem to be well recognised within the Singapore healthcare landscape – tellingly, only 1 of the 16 Clinical Practice Guidelines published by the Ministry of Health over the past 5 years mentions the restoration of occupational function as a treatment objective (MOH CPG 1/2012 on Depression).

We believe that there is potential for doctors to improve return-to-work outcomes in 3 ways. First, clinicians should avoid unhelpful terminologies and therapeutic approaches from the outset. In general, those who receive a diagnosis will develop beliefs about their condition, and patients who

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hold negative illness perceptions are more likely to have slower recovery times and future disability, independent of the initial objective severity of their condition.<sup>15</sup> To minimise such catastrophising, alarming terms such as “disc rupture” and “muscle tear” should be avoided. For the majority of common health problems, we should move from the traditional biomedical model that takes a purely mechanistic view of a broken human body with faults to be fixed, to a biopsychosocial model that aims to also identify and address patients’ perceptions and beliefs, as well as possible obstacles at home or in the workplace that may impede recovery and work rehabilitation.<sup>16</sup> An expectation of early return to work should be encouraged, as there is evidence to suggest that such expectations improve the likelihood of and time to return to work.<sup>17</sup> In this regard, the Royal College of Surgeons of England, and the Royal College of Obstetricians and Gynaecologists have developed and published on their websites useful consensus-based guidelines on the usual timescales for resuming work after common procedures.

This brings us to our second point: individuals do not have to be 100% fit before returning to work. Rather, appropriate work can be therapeutic in recovery and should be viewed as an essential part of rehabilitation.<sup>16</sup> In supporting a patient’s return to work, one should consider the patient’s current and anticipated functional ability vis-à-vis his or her job demands. If there is a mismatch between the individual’s functional ability and job demands, workplace adjustments may be recommended to the employer. Alternatively, should the doctor be unable to ascertain the work environment, he or she can clearly communicate the functional limitations of the individual to the employer (e.g., “unable to perform tasks that involve overhead activities” for a worker recovering from a shoulder problem) to guide the latter on possible adjustments in the context of the individual’s job role. While workplace interventions may seem more relevant to physical conditions, a recent Cochrane review found moderate quality evidence to suggest that adding a work-directed intervention reduces the sickness absence duration of individuals with depression.<sup>18</sup>

Thirdly, Singapore’s current MC-based system of sick certification is unhelpful in facilitating early return to work, as it tends to force doctors to dichotomise patients as being either completely fit or completely unfit for work. Although there is a middle-of-the-road option of certifying an individual as being fit for “light duties”, the usual format of MCs does not aid doctors in communicating their patient’s functional ability and limitations to employers. This has been increasingly recognised by other jurisdictions, with some moving to replace “sick notes” with “fit notes” in recent years.<sup>19</sup> The prescribed structure of such fit notes encourages doctors to explore with patients options for

their prompt return to work, and aids in the transmission of relevant advice to employers. For instance, the recent WSHI study found that 44% of injured workers who subsequently returned to work reported fatigue symptoms, while 39% of them experienced initial difficulty in performing their original work<sup>10</sup>—with appropriate workplace interventions on the advice of doctors (e.g., “phased return to work”), some of these workers may have been able to return to work earlier or increase their likelihood of maintaining lasting return to work despite having residual symptoms.<sup>20</sup>

To strengthen the delivery of work-focused healthcare, Singapore needs doctors who understand the bidirectional relationship between health and work. In this regard, more should be done to train medical students and practising clinicians in occupational medicine; this will also benefit the ongoing total workplace safety and health drive in the country.<sup>21</sup> In the same vein, we should start integrating return-to-work services as a part of mainstream healthcare in tandem with the evolution of Singapore’s regional health systems-based model of care. For example, return-to-work coordinators could be deployed to liaise internally with healthcare professionals and externally with employers to find return to work solutions for patients, with findings from a locally conducted randomised controlled trial supporting this approach as an effective means of improving return-to-work timings among injured workers.<sup>22</sup> As the cadre of doctors with qualifications in occupational medicine grows, restructured hospitals can further enhance their provision of work-focused healthcare by developing referral occupational health clinics to offer specialist fitness for work assessments undertaken by physician-led multidisciplinary teams.

## Conclusion

With Singapore’s re-employment age ceiling being increased to 67 from 1 July 2017 and indications that even this raised age ceiling may be abolished in time, it is imperative for doctors to recognise our role in sustaining this country’s ageing local workforce by keeping them healthy when well and facilitating their early return to work when ill. Through the sum of efforts at the clinician and system levels, we will build a more work-focused healthcare system that benefits individual patients and contributes to overall national resilience.

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## Do Obstetric Patients Opt to Undergo General Anaesthesia to Avoid Being Conscious Despite Safer Alternatives?

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### Abstract

There are various modes of anaesthesia available in the community today. This gives anaesthesiologists the freedom to select those that are safe, efficacious and most suitable for patients. However, patients may not always agree with their anaesthesiologist on the preferred mode of anaesthesia because they may have a different set of priorities, with many of them electing to have the lack of intraoperative awareness as the primary objective. Hence, disagreements between anaesthesiologists and patients may arise and could potentially disrupt doctor-patient relationship. This paper attempts to explore the possible reasons for obstetric patients championing for certain modes of anaesthesia and to provide an insight into the need for adequate patient education.

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**Key words:** Ethics, Safety, Informed Consent, Patient Preference, Intraoperative Awareness, Preoperative Anxiety

### Introduction

Anaesthesia today comes in many forms, ranging from a local injection of anaesthetics to numb the skin, a nerve block to provide anaesthesia to a region of the body, to general anaesthesia (GA) in which the patient is rendered unconscious. From an anaesthesiologist's perspective, patient safety comes first and hence, some options of anaesthetic delivery are favoured over others. However, the same cannot be said from the patient's perspective where comfort and lack of intraoperative awareness are top priorities. Patients are generally afraid of surgeries and do not wish to have any recollection. Hence, many patients would generally prefer GA over regional anaesthesia (RA). This is despite the fact that receiving GA could arguably be more dangerous and life-threatening to the patient. This begs the question, "Do obstetric patients opt for a more dangerous mode of anaesthesia just so that they prevent recollection from the surgery?" This paper serves to expound on the rationales of patients, and the methods that can be attempted in order to minimise differences in opinion between patients and physicians.

The significance of this paper extends into many aspects of medicine. We shall be focusing on obstetric anaesthesia to help elucidate the differences in priorities and opinions between physicians and patients. In obstetric anaesthesia, GA in caesarean section involves induction with hypnotics, tracheal intubation facilitated by suxamethonium, and ventilation with nitrous oxide and oxygen mixture which includes a volatile agent and muscle relaxant.<sup>1</sup> On the contrary, RA in caesarean section such as spinal and epidural anaesthesia involve injecting of local anaesthetics into the spinal column to achieve preferred regions of local anaesthesia.<sup>2</sup> RA is generally preferred over GA due to certain risks and complications that GA carries in the obstetric population. These risks and complications include gastric aspiration and difficult intubation due to laryngeal oedema, enlarged breasts and reduced respiratory reserves.<sup>3</sup>

### Search Strategy and Selection Criteria

We searched electronic databases including MEDLINE, EMBASE, PubMed and Google Scholar for studies evaluating the choice of anaesthesia amongst patients and anaesthesiologists. The search was performed using the

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following search terms: “conscious surgery”, “general anaesthesia”, “regional anaesthesia”, “preoperative anxiety”, “intraoperative awareness”, “public perception of anaesthesia” and “fears of anaesthesia”. Additionally, bibliography searching of all explored literature was performed to augment the citation searching.

### **Evolving Away from General Anaesthesia as the Sole Option**

Current expert opinions favour RA based on their knowledge from dated evidence. Old meta-analyses showing that RA is safer than GA were based on data collected from the 1970s to 2000s.<sup>4</sup> On the contrary, recent meta-analyses such as the Cochrane Review do not conclusively show that GA is more dangerous than RA.<sup>5</sup> We do not deny that patients who underwent GA today have better recovery profile credited to improved monitoring, updated protocols and perioperative surgical homes. The differences in safety profiles between GA and RA may be similar when compared with healthy patients. However, these differences become significantly clearer when patients come with comorbidities. In such patients, RA is a safer alternative and should be explored. Therefore, we aim to explore the reasons why patients may choose GA over RA in the hope that we can better understand and provide patients with well informed choices.

In obstetrics, patients are encouraged to undergo RA rather than GA to avoid life-threatening complications such as difficult intubation and aspiration.<sup>6</sup> RA in obstetric anaesthesia is the current preferred route of many physicians in their priorities to provide the best surgery outcome and patient care. However, for patients, sharing the same mentality and agreeing with the physicians' priorities may not be that simple. This is because many patients would prefer to undertake the risks of GA, even when there are safer options available, just so that they could be rendered unconscious and oblivious to their fears during the surgery.

### **Preoperative Anxiety Influences Patient's Selection of Anaesthesia**

As with any decision-making, anxiety has always been a major psychological influence on people. This is especially evident in making decisions on one's surgery including the choice of anaesthesia employed. Patients scheduled for surgery undergo a spectrum of anxiety levels depending on age, gender, previous anaesthesia experience, type of surgery performed, type of anaesthesia employed and preoperative information.<sup>7</sup> Interestingly, risk factors that predispose patients to preoperative anxiety include female gender, level of education, history of cancer, psychiatric disorders, depression, history of smoking and pain.<sup>8</sup>

Regardless of the level of anxiety or the risk factors that

predispose patients to experience preoperative anxiety, it is undeniable that preoperative anxiety is widely accepted as an expected response to arguably any surgery. Whilst many studies have shown that preoperative anxiety has led to increased postoperative analgesia, prolonged hospital stay, perioperative adverse outcomes and poor patient satisfaction,<sup>9-12</sup> there have also been studies to suggest an association between preoperative anxiety and selection of anaesthesia type—particularly, preference towards GA. For example, in a cross-sectional study scheduled for elective caesarean surgery, preoperative anxiety was significantly higher in patients who underwent GA compared to RA.<sup>13</sup>

However, we also recognise factors that may influence patient's selection of anaesthesia independent of preoperative anxiety. For example, a cross-sectional survey conducted by Ahmad and Afshan showed that younger women who are more tech-savvy are seemingly able to acquire medical information and become more knowledgeable in anaesthesia techniques, influencing their selection of anaesthesia, independent of preoperative anxiety.<sup>14</sup> In addition, they also found that previous surgical experience enhanced women's knowledge of anaesthesia options, influencing their selection of anaesthesia. Finally, their study also showed that patient demographics such as country of birth and cultural background play a role in patient selection of anaesthesia.<sup>14</sup> Their study concluded that 48.3% opted GA as compared to 33.4% of RA in Pakistan, a developing country. This is contrasted to developed countries where the rate of RA exceeded 90% for elective caesarean section.<sup>14</sup> Having said that, it is noteworthy that even developing countries are trending towards the use of RA in caesarean section.<sup>15</sup>

While we are moving away from paternalistic decision-making towards a more balanced, shared decision-making between physicians and patients in surgery options and medical therapies,<sup>16,17</sup> there remains some evidence on the influence of physicians, specifically anaesthetists, on patients' decision of their anaesthetic care. However, there is a significant influence that anaesthetists have on patients' anaesthetic care preferences. For example, a study in Hong Kong found that anaesthetists influenced the decision of a higher proportion of patients who had RA (51.5%) compared with those who had GA (38.7%). Interestingly, obstetricians influenced the decision of a lower proportion of patients who had RA (40%) and a higher proportion of patients who had GA (46.7%).<sup>18</sup> As such, anaesthetists play a strong role in educating and influencing patients' preference of anaesthetic care. Similarly, obstetricians also exert some influence on patients' preference and this can be further explored in future studies.

Nevertheless, preoperative anxiety remains a strong influence on patients' preference of anaesthesia. While we establish that preoperative anxiety contributes greatly to



patients' selection of GA over a safer and doctor-preferred alternative like RA, it is important to explore the reasons behind patients' anxiety and fears that influence them to undergo GA instead.

### **Fear of Being Conscious during Surgery**

Amongst the many reasons for electing GA over RA, being conscious intraoperatively has shown to be one of the most prominent factors eliciting patient anxiety. With patients already feeling distressed over undergoing surgery, being conscious and aware intraoperatively only serves to accentuate the anxiety.

Previous studies by Mitchell and available literature show that the majority of patients view their surgery with local or RA as anxiety provoking, with the thought of being conscious, ability to feel the surgeon, seeing their body open and the surgery being more painful due to local or RA and numbness wearing off too quickly as the most significant influences.<sup>19</sup>

Other researchers of the field have also revealed similar findings that increase patient anxiety. Gajraj et al uncovered from a study involving 100 obstetric patients who refused RA for elective surgical procedures, that the possibility of viewing events and hearing intraoperative conversation were influential in their decision to undergo GA despite having anaesthesiologists enthusiastically promote the benefits and safety of RA over GA.<sup>20</sup> Muneer et al also discovered similar results from a survey of patients scheduled for elective caesarean section who had refused RA due to fear of intraoperative awareness.<sup>21</sup>

In addition to the overwhelming response from patients, there have also been reports of similar concerns from the general public. Matthey et al conducted a province-wide telephone survey of 1216 participants in Canada showing that the majority were fearful of RA because they are concerned with "seeing the surgery". Moreover, the authors also expressed that this fear would have been greater reported had they included the ability to listen during surgery.<sup>22</sup>

Therefore, the vast literature suggests the fear of intraoperative consciousness as a significant reason for patients' preference of GA over RA despite the higher risks associated with the former.

### **Possible Solutions for Exploration**

To help patients and physicians reconcile their differences in priorities and opinions regarding the choice of obstetric anaesthesia, it is vital that education and communication be established between the parties. Many patients who experience a high degree of preoperative anxiety may impulsively select an option they deem to be the safest and most comforting. Unfortunately, the choice made by these

patients may not be the safest option in reality.

Previous studies have shown that anaesthetic provision information provides significant alleviation of anxiety.<sup>23,24</sup> Lee et al carried out a systematic review that supports the use of video and printed information about the overall process of anaesthesia and its risks prior to surgery for reducing patient anxiety while improving patient knowledge.<sup>24</sup> To further provide effective management of patient anxiety, concerns relating to local or RA can be explored while common misconceptions can be discussed.

By investing in patient information, patients are less anxious and more inclined to undergo regional or local anaesthesia for their surgeries. Karaaslan et al conducted a survey for 150 obstetric patients who were scheduled for elective caesarean sections and revealed that 66% of them who had previously refused RA for reasons such as intraoperative awareness and fear of permanent nerve damage, later agreed to undertake it after proper education was provided by the anaesthesiologist.<sup>25</sup>

Therefore, perioperative education is important in not only providing accurate and adequate information for maximal informed consent, but also in allaying the patients' fears and concerns of the surgery.

### **Conclusion**

Patient autonomy, one of the 4 main pillars of medical ethics, is constantly upheld by medical professionals. It is the cornerstone of how we strive to do our best for patients, and is the motto we live by as medical professionals. However, when a patient advocates for a treatment option that is more dangerous than other available alternatives, the ethos of decision-making for the best of the patient becomes torn between upholding patient autonomy versus ensuring beneficence. We must ensure that such decisions made by patients are not made impulsively without adequate education and a conducive environment. Our paper has shown that GA is not the best option for obstetric patients, and that anaesthetic alternatives can be considered. More importantly, our paper has highlighted the many factors that influence patients' decision in selecting their mode of anaesthesia, specifically the overarching influence – preoperative anxiety – that remains prevalent. As such, there exists a difference in priorities between physicians and patients regarding the mode of anaesthesia.

Therefore, it is important to ensure that adequate time is given for preoperative consultations, both in proper education and anxiety relief for the patient. In doing so, such ethical dilemmas can potentially be resolved effectively. This may be difficult to carry out in today's time when patient load is heavy and there is arguably lesser time allocated for preoperative consultations so that more surgeries can



be performed in a shorter amount of time. Nevertheless, it remains important that we prioritise patient care above all and ensure that effective communication is achieved between patients and doctors, adequate time is given for proper procedure consent-taking and that information is available and transparent to our patients. While Medicine continues to evolve, such as in the case of GA moving away from being the only option available in obstetric anaesthesia, we too must continue to evolve our mindsets into one that is current and open to change. As time has shown us repeatedly, people embrace change differently. The struggle between patients and doctors in deciding what is best for patients exists even when it is not acknowledged. It is therefore our duty as practising physicians to combine the knowledge of the past and evidence of the present, and apply it to the individual patient.

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## Pancreatic Panniculitis Sans Pancreatitis in a Patient with Diabetic Ketoacidosis

### Dear Editor,

A 23-year-old Malay woman with no past medical illness was admitted for a 4-day history of epigastric pain, vomiting and drowsiness. Investigations showed a high anion-gap metabolic acidosis with elevated serum ketones and hyperglycaemia, consistent with diabetic ketoacidosis (DKA). Anti-glutamic acid decarboxylase autoantibodies were positive, consistent with type 1 diabetes mellitus.

In the first week of admission, the patient had hyperamylasaemia (670 units/L, upper limit 100 units/L) and hyperlipasaemia (>400 units/L, upper limit 40 units/L) accompanying her epigastric pain, fulfilling the diagnosis of acute pancreatitis.<sup>1</sup> The gastroenterology consultant who reviewed the patient, however, requested for contrast-enhanced computed tomography (CT) scan of the abdomen to confirm the diagnosis as he felt the patient's DKA could have accounted for the elevated serum amylase and lipase levels, with similar epigastric pain. Two contrast-enhanced CT scans performed 6 days apart were negative for acute pancreatitis. The patient's hyperamylasaemia and hyperlipasaemia, together with epigastric tenderness, was attributed to DKA by the reviewing gastroenterologist.

Two weeks into admission, dermatology consult was sought for a 4-day history of painful lesions over the patient's legs, associated with bilateral ankles arthralgia. On examination, multiple discrete tender erythematous nodules were present over her shins and dorsal feet (Figs. 1a and 1b). Septic workup was unremarkable. Anti-streptolysin O titre was <200 IU/mL. Serum alpha-1 antitrypsin level was not performed. Clinical differentials considered included pancreatic panniculitis, erythema nodosum, erythema induratum, other causes of panniculitis, and cutaneous polyarteritis nodosa. A 6 mm punch biopsy was performed over one of the patient's right leg nodules. Histology showed lobular panniculitis with fat necrosis and neutrophils. Bluish saponified fat, basophilic deposits of calcium and ghost cells were present. No vasculitis was seen (Fig. 2). This was consistent with pancreatic panniculitis. No tissue was sent for direct immunofluorescence.

The patient was treated with indomethacin 25 mg thrice a day for symptomatic relief of her painful leg nodules. On outpatient review 2 weeks later, the patient was well. Nodules over her legs were less painful with flattening

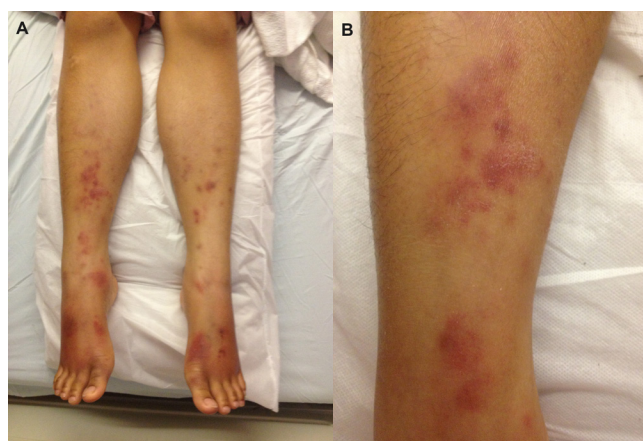


Fig. 1. A) Multiple erythematous nodules are seen over the patient's shins and dorsal feet. B) A close-up view of the erythematous nodules over the patient's right shin.

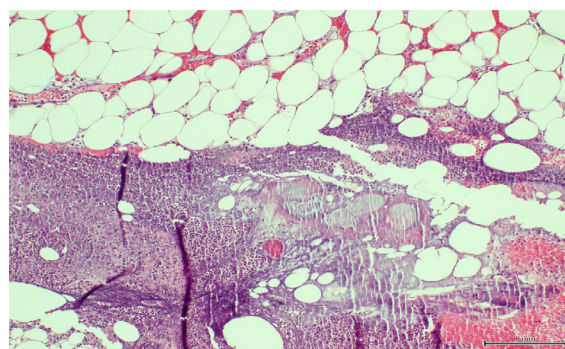


Fig. 2. Lobular panniculitis with fat necrosis and neutrophils. Bluish saponified fat, basophilic deposits of calcium and ghost cells seen. No vasculitis is seen (haematoxylin and eosin, original magnification x 200).

and post-inflammatory hyperpigmentation changes were seen.

The diagnosis of acute pancreatitis requires 2 of the following 3 features: 1) abdominal pain consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to back); 2) serum lipase or amylase activity at least 3 times greater than the upper limit of normal; and 3) characteristic findings of acute pancreatitis on contrast-enhanced CT and less commonly magnetic resonance imaging (MRI) or transabdominal ultrasonography.<sup>1</sup>

Pancreatic panniculitis is rare, affecting 0.3% to 3% of all patients with pancreatic disease, ranging from pancreatitis to pancreatic carcinoma.<sup>2</sup> It tends to affect the distal lower limbs, presenting with tender erythematous subcutaneous nodules that may spontaneously ulcerate with thick oily discharge.<sup>2</sup> Other possible sites of involvement include breasts, buttocks, thighs, and abdomen. Pancreatic lipase and amylase have been postulated to cause subcutaneous fat necrosis via enzymatic destruction of fat, supported by findings of these enzymes in lesional biopsies.<sup>3</sup>

Hyperamylasaemia and hyperlipasaemia are known to occur with DKA (16% to 25% of cases).<sup>3</sup> Three times the upper limit of normal for these enzymes is thought to be suggestive of pancreatic involvement since acute pancreatitis can precipitate or coexist with DKA.<sup>4</sup> However, hyperamylasaemia and hyperlipasaemia have been reported without pancreatitis findings on clinical examination or CT scan (gold standard for confirmation).<sup>4,5</sup> The source of these elevated enzymes in DKA patients without acute pancreatitis remains uncertain. Possibilities include subtle injury to pancreatic acinar cells, dysmetabolic state with release of salivary gland amylase or its accumulation from suboptimal urinary excretion, and release of lipolytic enzymes from other non-pancreatic sources (e.g. tongue, oesophagus, stomach, small bowel, liver).<sup>4,5</sup>

Although our patient presented with epigastric pain (not uncommon with DKA) with elevated serum amylase and lipase levels, contrast-enhanced CT scans of the abdomen did not reveal any pancreatitis. Pancreatic panniculitis lesions can precede the development of pancreatic disease in 40% of cases by 1 to 7 months.<sup>2</sup> However, in our patient, we postulate that her lesions were likely secondary to hyperlipasaemia associated with DKA and not due to underlying pancreatic disease per se. Patient's epigastric tenderness resolved shortly after her second CT scan. Her serum lipase level, which was persistently >400 units/L, only downtrended 1 week after resolution of her epigastric tenderness. Ten months on, there was no development of pancreatitis or other pancreatic disease clinically.

We report, to the best of our knowledge, the first case of pancreatic panniculitis sans pancreatitis in a newly diagnosed type 1 diabetes mellitus patient presenting with diabetic ketoacidosis.

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## The Early Effect of Laparoscopic Sleeve Gastrectomy on Taste Change in a Multiethnic Asian Cohort

### Dear Editor,

Bariatric surgery results in greater and lasting weight loss as well as reduces the severity of certain comorbidities.<sup>1</sup> The limited literature which has studied taste perception following Roux-en-Y gastric bypass (RYGB) and laparoscopic sleeve gastrectomy (LSG)<sup>2</sup> hypothesises that the consequent taste dysfunction influences food preferences, which prevents postoperative overeating of calorie-rich foods leading to greater weight loss.

As there are no similar investigations done in an Asian cohort, this Domain Specific Review Board (DSRB)-approved prospective study examined if there are any taste alteration for sweet, sour and salty food; and their influence on eating behaviour and weight loss outcomes after LSG in a multiethnic Asian cohort at the National University Hospital between 2012 to 2014. Questionnaires were administered 3 months post-LSG. The demographic and characteristics of the study participants are shown in Table 1.

Sensory change in taste was reported by 33 (27.5%) patients. Changes in taste perception for sweet, salty and sour food was 90.9% (n = 30), 57.6% (n = 19) and 21.2% (n = 7), respectively. Most subjects experienced heightened sensitivity to the respective taste: 28 (93.3%), 19 (100%),

and 6 (85.7%). The taste dysfunction compelled 28 (100%), 16 (84.2%) and 5 (83.3%) subjects consuming sweet, salty and sour food to reduce their intake. However, independent samples t-test analysis found no significant difference in postoperative weight loss between those who experienced taste change versus those who didn't ( $18.9 \pm 7.2$  kg vs  $19.5 \pm 8.0$  kg,  $P = 0.70$ ).

This study is limited by the ambiguous influence of recall bias and the precise time point of the taste dysfunction manifestation is unknown. Hence, future studies should explore participants' ability to identify varying concentrations of the respective tastes pre-LSG and retest at 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 6<sup>th</sup>, and 12<sup>th</sup> months post-LSG. It will be beneficial to use standardised tests to assess both taste and olfactory functions, as olfaction is an inseparable component of taste perception and alimentation.<sup>3</sup> Additionally, potential aetiologies for taste dysfunction such as medication and recent upper airway infection should be excluded.<sup>4</sup>

An improved study design to elucidate the mechanisms which lead to altered taste detection threshold and how it may affect food selection and weight changes is required as the gustatory system provides critical information about the quality (toxic exposures or spoilage indicators) and nutritional value of food.<sup>5</sup> We recommend that pre-LSG patients be informed about potential sensory changes as part of the informed consent process for surgery to prevent any eating disorders, anxiety, frustration or other related complications which may affect quality of life.

Table 1. The Demographic and Baseline Characteristics of Participants

Patients (n = 120)	
Age (years)	37.1 $\pm$ 12.3
Gender	
Female	n = 68 (56.6%)
Male	n = 52 (43.4%)
Preoperative body weight (kg)	115.2 $\pm$ 25 (n = 120)
Postoperative body weight (kg)*	96.2 $\pm$ 21.6 (n = 110)
Preoperative BMI (kg/m <sup>2</sup> )	42.3 $\pm$ 7.2 (n = 120)
Postoperative BMI (kg/m <sup>2</sup> )*	35.3 $\pm$ 6.1 (n = 110)
Ethnicity	
Chinese	34.1% (n = 41)
Malay	40.8% (n = 49)
Indian	21.7% (n = 26)
Others	3.3% (n = 4)

BMI: Body mass index

\*3 months post-surgery.

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## Asia's First Minimal-Access Left Ventricular Assist Device Implantation

### Dear Editor,

Left ventricular assist device (LVAD) has become an established therapy for end-stage heart failure, bridging patients to cardiac transplantation or to destiny in transplant-ineligible patients. New generation pumps continue to improve outcomes with 84% 1-year survival reported for the HeartWare Ventricular Assist Device (HVAD, HeartWare Inc, Framingham, MA).<sup>1</sup> Minimal access implantation hopes to further improve outcomes by minimising surgical insult and blood transfusion in these fragile patients.

### Case Report

We report a 47-year old male with hypertension for 20 years, viral myocarditis 8 years earlier and dilated cardiomyopathy. He was New York Heart Association functional class II in 2008 but had deteriorated for 1 year with recurrent admissions for congestive heart failure. He was referred for LVAD implantation as a bridge-to-transplant.

Minimal access HVAD implantation was performed via 2 small incisions. A left anterolateral mini-thoracotomy exposes the apex of the left ventricle for the sewing of a “docking mechanism” onto its surface. The heart muscle in the middle of this docking ring is then cored to facilitate the insertion of the LVAD inflow-cannula directly into the left ventricular apex (Fig. 1). An externalised power supply

cable then drives the hybrid rotating impeller within the LVAD in order to flush the patient's blood via centrifugal force through the outflow vascular graft. Blood is hence pumped forward through this graft that is sewn directly onto the ascending aorta beyond the aortic valve. The aortic outflow graft anastomosis was performed through a partial upper midline mini J-sternotomy (Fig. 1).

The procedure was completed with the heart beating without the need for a heart-lung machine. The patient did not require blood transfusion and was discharged home 2 weeks later having made an uneventful recovery. The patient remains well 18-months post-implant with normal functional status. Specifically, he was free from any driveline infection, bleeding or thromboembolic complications.

### Discussion

Minimal access cardiac surgery performed through the apex of the left ventricle via a left anterolateral mini-thoracotomy is routinely performed nowadays.<sup>2,3</sup> Less invasive approach has also been successfully used to explant LVAD.<sup>4</sup> Familiarity with these surgical techniques and modern LVAD-pumps facilitate the development of minimal access LVAD implantation.<sup>5</sup>

The LVAD off-loads the left ventricle, hence resting the heart and assists the left heart to maintain normal

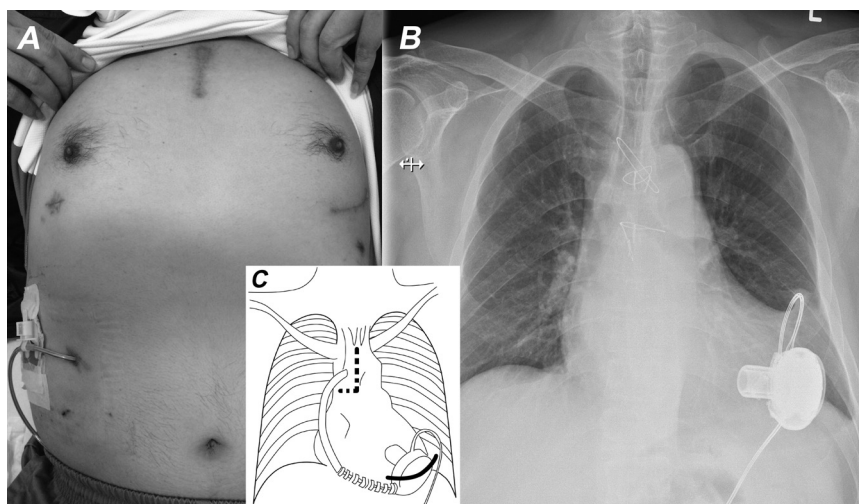


Fig. 1. A) Photograph of healed surgical scars with the LVAD driveline (connecting to batteries and control module) exiting patient's right hypochondrium. B) Radiograph showing the intrapericardial pump and manubrial sternal wires. C) Line diagram indicates surgical incisions (partial sternotomy = broken line; mini-thoracotomy = solid line) overlying both surgical sites.

organ perfusion. The potential benefits of this approach includes minimal surgical dissection, complete avoidance or shortened duration of use of the artificial heart-and-lung machine circulation during implantation and reduced blood loss.<sup>5-7</sup> Subsequent transplantation may be easier with less adhesion.

## Conclusion

Heart failure is a significant burden across Asia due to changing lifestyles and increasing prevalence of obesity, hypertension, diabetes and coronary artery disease in this populous part of the world.<sup>8</sup> We are encouraged by the outcome seen in this new procedural variation that uses a modern generation life-saving LVAD technology.

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## Inaugural Chee Kuan Tsee Lecture: Mental Health Care for the 21<sup>st</sup> Century\*

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### Introduction

Associate Professor Chee Kuan Tsee, President, College of Psychiatrists, distinguished guests, colleagues, ladies and gentleman.

I am honoured to be invited to deliver the inaugural Chee Kuan Tsee Lecture. This lecture has been established to honour and celebrate the achievements of an esteemed psychiatrist and clinician mentor, Associate Professor Chee Kuan Tsee. A/Prof Chee, an Emeritus Consultant at the Institute of Mental Health (IMH), has made outstanding contributions to the development of psychiatry in Singapore and has provided invaluable leadership to the psychiatric community as the founding president of the Singapore Psychiatric Association, and past chairman of the Chapter of Psychiatrists, Academy of Medicine. Building upon the foundation laid by our psychiatry pioneers, such as A/Prof Chee and many others, I hope to share on the Ministry's vision and strategy for mental health to guide the future development of psychiatry in Singapore.

### *Impact of Mental Illnesses*

Mental illnesses are major causes of morbidity and mortality in Singapore. More than 1 in 10 Singaporeans will experience a mental illness in their lifetime.<sup>1</sup> Currently, 1 in 10 Singaporeans aged 60 years and above suffer from dementia<sup>2</sup> and this number is expected to increase as we age. Alongside the high disease burden, a large treatment gap needs addressing as reported by the Singapore Mental Health Study.<sup>3</sup> Recognising the high burden of mental illnesses and the need to reduce the large treatment gap, the Ministry of Health (MOH) has significantly invested in mental health and will continue to do so through better resourcing and increasing services for mental health.

### *Development of the Singapore Mental Health Strategy and Plans*

What did we do? We started, about a decade ago, with the

National Mental Health Blueprint (NMHBP). There are 3 key aims under the Blueprint – promoting mental health, preventing the development of mental health problems and reducing the impact of mental health disorders. Under the Blueprint, we began developing community capability, a key shift that entailed moving from an acute-centric institutionalised model to a community-based model that is supported by hospital specialists. Subsequently, through the Community Mental Health (CMH) Masterplan, mental health care in the community was further strengthened, with the ultimate aim to improve the care of people with mental illness and dementia in the community. As we found out, this was a prescient move and preceded many of the other things that we now have to do.

### **Mental Health Care for the Future – Where Do We Go From Here?**

#### *Enhanced CMH Masterplan*

While these plans were the foundation, new challenges in our changing environment require the timely recalibration of our mental health plans. In line with the 3 strategic MOH shifts – to move beyond the hospital to community, beyond quality to value and beyond health care to health – we are enhancing the CMH Masterplan over the next 5 years to focus on adopting a collective front to better integrate health, social and community support.

#### *Beyond Hospital to Community – Integrating Mental Health in Primary Care*

We now have a much better understanding of the complex interrelationship between physical and mental health and how they influence each other. There are bidirectional links between mental and physical health and the high percentage of comorbidity of mental and physical illnesses are now well established. The Singapore Mental Health Study found that 14.3% of people with a chronic physical illness also had a mental illness while among those with mental illness,

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50.6% had a chronic physical comorbidity.<sup>1</sup> Our mental health services should thus be organised in a manner that can address this high comorbidity holistically rather than in silos and I think we spent too long in specialty silos. So what does this integration implies?

The family doctor is often the primary point of contact for many people with psychological symptoms. Integrating mental health services in primary care enables access in a setting that minimises stigma and discrimination, reducing the barriers to seeking treatment and providing an opportunity for early identification and intervention. We were able to start to address how to better our efforts under the CMH Masterplan, in part by addressing a “missing tier” of mental health care in the community that is accessible to patients requiring mental health care but who are not keen to visit the IMH because of stigma. This reinforces the need to strengthen and expand mental health services within primary care.

Over the next 5 years, we will work to enhance access to mental health care by increasing the number of mental health and dementia clinics in polyclinics. By 2021, we aim for 1 in 2 polyclinics to operate these clinics which will be run by family physicians with support from mental health and dementia specialists from partner hospitals. In parallel, we will expand the Mental Health General Practitioner (GP) Partnership Programme (MHGPP) where IMH and acute hospitals partner GPs and Family Medicine Clinics (FMCs) in their regions to manage patients with mental health conditions such as depression, anxiety and insomnia. Over 120 GPs have joined this programme, to provide integrated care for patients with mental health conditions. By 2021, we aim to increase the number of GP partners to 180.

We will also partner GPs in Primary Care Networks (PCNs) which we plan to set up by the end of this year. PCNs are groups of GPs who are linked together and provided through MOH funding with team-based support for chronic disease management. We will extend support for GPs in PCNs who are interested in providing basic screening for mental health conditions. To support GPs to manage people with mental illness in the community, we will be increasing the number of Community Intervention Teams (COMIT) made up of allied health professionals from 14 to 18 teams by 2021. Through these initiatives, we hope to enable people with mental illness or dementia to easily access mental health services in the various primary care settings and facilitate the holistic management of physical and mental health needs.

*Moving Beyond Healthcare to Health – Addressing the Whole Spectrum of Mental Health Needs, from Prevention to Recovery and Rehabilitation*

In tackling mental illnesses, we need to shift our focus

beyond healthcare to health and consider the whole spectrum of needs, from prevention, early intervention and treatment, to facilitating recovery and supporting rehabilitation. Mental illnesses affect individuals to varying degrees. Oftentimes, people with mental illness can overcome their conditions with minimal support and continue to lead productive lives. Unfortunately, a significant proportion will suffer from disabling effects which require complex long-term support and engagement. For this group of patients, support through recovery and rehabilitation is crucial. The World Health Organisation (WHO) calls for a balanced combination of 3 fundamental ingredients of care – pharmacotherapy, psychotherapy and psychosocial rehabilitation.<sup>4</sup> Mental health care must, therefore, extend beyond treatment to a recovery-based model that facilitates the creation of a supportive social environment for people with mental illness to rehabilitate back into. This includes providing postdischarge support, extending beyond healthcare, and establishing social services which provide vocational rehabilitation, employment and education support and housing.

To facilitate recovery and rehabilitation, we have 3 psychiatric rehabilitation homes operated by the Singapore Association for Mental Health (SAMH) and Singapore Anglican Community Services (SACS) which provide training on self-management and community living skills in a residential setting. These Voluntary Welfare Organisations (VWOs) also operate psychiatric day centres for patients to receive ongoing psychosocial rehabilitation, after discharge from the hospitals or the psychiatric rehabilitation homes. For those who can transit back into the community, but still require accommodation and some social support, a psychiatric shelter home will be ready in 2017. Following feedback on the need to improve postdischarge support and allow patients to transition smoothly to home and their community, we will be strengthening IMH’s postdischarge support beyond patients with very severe mental health conditions to also include an additional 3000 patients over the next 5 years. The level of support will be based on the patient’s need and severity of the condition and will include a focus on patients with a combination of physical and mental health conditions, and those who have high social and community risks.

At the national level, it is vital to not only meet the needs of people with mental illness, but also protect and promote mental well-being of Singaporeans through upstream prevention. Mental well-being enables us to lead meaningful lives and strengthens our ability to overcome challenges in life. Part of building emotional and mental health resilience involves raising awareness of mental well-being through providing the public with mental health knowledge and coping skills and facilitating help-seeking when necessary.



Another aspect of promoting mental well-being involves creating inclusive communities where people with mental illness are empowered to live safely and confidently within their communities. Empowering begins during the early childhood formative years by creating a nurturing core. Subsequently, the provision of healthy living and working conditions supported by workplace programmes, and in the older years, protective and supportive community networks. To build a mentally resilient community, we have piloted 3 Dementia-Friendly Communities (DFCs) to increase awareness and train residents, businesses and other partners to create supportive and inclusive environments for people with dementia and their caregivers. To date, over 7000 people have been trained. Over the next 5 years, we aim to increase the number of DFCs to reach out to more people.

### *Investing in Social Capital*

Recently, I had the privilege to visit Scotland and we heard about how they have embarked on what is known as the “Realistic Medicine” initiative which places the preferences of people receiving care at the heart of decision-making. “Realistic Medicine” is a description of their aim for patient-centricity such that patients are engaged and understand the care received. In delivering value-based care, we often neglect that what is interpreted as value to the individual is highly subjective, and may not always be congruous to the “best” medical option which is what we, as specialists, often talk about. Mental health is and remains a delicate topic in Singapore. One key challenge in addressing mental health is overcoming the stigma associated with it. Stigma results in discrimination and people with mental illness are often excluded or ostracised by society, rather than engaged and placed in the centre of their care. This rejection is also often experienced by caregivers and their family. Stigma often deters the public from getting involved in the care of people with mental illness and is a hindrance to their successful recovery and reintegration.

We will need to find ways to improve the mental health literacy of our people and involve the wider community to engage in conversations about care, though this is often difficult—probably our greatest challenge. In order to create stronger communities, we need the concerted effort and commitment from the government, healthcare providers, caregivers, family members and members of each community to come together to overcome mental health challenges and forge stronger bonds. Unfortunately, social capital is an important resource that we tend to overlook. In our culture, the family is often included in the treatment process and as we move to a community-based system, much of the responsibility of caring for people with mental illness will fall on the shoulders of their families and caregivers. I cannot overstate the importance of family members,

caregivers and a socially inclusive community in supporting people with mental illness. Our vision should be for a more participatory healthcare culture, where patients, their families, and the community are joined up in partnership with our healthcare providers. We can learn from and anticipate the release of the next Scottish Government Mental Health strategy, which will be published this year, and will reflect the philosophy of Realistic Medicine.

### *Creating Value for Our Patients – Breaking Silos and Improving Outcomes*

The reorganisation of the healthcare system into 3 integrated clusters presents an opportunity to redefine how mental health services are structured within each cluster and how service providers are engaged. Each integrated cluster will now have a comprehensive range of facilities, capabilities, services and networks across different care settings. Clusters will be better equipped to deliver more comprehensive and integrated care at the most appropriate care setting that is centred around patients’ needs, bringing the most value to their patients. Our healthcare institutions and professionals will need to break out of the silos within their organisations and fields of expertise, and perhaps our mindsets. As we are integrating mental and physical healthcare in primary care, this integration needs to extend to other levels of healthcare where patients with physical health conditions are actively screened and managed for psychiatric comorbidity and vice versa. In other words, psychiatrists will play an important role in promoting “psychiatric-mindedness” and rousing support from non-psychiatry colleagues and other stakeholders, including their management to break these silos.

Private psychiatrists see a significant proportion of our mental health patients. With many new providers taking on new roles in the mental health ecosystem, private psychiatrists will need to be aware of the various providers and services. I would like to add here that from the MOH’s perspective, we actually look at it as one healthcare system. While we spend a lot of time talking about public healthcare, we consider our colleagues in the private sector to be part of that same system as I earlier alluded to, where we have actively engaged our GPs to build rapport and a common mission for where we are headed. Primary care mental health providers, community allied health teams, and family and social support services in the community, all these are where we can refer patients to, when such support is required. Fostering effective partnerships across care boundaries and between public and private sectors is integral to the success of our mental health care system and I hope to see closer working ties between the 2 sectors. Associations like yours and the Academy are very important to continue to build on these partnerships.



I have quoted some statistics earlier from the work that Prof Chong Siow Ann has helped to helm. So, mental health research is another important area that we need to develop. As we seek to shift beyond quality to value, we need to be able to define and accurately measure patient-centred care outcomes to assess the effectiveness of our mental health policy and align our reimbursement model to improve outcomes while keeping costs affordable for Singapore. Research and better understanding of the epidemiology and risk factors for mental illnesses and the effectiveness of care models and treatment approaches are necessary to guide priorities for policy and service development and inform their implementation.

### *Furthering Professional Development*

Delivering a holistic patient-centred mental health care in our envisioned model that is anchored in primary care and the community requires new skills and competencies. To function effectively, psychiatrists will need to be familiar and up-to-date with the management of chronic diseases such as diabetes and geriatric conditions as these patients will present with psychiatric comorbidities. I heard from A/Prof Chua Hong Choon earlier that he is running a chronic disease and an acute medicine setup in IMH as well. So it is no longer a situation where we can ignore this. As patients with chronic diseases will also present with psychiatric comorbidities, you will need to be able to communicate, collaborate, establish rapport and function effectively in multidisciplinary teams as part of a network with primary and community care providers. Care planning and coordination to create and implement integrated care plans will be an integral part of practice under shared care teams for mental health and dementia. Then, there is familiarity with the social service sector, which will be necessary to address the psychosocial needs of your patients. Beyond providing care, you will be expected to train and support the capability building of other providers, including primary care, community and intermediate and long-term care providers to empower these providers to deliver better mental health and dementia care for patients in the primary and community settings, and facilitate patients' successful recovery and rehabilitation in the community. The psychiatry specialty and residency programme will need to effectively train the next generation of psychiatrists in such interdisciplinary professional and holistic way to better support our mental health needs and shifts in the model of care.

To address this, we have increased psychiatry specialist training capacity from 5 a year in 2012, to approximately 15 psychiatrists a year. From now till 2020, we will be exiting about 50 psychiatrists through the residency programme. Apart from training more psychiatrists, we have also increased the capability of our family doctors to identify and

manage common mental health conditions in the community. Since its first intake in 2011, over 100 family doctors have graduated with the Graduate Diploma in Mental Health (GDMH), offered by the Division of Graduate Medical Studies, National University of Singapore in conjunction with the IMH. As doctors do not work alone, we will also have to work on community nursing and other partners as part of this inter-professional capability.

### *Role of the College*

As we seek to transform our mental health landscape, there is no doubt that an important role of the College will be to further professional development, especially in equipping the psychiatric community with the knowledge and skills to meet future needs, not just in cutting edge psychiatry but also redefining the role of the psychiatrist within the team of mental health providers, and building the capability of primary care and community providers. The College provides professional leadership in the development of psychiatry and MOH will continue to call on many College Fellows as psychiatry clinician leaders to advise on mental health policy matters and co-create mental health care in Singapore. I hope to see College Fellows assuming leadership roles to challenge current boundaries in psychiatry through research and innovation, public and private sector collaboration, and experimenting new models of integrated health and social care. These clinician leaders will need to champion for mental health and persons with mental illness, to promote greater understanding and acceptance of those with mental illness, reduce stigma and social exclusion, and sustain advocacy to position mental health in our agenda, be it at the community, hospital, cluster or national level.

### **Conclusion**

Mental health care in Singapore is evolving and there is a huge amount that we need to do. I have just outlined our policy intent but implementation will be the tougher job. There are key shifts in the model of care. Firstly, care is shifting from the hospitals into the community with the attendant increased focus on care integration, not just across the healthcare continuum, but extending to other sectors, addressing needs beyond healthcare to health. We will need to move beyond reducing disability to creating value for patients, helping them achieve a better quality of life, and lead productive lives in the community. The medical profession will need to evolve with these shifts.

There are role models who have made outstanding contributions to the development of psychiatry and mental health whom we can look up to as we continue on this transformative journey:

a) Today we honour A/Prof Chee Kuan Tsee, one such role model. An astute clinician, he was one of the team members dealing with the Koro epidemic in 1969. Apart from being an outstanding clinician and mentor, I note that A/Prof Chee has also authored a well received reference handbook, 'Guide to Psychiatry', which is now, I believe, is in its 15<sup>th</sup> revision, and is a popular resource material used by psychiatry and mental health professionals and trainees.

b) A/Prof Wong Kim Eng, an outstanding clinician mentor from IMH, another pioneer in the field of psychiatry who has played an integral part in shaping our mental health plans, as the chairperson of the mental health committee that produced the NMHBP which we are still working on.

c) Prof Kua Ee Heok, a Senior Consultant from the National University Hospital, renowned author and researcher who has made invaluable contributions in the field of geriatric psychiatry.

And there are many more who are not mentioned. I would like to applaud your hard work and dedication in psychiatry and mental health. Working with many different stakeholders and delivering mental health care that extends beyond its traditional boundary will undoubtedly be challenging as many factors lie beyond your direct control. I am, however, confident that with such a rich heritage, psychiatry will rise

to these challenges. There is a long way to go before we achieve the models of excellence in mental health care but my colleagues in the Ministry and I are committed to this journey with you. Thank you.

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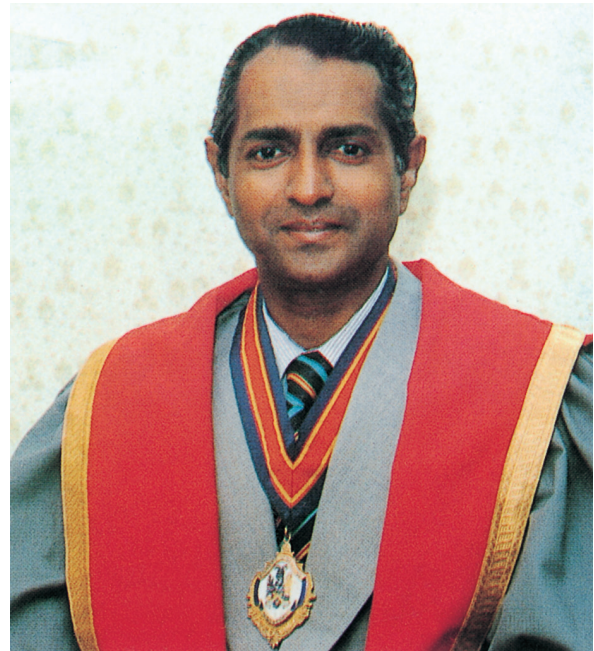
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## Professor Vettiveloo Kandasamy Pillay (1929 – 2016)

Professor “Kanda” Pillay, the 11<sup>th</sup> Master of the Academy of Medicine, Singapore (1978-1980), originally hailed from Seremban, Malaysia,<sup>1</sup> and was admitted to the King Edward VII College of Medicine in Singapore in 1948.<sup>2</sup> He graduated from the renamed Faculty of Medicine, University of Malaya in 1954. In 1958, he became one of the first 3 Orthopaedic Trainees with the Department of Orthopaedics together with William Fung (the first local head of the Government Department of Orthopaedics – the ‘O’ unit) and Yeoh Kean Hong. The trio obtained their Final Fellowship in Surgery in 1960 and MCh (Orth) Liverpool (Masters of Surgery in Orthopaedics) in 1961 together.<sup>1,2</sup> Thereafter, they joined the orthopaedic service. He had a keen interest in genetic, congenital and developmental deformities in orthopaedics, as was demonstrated by his publications.

Between 1967 and 1974, he became head of the ‘C’ unit – the University Department of Orthopaedics (renamed as the University of Singapore), succeeding Professor Donald Gunn as the first Local Professor of Orthopaedics.<sup>3</sup> During this period, he built the foundation for the local postgraduate programme in Orthopaedics and was instrumental in getting the local Master of Medicine in Surgery degree recognised as equivalent to that of the Fellowship of the Royal College of Surgeons in the United Kingdom.<sup>1</sup> Together with P Chacha, N Balachandran and KH Yeoh, he was involved in postgraduate orthopaedic training programmes in Indonesia in the 1970s.<sup>2</sup> He was conferred the title of Honourable Academician of Makassar University in 2002 in recognition of his efforts to establish postgraduate orthopaedic training in Jakarta and Makassar.<sup>4</sup>

In 1967, he was involved in the formation of the Singapore Orthopaedic Association (SOA) and elected as the first vice-president of the association.<sup>5</sup> He established the SOA Donald Gunn Gold Medal in 1989 in honour of his teacher and mentor.<sup>1</sup> The same year, he was also elected as a founding committee member of the Singapore Surgical Society. He was a founding member of the World Orthopaedic Concern which was established in Singapore in 1975. This international organisation, mooted in 1973 at Oxford, was focused on improving the healthcare of



orthopaedic patients in developing countries. In 1976, through his strong association with the Chairmen of the Lee and the Shaw Foundations, he established the Lee-Shaw Foundation Fellowship which allowed regional orthopaedic surgeons to do orthopaedic fellowships in Singapore, which continues on to this day.<sup>2,6</sup>

VK Pillay became a fellow of the Academy of Medicine in 1963 and was selected as the Galloway Lecturer (The Galloway Lecture is in memory of Sir David Galloway, an eminent physician and teacher of the Singapore Medical School, instituted in 1959 after a gift of \$2000 from Lady Galloway)<sup>6</sup> the same year, which he delivered on the topic of ‘Congenital (Developmental) Deformities of the Elbow Joint’.<sup>7</sup> He became the Chairman of the Chapter of Surgeons (which was founded in 1966 and eventually led to the disbandment of the Singapore Surgical Society) between 1971 and 1973.<sup>8</sup> During his leadership as the 11<sup>th</sup> Master between 1978 and 1980, the building fund was initiated. As Master, he obtained commitments from Shaw

Foundation and Lee Foundation to donate \$2m each over a period of several years.<sup>9,10</sup> The donations were contingent upon the Academy members collecting/contributing at least \$0.5m first. These donations and funds led to the eventual purchase by the Academy of the Runme Shaw Building at 142, Neil Road in June 1999.

He was honoured by the then Chapter of Surgeons (which became the College of Surgeons in 2004)<sup>8</sup> and awarded the Chapter of Surgeons Lectureship which he delivered on the topic of ‘Dilemmas in Surgery’ in 1995.<sup>8,11</sup> In 1997, he set up the Chapter of Surgeons Travelling Fellowship (now known as the College of Surgeons Travelling Fellowship). It provides funding to members of the College for their participation at conferences/seminars/workshops/teaching programmes to have further understanding of the surgical problems in the developing world and gain knowledge on the development/advancement of the surgical specialties.

Besides those of the Academy and Chapter, he was similarly honoured by the Singapore Medical Association (SMA) as the 19<sup>th</sup> SMA Lecturer in 1986 which he delivered on the topic ‘Excellence in Medicine’.<sup>12</sup> The SOA honoured him in 1990 as the Donald Gunn Lecturer.<sup>1</sup> The University Department of Orthopaedics honoured him as one of the pioneers in Singapore orthopaedic academics by establishing the VK Pillay Lectureship at the National University of Singapore in 2004.<sup>4</sup> Renowned orthopaedic surgeons from abroad are invited every year to spend about a week to deliver lectures, teach postgraduates and orthopaedic trainees and exchange scientific advancements in orthopaedics with staff members.

Kanda Pillay was both a spiritual and a family man. He is acknowledged as one of the pioneers who helped to set up the Hindu Centre in Singapore in 1978.<sup>13</sup> A devotee of Satya Sai Baba, he spent a lot of his spare time in providing orthopaedic expertise to the Satya Sai Baba Hospital in Puttaparthi in India. He was also involved in setting up the Sai Centre in Singapore in the 1980s.<sup>14</sup>

Professor Pillay was a faithful proponent of the art of Orthopaedics as oft quoted by him – “At one time, it was considered that to be an orthopaedic surgeon you needed more brawn than brain. I kept telling my colleagues that in orthopaedic, things are done not with Force but with Art — Non Vis Sed Arte.”

His contributions to the Academy and to the art, practice and teaching of Orthopaedics in Singapore serve as inspiration to generations of orthopaedic surgeons and academicians to come.

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