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Regulating, implementing and evaluating AI in Singapore healthcare: AI governance roundtable's view

A roundtable discussion developed a structured set of statements for regulation, implementation and evaluation of AI models in healthcare (See full article, p. 428)

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Caring for the sexually assaulted child: Follow-up matters

Rie Aoyama¹ MRCPCH (UK), Olivia Leow¹ MRCPCH (UK), Si Min Chan^{1,2} FRCPCH (UK)

In 2024, the United Nations Children's Fund (UNICEF) reported that 1 in 8 women (370 million) experienced sexual assault before the age of 18 years, and 8% of these are from East and Southeast Asia.¹ In Singapore, 38.6% of 11,868 sexual assault cases from 2018 to 2022 involved children aged under 16 years.² These children are at risk of pregnancy, sexually transmitted infections (STIs) and post-assault trauma in the short term, and face wide-ranging long-term psychosocial and health consequences, including psychiatric disorders and human immunodeficiency virus (HIV) infection.³ A systematic review of children and adolescents exposed to sexual abuse found that STI detection varied from <1% to 61% in different settings and by type of STI.⁴ In a Singapore review of 790 patients aged 0 to 16 years who presented to a paediatric emergency department (ED) for sexual abuse/assault from 2016 to 2020, 6.2% had an STI, with the majority having chlamydia followed by gonorrhoea.⁵

Yao et al. studied the medical records of 278 children and adolescents aged 0 to 16 years, in 292 paediatric ED encounters for non-consensual sexual assault over 20 months.⁶ They described patient and assault characteristics, the use of post-exposure prophylaxis (PEP) for STIs and follow-up. Patient demographics were similar to those in previous national and global studies.^{1,5} Most were female (96.2%), with a median age of 14.0 years old. Most (64.7%) presented more than 7 days post-assault, well beyond the recommended 72-hour window for HIV PEP and emergency contraception; 61.7% had penile-vaginal exposure and only 7.2% used barrier contraception. Nearly one-third of female patients had no urine pregnancy test done. Baseline STI screening ranged from 83.9% (HIV and hepatitis C) to 85.9% (chlamydia and gonorrhoea). Institutional protocol mandated this only if required by the police. The only STIs diagnosed were *Chlamydia trachomatis* (27/251, 10.8%) and *Gardnerella vaginalis* (102/214, 47.7%).

The first striking finding was inconsistent prescribing and poor adherence to HIV PEP. HIV PEP was

recommended for those who had a penetrating sexual encounter within the last 72 hours with an assailant who had known high-risk factors or multiple assailants. Of 40 eligible patients (13.7%), 35 were offered PEP; 29 started, but only 10 completed the 28-day course. Five eligible patients were missed and left untreated, and another eight patients who started HIV PEP were later deemed ineligible, reflecting the difficulty in accurate risk assessment based on the initial assault history taken, and highlighting a potentially serious gap in treatment. Nearly all assailants were male, and half were over 18 years old or of unknown age. None were known to be HIV- or hepatitis B virus (HBV)-positive, but it was not specified how many were known to be negative or of unknown status. Considering that 1 in 4 assailants were strangers and hence likely to have unknown or unascertainable risk factors, it is surprising that only 40 patients were eligible for HIV PEP, and many were likely ineligible because they presented beyond 72 hours. The authors suggest that clinical decision-making for HIV PEP is complicated by the uncertain history obtained from children regarding assault characteristics. Although risk of HIV transmission is likely low, specific circumstances conferring higher risk, such as traumatic penetration or bleeding, sites of exposure to ejaculate, and assailant's genital lesions may be unknown. Both the World Health Organization and the US Centres for Disease Control and Prevention (CDC) recommend HIV PEP regardless of the type of sexual assault and whether barrier protection was used.^{7,8} This includes non-penetrating sexual assault involving any mucosal exposure.

Patients who completed PEP had at least 1 protective social factor, but the study did not evaluate whether drug adverse effects or poor social factors were the main cause of poor adherence. Overall, 51.7% of patients had high-risk behaviours or family/social circumstances, and 10.6% had a comorbid psychiatric illness. Although logistical and financial support is always helpful, children and adolescents may have chaotic lifestyles and a lack of personal responsibility.

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Provision of a 28-day PEP supply, close caregiver supervision or regular phone/video monitoring by a nurse/social worker may improve compliance. A longitudinal cohort study reported that 38% developed post-traumatic stress disorder.⁹ Patients may be more receptive only later to enhanced adherence counselling and support. This should be tailored to age-specific needs, for example, involving a responsible caregiver for younger children, and engaging and respecting the autonomy of adolescents.⁴ Further work is needed to identify specific social interventions that are effective in supporting a child post-assault.

Similarly, PEP management in HBV non-immune patients was inconsistent; only 61% were offered booster vaccination and 20 of 27 with high-risk encounters received hepatitis B immunoglobulin. HBV waning immunity in this study was consistent with 2018 national seroprevalence surveillance rates of 45.7% in children aged 1 to 17 years and 24% in those aged 13 to 17 years,¹⁰ and raises the question of whether to recommend empiric booster vaccination for high-risk adolescents or routine booster for all.

Another important finding was poor follow-up of STI seroconversion at 2- and 6-months post-assault, and patient well-being. Fewer than 1 in 5 patients (18.8%), regardless of PEP eligibility or administration, had any repeat HIV serology tests done. Similarly, 1 in 5 patients had hepatitis C or HBV serology repeated. All tested negative, but low testing rates reflect missed opportunities for early diagnosis and the inability to ascertain true STI transmission rates post-assault. Although all patients should have medical and social follow-up, about 1 in 10 were not referred to any clinic and just over half (57.7%) attended any clinic follow-up at all. In patients eligible for HIV PEP, poor infectious disease clinic attendance likely contributed to the 2 in 3 who failed to complete PEP. Teleconsultation may improve compliance, but not serological testing.

Referral and follow-up rates with a medical social worker were not reported. The majority of perpetrators of child sexual assault are people known to the patient and frequently from within their household.^{5,6} Most patients are already known to community/social services, and many have multiple episodes of sexual assault,^{5,6} suggesting that we are missing opportunities to identify at-risk children and intervene appropriately.

HIV PEP should be initiated as early as possible, ideally within 72 hours of exposure. Few patients presented in a timely manner, consistent with previous studies that report presentation within 3 to 5 days by less than one-third of patients in Africa, 56% in Thailand and 80% in Brazil.⁴ In a study of 252 cases of child sexual abuse in Singapore, delayed disclosure occurred at a mean of 32 months and was associated

with younger female victims, more severe abuse, and abuse by in-home caregivers.¹¹ Hesitancy to report sexual assault underscores the need to improve preventive education on sexual violence and address age-specific barriers to reporting. School-based programmes can improve children's knowledge and protective skills,^{11,12} and recognition and reporting may be improved by early childhood home visits, and parent and teacher education.³ Sexual assault is associated with the taboo and secrecy surrounding sex in the Asian cultural context¹¹; this unpleasant subject requires more visibility and less stigma, with more avenues for children to disclose their experiences safely.

In this study, rates of empiric treatment for chlamydia, gonorrhoea and trichomoniasis all differed, suggesting that not all treatments were offered by physicians or accepted by patients. Although the study's institutional guidelines did not offer STI treatment to children younger than 13 years and to those presenting beyond 72 hours, STI treatment may be considered for all children regardless of age and time of presentation.⁴ There is little direct evidence comparing the test-and-treat approach with presumptive STI treatment/prophylaxis.⁴ Presumptive treatment may not be required in pre-pubertal girls if incidence is low and regular follow-up can be assured. Holistic care plans should also include guidance on the use of emergency contraception and the HPV vaccine; the CDC recommends a dose for all unvaccinated patients aged 9 to 26 years at initial assessment, with follow-up doses later.⁸

Overall, we need to pay greater attention to sexually assaulted children. Medical care should continue beyond disclosure. Early identification, robust STI/PEP management and psychosocial care are a priority. Poor compliance and follow-up are affected by pre-existing vulnerabilities and by the challenges of navigating multiple medical and social visits over months. Financial burden, poor understanding of the purpose of outpatient follow-up, Asian cultural perceptions and family dynamics all play a role. In Singapore, the Child Protective Service, which is part of the Ministry of Social and Family Development, offers statutory interventions and specialised school and community interventions. It is important that post-disclosure management is handled sensitively and seamlessly between community and hospital services, focusing on the child's well-being. One-stop multidisciplinary outpatient clinics could streamline follow-up.

The ED visit may ultimately be the only medical encounter and the only window of opportunity to maximise care. We need better coordination among the child, family and professionals in healthcare, social and law enforcement systems; and research to understand barriers in the Singapore context, not

limited to timely presentation but also subsequent compliance. Every sexually assaulted child is one too many, we must do better to reduce their risk of poor outcomes.

Ethics statement

Not applicable.

Declaration

The authors declare there are no affiliations with or involvement in any organisation or entity with any financial interest in the subject matter or materials discussed in this manuscript.

Keywords: hepatitis B, HIV, infectious diseases, paediatrics, sexual assault

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Diagnostic patterns and predictors of cognitive outcomes in autistic children in Singapore

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ABSTRACT

Introduction: This study aimed to examine patterns of diagnosis, cognitive and adaptive functioning, and school placement outcomes in autistic children in Singapore, and to assess earlier predictive factors of cognitive outcomes.

Method: Retrospective data were extracted from medical records of a specialist developmental paediatrics service for children born in 2008–2011 and referred to the autism clinic or were given a diagnosis of autism. Data items included demographic data, diagnostic methods, psychological assessment results, early intervention attendance and school placement outcomes.

Results: A total of 2124 children (82.6% male; 66.4% Chinese, 13.4% Malay, 9.8% Indian and 10.5% Others) were diagnosed with autism from the 4 birth-year cohorts. The mean (SD) age of the first clinical diagnosis of autism was 3.56 (1.14) years, with 81.0% of children receiving a concordant initial clinical diagnosis. A total of 1811 (85.2%) had a formal diagnostic assessment using the Autism Diagnostic Observation Schedule (ADOS) at a mean (SD) age of 4.16 (1.11) years. Of 1326 with cognitive and adaptive assessment results, 16.6% had mild and 19.8% had moderate-severe cognitive impairment. Of 1483 with school placement outcomes, 45.9% went to mainstream schools, 21.8% entered SPED schools offering the national curriculum and 32.3% required customised curriculum SPED schools. Logistic regression showed that factors predicting intellectual impairment included higher ADOS scores (aOR 95% CI 1.13 [1.08–1.19] for Comm+SI total and 1.53 [1.33–1.75] for SBRI total), higher social communication level of support (based on the DSM-5 criteria) (aOR [95% CI] 2.14 [1.10–4.16] for level 2 and 14.94 [5.77–38.64] for level 3), and minority race (aOR [95% CI] 2.82 [1.52–5.20] for Malay, 5.19 [2.36–11.44] for Indian, and 4.54 [1.91–10.79] for Others).

Conclusion: These findings could guide policymakers and practitioners worldwide to strategically allocate diagnostic, intervention and educational resources, maximising developmental outcomes for autistic children across diverse settings.

Keywords: autism spectrum disorder, children, diagnosis, outcomes, special education

CLINICAL IMPACT

What is New

- This study is one of the largest to track school-age outcomes of autistic children in Singapore.
- In the absence of any other national prevalence or outcome data, the current study provides useful insights into the patterns of diagnosis, cognitive and adaptive functioning, and cognitive and school placement outcomes.

Clinical Implications

- Information from this study can be useful for resource planning purposes for national agencies or ministries involved in providing autism diagnostic, early intervention and educational services.

INTRODUCTION

Autism spectrum disorder (ASD or autism) is a neurodevelopmental condition characterised by differences in social communication and social interaction, with restricted, repetitive behaviours (RRBs).¹ The prevalence of autism in Singapore is estimated to be 1 in 100,² which is similar to that quoted by the World Health Organization based on global data,³ but lower than the 1 in 36 reported by the US.⁴

In 1998, a national child development programme (CDP) was established by the Ministry of Health, Singapore, and has evolved into a nationwide community-based, family-focused and child-centric collaborative service network involving government bodies and voluntary welfare organisations.^{5,6} The Department of Child Development (DCD) in KK Women's and Children's Hospital (KKH) and the Child Development Unit (CDU) of National University

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Hospital are the 2 national CDUs in Singapore. In 2007, they received 1200–1400 new preschool referrals and saw 4000–5000 follow-up consultations per year.⁵ Today, new referrals in KKH alone have increased to approximately 5000 children per year with 13,000 follow-up consultations. Autism comprises approximately 28% of CDP diagnoses, with 360–500 children diagnosed annually in the mid-2000s to an estimated 1200–1400 today.

Following a diagnosis of autism in early childhood, most toddlers and preschoolers in Singapore are typically referred to a government-funded Early Intervention Programme for Infants and Children (EIPIC), which provides specialised therapy and educational support for 6–8 hours per week to those requiring medium to high levels of support. While waiting for an EIPIC placement, hospital-based interim therapy incorporating caregiver training is usually provided, but at much lower intensity. Children with milder needs, however, might only require isolated speech-language, occupational or behavioural therapy provided in either hospital or preschool settings, rather than EIPIC. Some parents may also opt for private services. Throughout this period, the children usually continue with medical follow-up at 1 of the 2 CDUs.

In Singapore, formal schooling starts in the year a child turns 7 years old, and children on the autism spectrum may attend mainstream schools, special education (SPED) schools offering the national curriculum, or SPED schools offering a customised curriculum. At about 5–6 years of age, most autistic children would be recommended to undergo a holistic needs assessment that takes into account the child's level of cognitive and adaptive functioning in order to inform on appropriate school placement needs.⁷ Usually, a cognitive profile indicative of normal intellectual ability would be required for a child to attend mainstream schools or the SPED schools offering the national curriculum. However, some children may not undergo the assessment, usually either because there are no significant concerns for the child needing SPED placement or because parents decline it.

Three published studies have reported on profiles of autistic children in Singapore. The first was by Bernard-Opitz et al. in 2001, at a time when Singapore's resident population was about 3 million.⁸ Survey data from 176 parents of autistic children 3–12 years old indicated that 81% of children were boys and 60% were diagnosed before 3 years of age. There was a high (39%) incidence of both parents working and the involvement of foreign maids as caregivers. Concerns were raised about a possible lack of stimulation in many homes and the influence of psychosocial deprivation on child development.

The second study was Lian and Ho who reported on 170 autistic children from a total of 542 children referred to KKH in 2003 and followed up after 1 year.⁹ The ratio of males to females was 4.5:1, and the median age of first consultation was 42 months (range 19–112 months). In addition, 74% received a psychological assessment confirming autism. Autism was moderate-to-severe in 86% of the children, and only 14% were deemed potentially capable of mainstream ability. Children with high-functioning autism presented at a higher median age (52 months) than children with more severe autism (38 months). The younger the child at presentation, the higher the likelihood of a diagnosis of at least a moderately severe variant of autism.

The most recent paper by Aishworiya et al. was a cross-sectional study in 193 autistic children on modifiable factors prior to early intervention that are associated with better adaptive skills.¹⁰ The mean age of diagnosis was 35.5 months and 84% were boys. The study found that shorter waiting times for entry into regular early intervention services were associated with better adaptive skills at 6 and 7 years old.

Early identification of children on the autism spectrum leads to early intervention during a critical period for brain development, and better outcomes due to earlier correction of developmental delays.^{11,12} Singapore is on its fourth Enabling Masterplan 2030 to build a more inclusive society and to improve the quality of life of persons with disabilities.¹³ The Academy of Medicine, Singapore published evidence-based recommendations in the Clinical Practice Guidelines on ASD in Children and Adolescents for gold-standard assessment, intervention and management.¹⁴ The recent years have seen increasing awareness of autism in Singapore,¹⁵ and the number of EIPIC centres in Singapore has ballooned from 2 therapy hubs in the mid-2000s to 27 across the island today. However, details on diagnostic patterns and longer-term outcomes of autistic children are less clear. Having large-scale Singapore data on these topics would greatly facilitate national resource provision and planning, as ethnic, cultural, healthcare provision and educational framework differences can result in the need for tailored policymaking and resource planning in Singapore and elsewhere in Asia.

Aims

The primary aim of this study was to examine patterns of diagnosis, cognitive and adaptive functioning, and school placement outcomes in autistic children in Singapore. A secondary aim was to examine for earlier predictive factors of cognitive outcomes.

METHOD

The study was conducted in KK Women's and Children's Hospital, which is a tertiary hospital that provides specialist developmental paediatrics services and is the largest diagnostic centre for autism in Singapore. It receives preschool-age referrals—mostly from primary care, for a wide range of developmental concerns—who are first seen in a triage clinic. Children with concerns for autism are then referred to an autism clinic for a detailed autism-specific interview conducted by trained developmental behavioural paediatricians (DBPs), who would then order the Autism Diagnostic Observation Schedule (ADOS)^{16,17} (conducted later by an ADOS-trained clinical psychologist) if a child showed features of autism. The DBP would also give a clinical diagnosis of autism first if the child met the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria based on the detailed interview and direct observations. Some children might instead be referred directly from the triage clinic for a full assessment (interview and ADOS) in a single session by a psychologist. The ADOS is a standardised, semi-structured, play-based behavioural measure that is one of the gold standard assessment tools used to aid in the diagnosis of autism.^{16,17} The ADOS Module 1 is used for children who have limited verbal communication, Module 2 for those with phrase speech but who are not yet verbally fluent and Module 3 for verbally fluent children. The Toddler Module is not used for diagnostic purposes by this centre.

Retrospective data were manually extracted from medical records for children meeting the following inclusion criteria: (1) born in years 2008–2011 and (2) referred to the autism clinic for further evaluation, or (3) ever given a primary or secondary diagnosis of autism. The birth years were selected such that the most complete data on cognitive assessments and final school placement outcomes could be obtained. Data items extracted included demographic data, diagnostic methods and dates, results of any psychological assessments (whether conducted in-house or externally), early intervention attendance and school placement outcomes.

Data extraction was conducted from 2019 to 2020 by a team of 2 associate psychologists and 4 medical students who were trained on how to find and extract data items thoroughly from both electronic and paper medical records. Data cleaning and reliability checks were conducted by the associate psychologists and principal investigator, and there was no imputation of missing data or patient contact to obtain additional data.

As the study cohort underwent diagnostic assessments over a period when the DSM, Fourth Edition

(DSM-IV-TR) was replaced by the Fifth Edition (DSM-5), the diagnosis conferred to each child varied between DSM-IV-TR and DSM-5 diagnostic terms. For data analysis, and as per the DSM-5 workgroup recommendations, all children given a DSM-IV-TR diagnosis of autistic disorder, Asperger syndrome or pervasive developmental disorder - not otherwise specified were grandfathered into a diagnosis of ASD under the DSM-5. Similarly, the ADOS version used changed from the ADOS-Generic (ADOS-G) to the current ADOS-Second Edition (ADOS-2) over this period.

Children were classified to have a diagnosis of intellectual disability (ID) if a formal ID diagnosis was given by the psychologist conducting the assessment of cognitive and adaptive functioning, or a diagnosis of intellectual impairment if there was no formal diagnostic statement of ID but the child's full-scale intelligence quotient (FSIQ) was <70; if FSIQ was not available, then the majority of IQ subscale scores and/or the adaptive skill subscale scores was <70. School placement recommendations were extracted from formal psychological reports, whereas actual school placement outcome was based on clinical follow-up information.

To ensure that the study cohort strictly comprised children with an accurate diagnosis of autism, the following were used as exclusion criteria and hence removed from the sample prior to data analysis: (1) children who did not meet autism diagnostic criteria following a full psychological assessment and in whom no further concerns for autism were raised on follow-up, (2) children who were only seen for a single clinic visit and (3) children with no concerns for autism beyond the initial appointment (Fig. 1).

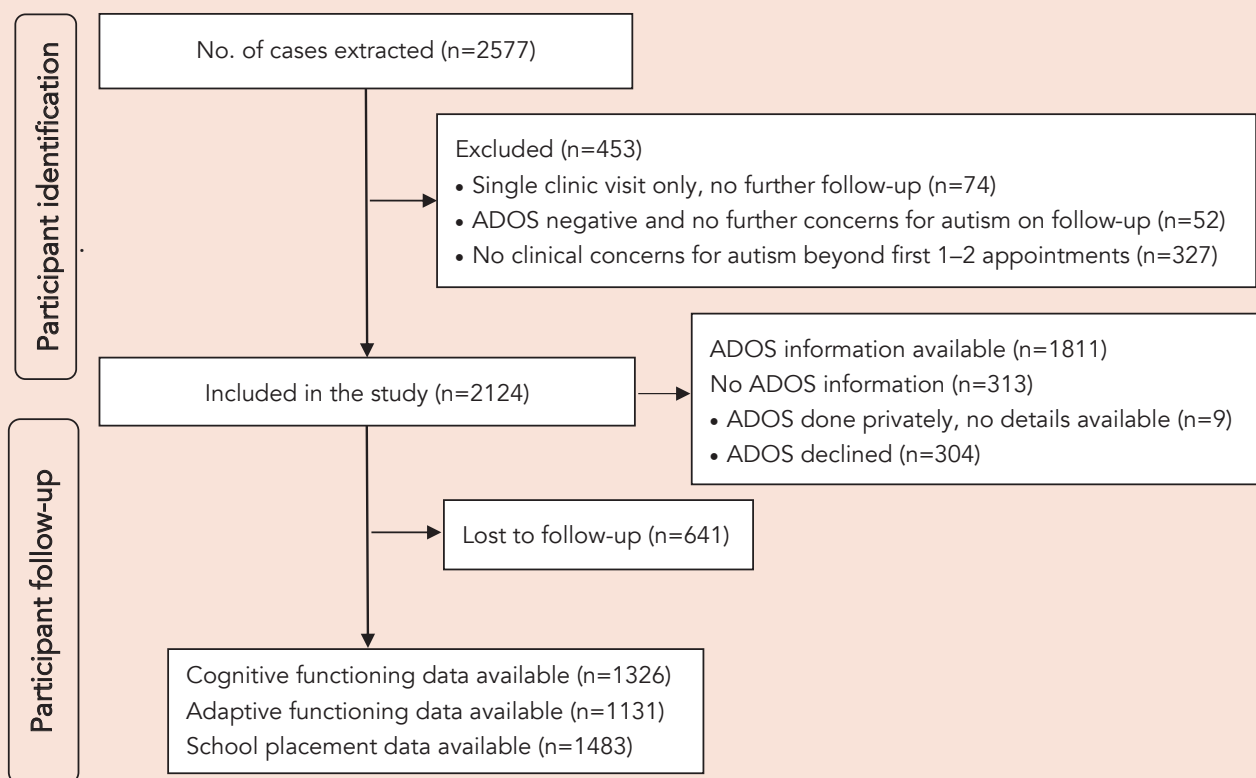
The study was approved by the SingHealth Centralised Institutional Review Board (2017/2103), and waiver of consent was granted in view of the retrospective and minimal risk nature of the study.

Statistical analyses were conducted using SPSS Statistics software version 28 (IBM Corp, Armonk, NY, US). Pearson correlation analyses were conducted to look for linear correlations between continuous variables, whereas independent t-tests and Pearson chi-squared (χ^2) tests were used to assess for differences between groups. Binomial logistic regression analyses were then conducted to analyse the relative contributions of proposed factors in predicting cognitive outcomes of ID/intellectual impairment versus (vs) no ID.

RESULTS

Using the inclusion criteria, 2577 children were identified, and data for all of these were extracted. After removing records for those who did not meet criteria for data analysis, a total of 2124 records

Fig. 1 Flowchart of study cohort.



ADOS: Autism Diagnostic Observation Schedule

were included (Fig. 1). Table 1 shows the demographic characteristics of the study cohort. The majority were male ($n=1754$, 82.6%), and there was a gradual increase in numbers diagnosed from years of birth 2008 to 2011. The ethnic group distribution was slightly different (fewer Chinese and more Others) to Singapore's resident population (74.1% Chinese, 13.5% Malay, 9.0% Indian, 3.4% Others)¹⁸ but was reflective of the ethnic composition of children seen under the national CDP services. Only 18 (0.8%) had genetic syndromes, of which 3 had no ID, and another 3 had no outcome data. They were not removed from the analyses as the numbers were very few.

Diagnostic data patterns

Table 2 shows the diagnostic and cognitive data of the study cohort. The mean (standard deviation [SD]) age at first clinic visit and first clinical diagnosis of autism were 3.23 (1.01) and 3.56 (1.14) years, respectively, with 718 (34.5%) being diagnosed before 3 years of age. The majority (81.0%) of children received a concordant clinical diagnosis before ADOS assessment was conducted. For those who only had a diagnosis of autism confirmed after the

psychological assessment, their clinical diagnoses were mainly global developmental delay or language delay.

A total of 1811 (85.2%) had ADOS assessments at a mean (SD) age of 4.16 (1.11) years, with most using Module 1 (70.9%). The vast majority had ASD or autistic disorder (97.4%). Three children were deemed to not meet full diagnostic criteria following their ADOS assessment, but eventually met clinical diagnosis on longer term follow-up when more symptoms emerged ($n=2$) or a private reassessment using additional diagnostic tools was conducted ($n=1$).

For children diagnosed by DSM-5 criteria, the levels of support for each domain (social communication and RRBs) are provided in Table 2. Most children were deemed to require level 2 (substantial) support for social communication and level 1 (some) support for RRBs.

Early intervention data patterns

Table 2 shows that the mean (SD) waiting time for EIPIC entry in a subgroup of 1194 children was almost a year. Of these, 390 were in an EIPIC centre for an average of about 2.5 years. However, this duration

Table 1. Demographic characteristics of study cohort (n=2124).

Demographic characteristics	No. (%)
Child	
Sex	
Male	1754 (82.6)
Female	370 (17.4)
Ethnicity	
Chinese	1410 (66.4)
Malay	284 (13.4)
Indian	208 (9.8)
Others	222 (10.5)
Year of birth	
2008	438 (20.6)
2009	549 (25.8)
2010	553 (26.0)
2011	584 (27.5)
Caregiver	
Highest educational level attained (mother), n=2086	
Primary	67 (3.2)
Secondary	473 (22.7)
A-level/diploma/ITE	552 (26.5)
Degree	842 (40.4)
Postgraduate	152 (7.3)
Highest educational level attained (father), n=2056	
Primary	65 (3.2)
Secondary	436 (21.2)
A-level/diploma/ITE	498 (24.2)
Degree	822 (40.0)
Postgraduate	235 (11.4)
Combined monthly household income (SGD), n=2077	
<3000	309 (14.9)
3000–4999	562 (27.1)
5000–9999	886 (42.7)
>10,000	320 (15.4)

ITE: Institute of Technical Education; SGD: Singapore dollar

should be interpreted with caution as there were no clear EIPIIC end dates for the other 804.

Cognitive and adaptive data patterns with school placement outcomes

There were 641 (30.2%) children who were lost to follow-up for school placement assessments and outcomes (Fig. 1). A total of 1285 (60.5%) and 1131 (53.2%) of the study cohort had information on cognitive and adaptive assessment results, respectively (Table 2). The mean (SD) age at which a cognitive assessment was conducted was 5.61 (0.76) years, and the most common assessment tool was the Wechsler Preschool and Primary Scale of Intelligence (79.0%). Some children with substantial developmental delays or behavioural difficulties could not complete a cognitive assessment. Instead, 143 (11.3%) were tested using developmental scales and 34 (2.7%) had testing abandoned.

The number of children with normal cognitive functioning was 622 (46.9%) and included 101 children with no clinical concerns for cognitive impairment and were deemed by the DBP to not need formal cognitive assessment. Another 222 (16.7%) had non-verbal intelligence quotient (IQ) subscale scores in the normal range but associated with a verbal IQ score of <70, indicating verbal impairment. Additionally, 220 (16.6%) had mild and 262 (19.8%) had moderate-severe cognitive impairment or ID. Mean Vineland Adaptive Behavior Scale scores ranged in the 70s. As expected, there was a high positive correlation between cognitive functioning and adaptive skill scores ($r=0.72$, $P<0.001$, $n=1081$).

School placement recommendations were recorded for 1282 (60.4%) children (Table 3). Actual school placement outcome was available for 1483 (69.8%) and indicated that 681 (45.9%) progressed to mainstream school, 323 (21.8%) entered SPED schools offering the national curriculum, and 479 (32.3%) went to customised curriculum SPED schools. Moreover, 16.8% obtained a deferment from commencement of Primary 1.

Predictors of cognitive outcomes

Although duration of EIPIIC attendance was considered one of the potential predictors of cognitive outcomes, the start and end dates of EIPIIC were available in only 390 children. Furthermore, the information collected was limited in that attendance rates and any breaks in the programme (e.g. due to holidays or illness) were not accounted for. Correlation analyses also showed that children attended EIPIIC for longer if they received a clinical diagnosis of autism at a younger age ($r=-0.325$, $P<0.001$), had higher ADOS scores (ADOS-G $r=0.153$,

Table 2. Diagnostic, early intervention, cognitive and adaptive data of study cohort.

Diagnostic data	No. (%)	Mean (SD)
Age at first clinic visit, n=2124		3.23 (1.01)
Age at first clinical diagnosis in years, n=2084		3.56 (1.14)
Diagnosed before 3 years of age	718 (34.5)	
When the first clinical diagnosis was made, n=2081		
Before ADOS: new case consultation	1567 (75.2)	
Before ADOS: autism clinic consultation	121 (5.8)	
Only once ADOS was done	393 (19.0)	
Age at ADOS in years, n=1809		4.16 (1.11)
DSM version, n=1806		
DSM-IV-TR	1204 (66.7)	
DSM-5	602 (33.3)	
ADOS version, n=1806		
ADOS-G	732 (40.5)	
ADOS-2	1074 (59.5)	
ADOS module, n=1803		
Toddler module	1 (0.1)	
Module 1	1278 (70.9)	
Module 2	468 (26.0)	
Module 3	56 (3.1)	
Diagnosis given after ADOS assessment, n=1811		
ASD, no subtype	781 (43.1)	
Autistic disorder	984 (54.3)	
Asperger syndrome	3 (0.2)	
PDD-NOS	40 (2.2)	
Not ASD	3 (0.2)	
Social communication level of support, n=581		
Level 1	142 (24.4)	
Level 2	282 (48.5)	
Level 3	157 (27.0)	
RRBs level of support, n=581		
Level 1	269 (46.3)	
Level 2	222 (38.2)	
Level 3	90 (15.5)	
ADOS-G scores, n=712		
Communication		5.65 (1.97)
Reciprocal social interaction		10.46 (2.89)

Table 2. Diagnostic, early intervention, cognitive and adaptive data of study cohort. (Cont'd)

Diagnostic data	No. (%)	Mean (SD)
Social communication total		16.12 (4.19)
Imagination/creativity		2.66 (1.26)
Stereotyped behaviours/restricted interests		2.43 (1.53)
ADOS-2 scores, n=1049		
Social affect		13.89 (3.87)
Restricted and repetitive behaviour		3.50 (2.02)
Overall		17.39 (4.64)
Comparison score		6.98 (1.58)
Early intervention data		
Waiting time for EIPIC entry in days, n=1194		334.9 (210.9)
Duration in EIPIC in days, n=390		946.6 (412.7)
Cognitive and adaptive data		
Age at cognitive assessment in years, n=1285		5.61 (0.76)
Cognitive assessment tool used, n=1269		
WPPSI	1003 (79.0)	
WISC	8 (0.6)	
SB-5	80 (6.3)	
BAS-3	1 (0.1)	
Griffith Mental Development Scales	1 (0.1)	
Bayley Scales of Infant and Toddler Development	142 (11.2)	
Testing abandoned	34 (2.7)	
Level of cognitive functioning, n=1326		
Normal ^a	622 (46.9)	
Normal non-verbal IQ but verbal impairment	222 (16.7)	
Mild impairment	220 (16.6)	
Moderate-severe impairment	262 (19.8)	
Adaptive functioning (Vineland), n=1131		
Communication standard score		79.3 (19.6)
Daily Living Skills standard score		77.6 (16.8)
Socialisation standard score		71.7 (12.8)
Motor standard score		80.4 (13.9)
Adaptive Behaviour Composite standard score		74.6 (14.7)

ADOS: Autism Diagnostic Observation Schedule; ADOS-2: ADOS-Second Edition; ADOS-G: ADOS-Generic; ASD: autism spectrum disorder; BAS-3: British Ability Scales, Third Edition;

DSM: Diagnostic and Statistical Manual of Mental Disorders; EIPIC: Early Intervention Programme for Infants and Children;

IQ: intelligence quotient; PDD-NOS: pervasive developmental disorder - not otherwise specified; RRBs: restricted, repetitive behaviours;

SB-5: Stanford-Binet Intelligence Scales,

Fifth Edition; SD: standard deviation; TR: text revision; Vineland: Vineland Adaptive Behavior Scale; WISC: Wechsler Intelligence Scale for Children; WPPSI: Wechsler Preschool and Primary Scale of Intelligence.

^aIncludes 101 children with no clinical concerns for cognitive impairment, and formal cognitive assessment was not required.

Note: 1081 children had data on both cognitive and adaptive functioning.

Table 3. School placement recommendations and outcome of study cohort.

Recommendations and outcomes	No. (%)
School placement recommendation, n=1282	
Mainstream school	252 (19.7)
SPED school offering national curriculum	502 (39.1)
SPED school offering customised curriculum	528 (41.2)
School placement outcome, n=1483	
Mainstream school	681 (45.9)
SPED school offering national curriculum	323 (21.8)
SPED school offering customised curriculum	479 (32.3)
Children placed in mainstream school despite an original placement recommendation of a SPED school offering customised curriculum	50 (3.4)
Deferred primary one, n=2124	356 (16.8)
SPED: special education	

$P=0.034$; ADOS-2 $r=0.233$, $P=0.002$), or had lower Vineland scores ($r=-0.246$, $P<0.001$), indicating that longer EIPIC attendance was likely associated with pre-existing higher support needs. Hence, duration of EIPIC attendance was not used in further regression analyses. Additionally, some children would have attended other forms of early intervention instead of EIPIC, and these data were not available to be extracted. Furthermore, the therapy that a child would receive differs depending on each child's unique presentation of autism symptoms and severity, overall making it impossible to analyse early intervention received as a predictor of cognitive outcomes.

Waiting time for entry into EIPIC was not correlated with Vineland Adaptive Behavior Composite scores or ADOS scores but was negatively correlated with age at first clinic visit ($r=-0.25$, $P<0.001$, $n=1194$), indicating that children presenting at older ages were more likely to be given expedited entry into EIPIC. Mean (SD) waiting time for entry into EIPIC was also no different between children with ID vs no ID (334.9 [227.8] vs 340.1 [216.2] days, $P=0.739$).

Table 4 shows the factors associated with whether a child was more likely to have ID or mild/moderate-severe impairment in cognitive functioning. Age at first clinical diagnosis and sex were not significant.

Table 5 shows 2 binomial logistic regression models examining predictors of ID or intellectual impairment. As parents' highest educational levels attained were strongly correlated with each other and with combined monthly household income, to avoid multicollinearity, only mother's educational level was retained in the regression models. For those assessed using the DSM-IV-TR criteria, ADOS-G scores were

used, whereas for those assessed using the DSM-5, levels of support were used. DSM-5 levels of support for social communication and RRBs were used as separate factors as some children may have very discrepant levels of support between the 2 domains. Both models were statistically significant.

In those diagnosed on the DSM-IV-TR, mother's educational level and higher ADOS-G scores in both domains were significant predictors of intellectual impairment (χ^2 [6]=97.406, $P<0.001$). While adjusted odds ratios showed that there seemed to be a trend towards minority races to be at increased odds of a child having intellectual impairment, these did not reach statistical significance in the model. Approximately 23.2% of the variability is accounted for by the model. However, in those diagnosed on the DSM-5, race and DSM-5 social communication level of support, but not RRBs level of support, were significant predictors of intellectual impairment (χ^2 [8]=111.374, $P<0.001$). Children given level 3 (very substantial) support for their social communication domain had 14.9 times the odds of having intellectual impairment, and children of a minority racial group had 2.8–5.2 times the odds. Approximately 32.9% of the variability is accounted for by the model.

DISCUSSION

This is the first large-scale study to examine patterns of diagnosis, cognitive and adaptive functioning in a clinically representative sample of autistic children in Singapore, and to explore predictors of cognitive outcomes. Despite being retrospective, detailed clinical data were obtained from 2124 autistic children with follow-up information until 9–12 years

Table 4. Factors associated with a diagnosis of intellectual disability or intellectual impairment.

Descriptive	No ID	ID or intellectual impairment		
Continuous variables	Mean (SD)	Mean (SD)	P value	Cohen's ω
Age at first clinical diagnosis in years	3.72 (1.18) n=830	3.63 (1.22) n=503	0.202	0.073
ADOS-G Comm+SI total	15.02 (4.06) n=343	17.23 (4.02) n=197	<0.001 ^b	-0.546
ADOS-G SBRI total	1.96 (1.34) n=340	3.02 (1.61) n=195	<0.001 ^b	-0.730
ADOS-2 Social Affect total	12.54 (3.68) n=441	15.39 (3.31) n=291	<0.001 ^b	-0.806
ADOS-2 RRB total	3.18 (1.96) n=441	3.96 (1.88) n=291	<0.001 ^b	-0.405
ADOS-2 Overall total	15.72 (4.34) n=441	19.35 (3.92) n=291	<0.001 ^b	-0.869
Vineland Communication standard score	91.14 (12.37) n=625	64.21 (16.70) n=455	<0.001 ^b	1.877
Vineland Daily Living Skills standard score	86.60 (12.67) n=625	65.87 (14.58) n=455	<0.001 ^b	1.536
Vineland Socialization standard score	78.20 (10.98) n=625	63.12 (10.01) n=454	<0.001 ^b	1.424
Vineland ABC standard score	83.15 (10.88) n=626	63.51 (11.62) n=458	<0.001 ^b	1.754
Categorical variables	No. (%)	No. (%)	P value	Cohen's ω
Sex			0.416	0.024
Male	695 (83.1)	412 (81.3)		
Female	141 (16.9)	95 (18.7)		
Ethnicity			<0.001 ^b	0.204
Chinese	649 (77.6)	301 (59.4)		
Malay	87 (10.4)	117 (23.1)		
Indian	53 (6.3)	51 (10.1)		
Others	47 (5.6)	38 (7.5)		
Highest educational level attained (mother)			<0.001 ^b	0.173
Primary	14 (1.7)	28 (5.6)		
Secondary	181 (22.0)	157 (31.6)		
A-level/diploma/ITE	237 (28.9)	135 (27.2)		
Degree	338 (41.2)	156 (31.4)		
Postgraduate	51 (6.2)	21 (4.2)		

Table 4. Factors associated with a diagnosis of intellectual disability or intellectual impairment. (Cont'd)

Descriptive	No ID	ID or intellectual impairment		
Categorical variables	No. (%)	No. (%)	P value	Cohen's ω
Highest educational level attained (father)			<0.001^b	0.163
Primary	20 (2.5)	25 (5.1)		
Secondary	158 (19.6)	152 (31.1)		
A-level/diploma/ITE	214 (26.5)	123 (25.2)		
Degree	338 (41.8)	155 (31.8)		
Postgraduate	78 (9.7)	33 (6.8)		
Combined monthly household income (SGD)			<0.001^b	0.200
<3000	96 (11.8)	116 (23.5)		
3000–4999	207 (25.3)	155 (31.4)		
5000–9999	372 (45.5)	179 (36.2)		
>10,000	142 (17.4)	44 (8.9)		
Social communication level of support			<0.001^b	0.428
Level 1 "Some"	100 (38.0)	19 (12.7)		
Level 2 "Substantial"	134 (51.0)	60 (40.0)		
Level 3 "Very substantial"	29 (11.0)	71 (47.3)		
RRBs level of support			<0.001^b	0.272
Level 1 "Some"	151 (57.4)	49 (32.7)		
Level 2 "Substantial"	87 (33.1)	62 (41.3)		
Level 3 "Very substantial"	25 (9.5)	39 (26.0)		

ABC: Adaptive Behaviour Composite; ADOS: Autism Diagnostic Observation Schedule; ID: intellectual disability; ITE: Institute of Technical Education; RRB: restricted, repetitive behaviours; SBRI: stereotyped behaviours and restricted interests; SD: standard deviation; SGD: Singapore dollar; SI: social interaction

Note: ^a $P < 0.05$, ^b $P < 0.01$ (2-tailed). Cohen's d effect sizes: 0.2 = small, 0.5 = medium, 0.8 = large, 1.2 = very large. Cohen's ω effect sizes: 0.1 = small, 0.3 = medium, 0.5 = large. For ADOS-G and ADOS-2 scores, children would only have been diagnosed using one or the other.

old. There was a gradual increase in the numbers of children with autism born in each year from 2008 to 2011, possibly reflecting improved identification of autism over the years, as well as a true increase in prevalence. Other data from our department have shown a substantial increase in annual numbers of children presenting with concerns for autism, from 540 in 2014, to 936 in 2020 and stabilising at around this figure since then. This is consistent with the rising prevalence of autism reported elsewhere.⁴

The mean (SD) age of first clinical diagnosis of autism was 3.56 (1.14) years, similar to a paper on 206 children who underwent diagnostic assessments for autism from 2012 to 2013,¹⁹ and not too different from studies by Lian and Ho and Aishworiya et al.^{9,10}

Interestingly, fewer children (34.5%) were diagnosed before 3 years of age compared to Bernard-Opitz's 2001 paper (60%), although that study was on a small, selected group of parents who completed a survey and the children appeared to have more severe autism, which might explain their earlier age of diagnosis. More importantly, majority (81.0%) received a concordant clinical diagnosis, given 0.6 years (7.2 months) before ADOS assessment was conducted. This emphasises the reliability of using a careful clinical diagnosis to initiate care plan discussions with caregivers and obtain access to early intervention. Currently, preschool children in Singapore can enter early intervention programmes for autism based on a clinical diagnosis of autism given by a DBP, even if a full psychological

Table 5. Logistic regression analysis of predictors of intellectual disability/impairment for those assessed using DSM-IV-TR criteria (n=524) and DSM-5 criteria (n=405).

Variables	Wald	aOR	95% CI for aOR	P value
Assessed using DSM-IV-TR				
Race				
Chinese	6.61			0.085
Malay	2.59	1.64	0.90–3.00	0.107
Indian	2.83	1.85	0.90–3.79	0.092
Others	2.43	1.91	0.85–4.30	0.119
Mother's educational level	4.12	0.86	0.74–1.00	0.042^a
ADOS-G Comm+SI total	23.70	1.13	1.08–1.19	<0.001^b
ADOS-G SBRI total	37.39	1.53	1.33–1.75	<0.001^b
Constant	32.85	0.04		<0.001^b
-2 Log likelihood 590.046; Nagelkerke R ² =0.232; $\chi^2(6)=97.406$, P<0.001				
Assessed using DSM-5				
Race				
Chinese	30.00			<0.001^b
Malay	10.94	2.82	1.52–5.20	0.001^b
Indian	16.69	5.19	2.36–11.44	<0.001^b
Others	11.73	4.54	1.91–10.79	0.001^b
Mother's educational level	3.64	0.84	0.71–1.01	0.056
SC level of support				
Level 1	32.90			<0.001^b
Level 2	5.00	2.14	1.10 – 4.16	0.025^a
Level 3	31.08	14.94	5.77 – 38.64	<0.001^b
RRBs level of support				
Level 1	2.08			0.353
Level 2	0.29	1.17	0.66 – 2.10	0.591
Level 3	0.92	0.63	0.24 – 1.63	0.339
Constant	10.400	0.23		0.001^b
-2 Log likelihood 420.375; Nagelkerke R ² =0.329; $\chi^2(8)=111.374$, P<0.001				

ADOS: Autism Diagnostic Observation Schedule; aOR: adjusted odds ratio; CI: confidence interval; SBRI: stereotyped behaviours and restricted interests; SC: social communication; SI: social interaction; RRB: restricted, repetitive behaviours

^aP<0.05.

^bP<0.01.

P values in bold indicate significance.

assessment has not been conducted yet. Hence, an accurate clinical diagnosis is vital for appropriate intervention programme referrals to be made.

Currently, the routine practice in Singapore is for all preschoolers with suspected autism to undergo a diagnostic assessment using the ADOS and a detailed autism-specific interview. This has led to resource constraints and long waiting times for psychological assessments, similar to that reported elsewhere. The 2023 Clinical Practice Guidelines on ASD in Children and Adolescents has highlighted that a single-clinician approach to diagnosing autism may be considered, provided that certain criteria on the experience of the clinician and the diagnostic procedure are met.¹⁴ The guidelines also state that standardised assessment tools are not always necessary, particularly in children with very clear features of autism. Given again that 81% of children with autism in this study received a concordant clinical diagnosis before ADOS was conducted, it is highly likely that a significant number of autistic children can be reliably diagnosed via a single-clinician approach, with consequential easing of the pressure on autism diagnostic services nationally. Careful selection of children who may be diagnosed this way is advised, but discussion of the selection criteria is outside the remit of this paper. However, it is noteworthy that as this study was conducted in a national CDU, most children in the sample underwent an ADOS Module 1 at a preschool age and the diagnostic concordance rate may be different for children detected later or with milder symptoms.

Only 85.2% of the cohort underwent the ADOS, which is higher than previously reported.⁹ The data included private diagnostic assessments for which data fields could be extracted from a psychological report. The main reasons for not having the ADOS done included caregivers declining the assessment, or care being transferred elsewhere, for whom school placement outcome data were usually also missing. It is recognised that autism diagnostic assessments are sometimes conducted during school-age years for some children in whom caregivers initially declined an assessment. This is usually due to a child having ongoing support needs, often as social and academic demands start to outweigh the child's abilities. The fact that 3 children did not meet diagnostic criteria following their ADOS assessment but eventually achieved clinical diagnosis later, highlights the importance of long-term follow-up for children in whom there remain ongoing concerns for social communication, behavioural or sensory difficulties.

Although most autistic children in Singapore undergo formal cognitive testing at 5–6 years of age to facilitate school placement, these data have highlighted that approximately 14% of children were unable to complete a standardised cognitive assessment, and either had testing abandoned or

required alternative tests (developmental or adaptive scales) to gauge their needs. However, for those who were able to complete cognitive assessments, almost half (46.9%) had normal functioning, and only 36.4% were confirmed to have intellectual impairment. This is quite different to the previous 2012 publication, which indicated that only 14% of autistic children in Singapore were considered of mainstream school ability.⁹ The current study cohort is more than 10 times the size of the previous study, and outcome data were tracked for a much longer follow-up duration, hence these findings are likely to be more accurate and hold important implications for SPED resource allocation at a national level. More children on the autism spectrum with milder needs are now being diagnosed compared to before, thus there are likely to be more children with autism without intellectual impairment in our sample.

Another important finding is that 16.7% had IQ subscale scores, which were in the normal range but associated with a verbal IQ score of <70, indicating significant verbal impairment. This is a group of autistic children who could potentially be supported more effectively towards better outcomes if their language needs are supported, for example through speech-language therapy or the increased use of visual-based pedagogical methods. SPED schools offering the national curriculum may offer this group of children the support needed to navigate the language-rich mainstream curriculum. Approximately two-thirds of children went on to attend schools that offered the national curriculum, whether in a mainstream or SPED setting. Although 16.8% obtained a deferment from commencement of Primary One, with the changes in the deferment processes of the Ministry of Education Singapore as of 2024,²⁰ this figure may change in the future.

The limited data available on the 390 children with EIPIIC attendance information did show that children attended EIPIIC for longer if they received a clinical diagnosis of autism at a younger age, had higher ADOS scores or had lower Vineland scores. These factors were likely to be reflective of them having higher support needs, resulting in them presenting earlier to services. As opposed to Aishworiya's paper, waiting time for entry into EIPIIC was not correlated with Vineland Adaptive Behavior Composite scores or ADOS scores, but was negatively correlated with age at first clinic visit, indicating that children presenting at older ages were more likely to need expedited entry into EIPIIC. However, that study was on a smaller cross-sectional sample, included only children with an ADOS-confirmed diagnosis of autism, and collected Vineland data at an older age.

In the logistic regression models, factors which were significant in predicting ID or intellectual impairment included lower mother's educational level, higher

ADOS scores and higher DSM-5 social communication level of support. Some of this information could be used to guide clinicians and begin conversations with parents about educational options for their child at appropriate times of school transition. Interestingly, race was also a significant predictive factor for ID or intellectual impairment in the DSM-5 regression model, with a trend towards significance in the DSM-IV-TR model. A separate paper has been published focusing on the ethnic group differences found in this same cohort of children.²¹

Limitations

Although the sample size was large, this was a single-centre study. However, this centre sees 70–80% of Singapore's CDP caseload. As this was a retrospective study conducted on available medical records data, there might be potential selection bias in that children referred for diagnostic evaluations at a preschool age may have more obvious symptoms of autism already, while those with milder symptoms may only be diagnosed if they continued to attend follow-up appointments. A total of 641 (30.2%) children were lost to longer term follow-up and hence did not contribute data to cognitive/adaptive assessments and school placement outcomes. Although the accuracy of the retrospective data is limited to the available information in each child's records, most children with longer-term follow-up had full psychological assessment results available. However, there was limited information on the duration of EIPIIC attendance as well as other interim or non-EIPIIC intervention received, hence it was not possible to evaluate early intervention received as a predictor of cognitive outcomes. There was also limited information on family history of autism. Another limitation is that there is a time lag between age at first clinic visit/first clinical diagnosis and age of ADOS of about 0.93/0.6 years respectively, meaning that the autism severity as captured by the ADOS might not be very representative of baseline severity. Finally, data were extracted when the children in the cohort were aged between 9 and 12 years, and hence further follow-up data beyond that are not available. It is not known how many children who started out in mainstream schooling eventually needed to be transferred to a SPED school, or vice versa. There was scant data on older-age onset co-occurring conditions, and the study cannot extrapolate to any conclusions on adult outcomes.

CONCLUSION

This study is one of the largest to track school-age outcomes of a sizeable population of autistic children in Singapore. In the absence of any other national

prevalence or outcome data, the current study provides useful insights into the patterns of diagnosis, cognitive and adaptive functioning, and school placement outcomes. Such information can be useful for resource planning purposes for national agencies involved in providing autism diagnostic, early intervention and educational services.

Ethics statement

This retrospective study was approved by the SingHealth Centralised Institutional Review Board (2017/2103). Informed consent was waived, as it involved no participant contact and had no effect on their usual care.

Declaration

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Post-exposure prophylaxis and follow-up in children and young persons presenting with sexual assault

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ABSTRACT

Introduction: Paediatric sexual assault (SA) victims should be assessed for post-exposure prophylaxis (PEP) to mitigate the risk of sexually transmitted infections (STIs). We describe the clinical characteristics of children and young persons (CYPs) presenting with SA at KK Women's and Children's Hospital in Singapore, viral PEP (human immunodeficiency virus [HIV] and hepatitis B virus [HBV]) prescribing practices, and STI evaluation at follow-up.

Method: Medical records of CYPs ≤16 years who presented with SA between January 2022 and August 2023 were reviewed, including assault and assailant characteristics, baseline and follow-up STI screening, PEP prescription, adherence and follow-up attendance. CYPs with SA in the preceding 72 hours by HIV-positive or HIV-status unknown assailants with high-risk characteristics were eligible for HIV PEP.

Results: We analysed 278 CYPs who made 292 SA visits. There were 40 (13.7%) CYPs eligible for HIV PEP, of whom 29 (82.9%) received it. Among those tested at baseline, 9% and 34.9% of CYPs tested positive for *Chlamydia trachomatis* and *Gardnerella vaginalis*, respectively. None tested positive for *Neisseria gonorrhoeae*, *Trichomonas vaginalis*, HIV, HBV or hepatitis C. Majority of CYPs tested were HBV non-immune (n=167, 67.6%); only 77 (46.1%) received the vaccine. Out of 27 CYPs eligible for HBV PEP with immunoglobulin, only 21 (77.7%) received immunoglobulin. A total of 37 CYPs received HIV PEP, including 8 who were retrospectively deemed ineligible. Only 10 (27%) completed the course. Overall, 153 (57.7%) CYPs attended follow-up, and none seroconverted for HIV or HBV.

Conclusion: We report suboptimal rates of HBV post-exposure vaccination, and low compliance to HIV PEP and follow-up among paediatric SA victims. Factors contributing to poor compliance should be examined to optimise care for this vulnerable population.

Keywords: hepatitis B, HIV, infectious diseases, paediatrics, sexual assault

CLINICAL IMPACT

What is New

- We report a large proportion of HBV non-immunity among our paediatric sexual assault victims.
- There was low compliance to HIV post-exposure prophylaxis and follow-up in our population.

Clinical Implications

- Rates of opportunistic HBV vaccination among HBV non-immune victims can be improved.
- Further studies should examine factors relating to non-compliance to devise interventions to optimise care for these patients.

INTRODUCTION

Sexual assault (SA) in the paediatric population is an under-recognised but significant public health burden.^{1,2} Effective management requires addressing the psychosocial issues involved and mitigating the risks of transmission of sexually transmitted infections (STIs) such as human immunodeficiency virus (HIV) and hepatitis B virus (HBV) with the appropriate use of post-exposure prophylaxis (PEP).¹

As the occurrence of STI transmission in children attributable to SA is low,^{3,5} the question is whether current strategies used to risk-stratify patients to determine the need for PEP, particularly for HIV, are well-informed.^{4,6} Making a decision is often challenging due to limited information on assailant risk,^{3,6} and lack of physician consensus beyond the first 72 hours of presentation post-assault.³ Additionally, despite increased accessibility to healthcare resources and advancements in sexual health education, compliance to HIV PEP remains poor.^{3,5,6}

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The primary objectives of our study were to describe the clinical characteristics of children and young persons (CYPs) presenting with SA in a multi-ethnic paediatric population in Singapore, and to describe PEP prescribing practices. We aimed to describe rates of medication adherence and follow-up, as well as identify gaps in care for future improvement.

METHOD

Study design, patient population and setting

A clinical audit was conducted using electronic medical records of CYPs aged ≤ 16 years who presented to the children's emergency (CE) of KK Women's and Children's Hospital (KKH), a tertiary paediatric institution in Singapore, between January 2022 to August 2023. CYPs with the CE diagnosis codes of "sexual abuse" and "sexual assault" were captured. Cases lacking sufficient information or determined not to involve assault were excluded. We defined sexual assault as any non-consensual sexual act, with or without penetration, including touching of ano-genitalia or breasts, which may have occurred because of physical or psychological coercion on victims, or any sexual act involving CYPs aged ≤ 16 years who cannot consent or understand the consequences of their choice because of their age.⁷

Data collection and variables

Data collected included CYP demographics, medical history, assault and assailant characteristics, results of baseline and follow-up STI screening, PEP prescription, adherence and follow-up. Information about the CYPs' social background was also collected to determine predisposing and protective social factors for PEP compliance. Predisposing social factors for poor PEP compliance included the presence of family history of mental health issues, domestic violence, high-risk behaviours (smoking, alcohol, vaping, self-harm) and/or residence in Girls' or Boys' Home (indicating previous juvenile delinquency or a complicated home environment).² Protective factors included regular follow-up with a medical social worker, psychologist or external community agency, active school attendance and/or presence of an intact family (defined as a complete nuclear family with paternal and maternal figures irrespective of biological relationship).^{2,7,8}

Definitions

CYPs were categorised into 2 groups based on eligibility for HIV PEP, determined by timing of presentation, the nature of SA exposure and assailant risk factors. CYPs eligible for HIV PEP were defined as CYPs with a penetrating SA encounter (genital-

genital, genital-anal, genital-oral) presenting within 72 hours and fulfilling the following criteria: (1) known HIV-positive assailant; (2) unknown HIV-status assailant aged >18 years; (3) assailant with multiple sexual partners or multiple assailants during the assault; (4) assailant who is a known intravenous drug user; or (5) male assailant known to have sex with men. CYPs were deemed to be HBV non-immune and eligible for vaccination if their hepatitis B surface antibody (HBsAb) levels were below 10 mIU/mL. Eligibility for HBV immunoglobulin (HBIG) as HBV PEP was determined based on the CYP's immune status, assailant HBV status and if unknown, high-risk assailant characteristics or high-risk exposures as defined in the guide to assess for HIV PEP eligibility (used as a proxy indicator) (Supplementary Appendix S1). This was adapted from guidelines on PEP by the Centres for Disease Control and Prevention (CDC) and World Health Organization (WHO).^{9,10}

At our institution, CYPs presenting with SA undergo a thorough medical evaluation and follow a protocol for STI screening (Supplementary Appendix S2), evaluation for PEP eligibility and outpatient follow-up (Supplementary Appendix S1). HIV PEP is offered to CYPs fulfilling the guiding points for HIV PEP eligibility who present within 72 hours, with varying regimen according to different weight bands (Supplementary Appendix S1). CYPs seen after 72 hours and before 7 days are reviewed on a case-by-case basis for eligibility for HIV PEP depending on the ascertained degree of risk of exposure for HIV. An initial 14-day medication supply is provided, followed by continuation of post-outpatient infectious disease specialist review. Follow-up serologies are routinely performed at 2 and 6 months post-assault or earlier if clinically indicated. Additionally, all CYPs are referred to a medical social worker. All CYPs undergo a comprehensive biopsychosocial assessment assessing for flashbacks and trauma symptoms, with further referral to community support services or a trauma-informed psychologist as needed.

Statistics

Pearson's chi-square or Fisher's Exact tests were used to evaluate for differences between 2 categorical variables. Non-normal continuous variables were expressed as medians with interquartile ranges. STATA version 18 (StataCorp, College Station, Texas, US) was used for statistical analysis. A *P* value of <0.05 was taken to be statistically significant.

This study was performed as part of a clinical audit for quality improvement; requirement for informed consent was waived by KK Women's and Children's Hospital, SingHealth (Reference number: KKH-2023-05-00148).

RESULTS

Demographics of CYPs presenting with sexual assault

Between January 2022 and August 2023, 297 CYPs made 325 visits for SA. Nineteen CYPs were found to have inconclusive evidence for SA and excluded from analysis. The remainder comprised 278 CYPs, accounting for 292 CE visits for SA, of whom 281 (96.2%) were females and the median age was 14.0 years (Table 1). A total of 189 (64.7%) CYPs presented more than 1 week post-SA. Among them, 129 (44.2%) were Malay and 122 (41.8%) were Chinese. Assault and assailant characteristics are detailed in Table 1. Penile-vaginal exposure was most common (n=180, 61.6%). Barrier contraception was reported in 21 (7.2%) of CYPs (Table 1). No assailants were known to be HIV- or HBV-positive. After retrospectively applying the criteria described in the Methods, 40 CYPs (13.7%) were eligible for HIV PEP.

Baseline screening and post-exposure prophylaxis for *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Trichomonas vaginalis*

Among 251 (85.9%) CYPs who received *Chlamydia trachomatis* and *Neisseria gonorrhoeae* polymerase chain reaction tests, 27 (9.2%) tested positive for *Chlamydia trachomatis* and none for *Neisseria gonorrhoeae* (Table 2). No cases of *Trichomonas vaginalis* were detected among those tested (n=214, 73.3%). Three CYPs tested positive on the *Treponema pallidum* particle agglutination assay and chemiluminescent microparticle immunoassay but had subsequent negative Venereal Disease Research Laboratory test results and *Treponema pallidum* antibodies, indicating false positives (Table 2). Among the 281 females, 196 (69.8%) received baseline pregnancy testing (Table 2 and Supplementary Appendix S2), with 5 (1.7%) testing positive, 4 (80%) of whom continued their pregnancies.

There were 85 (29.1%) CYPs who received empirical oral azithromycin against *Chlamydia trachomatis*, 68 (23.2%) who received parenteral ceftriaxone for prophylaxis against *Neisseria gonorrhoeae*, and 75 (25.7%) who received oral metronidazole for prophylaxis against *Trichomonas vaginalis*.

Baseline testing and post-exposure prophylaxis for hepatitis B (HBV)

Fig. 1 summarises the baseline HBV and HIV serological status of our population, PEP prescription and subsequent follow-up. Two hundred and forty-seven (84.6%) CYPs received a baseline HBV serology where none had detectable hepatitis B surface antigen (HBsAg). One hundred and sixty-seven (67.6%) CYPs were found to be HBV non-immune, of whom 102 (61%) were offered HBV vaccination

(Fig. 1). Of these 102 patients, 77 (75.0%) received the vaccine within our institution while the remaining 25 (24.5%) were instructed to receive HBV vaccine from primary care clinics. Among the 40 CYPs eligible for HIV PEP, there were 27 (67.5%) CYPs who were also HBV non-immune; 23 were given the HBV vaccine, 3 were instructed to receive the vaccine at a polyclinic and 1 absconded from the CE. Twenty (74.0%) out of 27 HIV PEP-eligible, HBV non-immune CYPs were also eligible for HBIG, due to the high-risk nature of the SA or the assailant (Fig. 1). Among the 252 CYPs ineligible for HIV PEP, 140 (67.6%) were HBV non-immune but only 75 (53.6%) were offered vaccination, of whom 54 (72.0%) received the vaccine at our institution. No person who received HBV immunoglobulin reported any adverse events. Of 77 HBV non-immune CYPs who received a HBV vaccine, 37 (48.0%) received a follow-up HBV serology test, of whom 33 (89.2%) achieved HBV immunity. All 37 CYPs with follow-up HBV serology tests were HBsAg-negative.

Baseline testing and post-exposure prophylaxis for HIV

Of 245 (83.0%) CYPs who had a baseline HIV serology, none tested positive (Fig. 1). Among the 40 CYPs eligible for HIV PEP, 35 (87.5%) were offered HIV PEP and 29 (72.5%) accepted it (Fig. 1). Six eligible CYPs declined due to financial constraints or parental perception that the assault was low risk. Five CYPs retrospectively deemed eligible were not offered HIV PEP due to initially underestimated risk or details that were disclosed only later. There were 9 (3.5%) CYPs retrospectively assessed to be ineligible for HIV PEP who were offered PEP—all of whom had presented within 72 hours post-SA but did not report additional high-risk assailant or assault characteristics. Of these 9 CYPs, 8 (88.8%) accepted the recommendation. All CYPs offered HIV PEP were female and older than 13 years.

Among the 37 CYPs who accepted and received HIV PEP, adherence dropped from 62.2% (n=23) at 14 days to 27.0% (n=10) at 28 days. Eight CYPs reported adverse effects, including nausea (n=6, 75.0%) and abdominal pain (n=3, 37.5%). Non-adherence was attributed to (1) forgetfulness (n=1, 3.7%); (2) nausea and abdominal pain (n=1, 3.7%); (3) competing priorities (n=2, 7.4%); and (4) financial constraints (n=2, 7.4%). Fifty-five (18.8%) CYPs received a follow-up HIV serology (irrespective of HIV PEP administration) and none were positive (Fig. 1). All CYPs who were PEP-compliant had at least 1 protective social factor, including established access to social services.

Baseline testing and follow-up testing for hepatitis C

There were 245 (83.9%) CYPs with negative hepatitis C serology at baseline; 54 (22.0%) had repeat serology

Table 1. Demographics and social background of children and young persons presenting to children's emergency with sexual assault.

	Total (n=292)	CYPs eligible for HIV PEP ^a (n=40)	CYPs ineligible for HIV PEP ^b (n=252)	P value ^c
Patient demographics				
Female, no. (%)	281 (96.2)	40 (100)	241 (95.6)	0.17
Age >13 years, no. (%)	209 (71.6)	35 (87.5)	174 (69.0)	0.02
Age, median (IQR), years	14.0 (12.0–15.0)	14.0 (14.0–15.0)	14.0 (12.0–15.0)	0.004
Ethnicity, no. (%)				
Chinese	122 (41.8)	17 (42.5)	105 (41.7)	0.92
Malay	129 (44.2)	16 (40.0)	113 (44.8)	0.56
Indian	21 (7.2)	5 (12.5)	16 (6.3)	0.16
Others	20 (6.8)	2 (5.0)	18 (7.1)	0.62
Presence of any comorbid psychiatric illness, no. (%)	31 (10.6)	12 (30.0)	19 (7.5)	<0.001
Depression/anxiety	21 (67.7)	7 (58.3)	15 (78.9)	0.01
Eating disorder	3 (9.7)	1 (8.3)	2 (10.5)	0.32
Attendance for multiple episodes of sexual assault, no. (%)	26 (8.9)	4 (10.0)	22 (8.7)	0.79
Assault and assailant characteristics				
Time of presentation to children’s emergency from assault, no. (%)				
<72 hours	93 (31.8)	37 (92.5)	56 (22.2)	<0.001
72 hours to 7 days	10 (3.4)	3 (7.5)	7 (2.7)	
>7 days	189 (64.7)	0 (0)	189 (75.0)	
Assailant characteristics, no. (%)				
Multiple assailants	28 (9.6)	7 (17.5)	21 (8.3)	0.06
Assailant with multiple partners	8 (2.7)	5 (12.5)	3 (1.2)	0.04
Stranger	71 (24.3)	23 (57.5)	48 (19.0)	<0.001
Male	282 (96.6)	39 (97.5)	243 (96.4)	0.05
Known HIV-positive assailant	0 (0)	0 (0)	0 (0)	NA
Male assailant known to have sex with men	5 (1.7)	1 (2.5)	4 (1.6)	0.38
>18 years or unknown age	134 (45.8)	34 (85.0)	100 (39.6)	<0.001
Known intravenous drug user	1 (0.3)	0 (0)	1 (0.4)	NA
Use of protection	21 (7.2)	3 (7.5)	18 (7.1)	0.94
Type of exposure involved, no. (%)				
Penile-vaginal	180 (61.6)	37 (92.5)	143 (56.7)	0.004
Penile-anal	14 (4.8)	1 (2.5)	13 (5.2)	
Others ^d	199 (68.2)	18 (45.0)	181 (71.8)	
Social background				
Presence of any protective social factors, no. (%)	274 (93.8)	39 (97.5)	235 (93.2)	0.30
Presence of intact family	141(51.5)	25 (64.1)	116 (49.4)	0.05
Regular follow-up with medical social worker/ psychologist/ external community agency	146 (53.5)	22 (56.4)	124 (52.8)	0.49
Active school attendance	253 (92.3)	34 (87.2)	219 (93.2)	0.74
Presence of any predisposing social factors, no. (%)	151 (51.7)	26 (65.0)	125 (49.6)	0.07
Presence of family history of mental health issues and/or domestic violence	68 (45.0)	10 (38.5)	58 (46.4)	0.78
Presence of other high-risk behaviours (smoking, alcohol, vaping, self-harm)	114 (75.5)	25 (96.2)	89 (71.2)	<0.01
Living in Girls’/Boys’ Home	25 (16.6)	3 (11.5)	22 (17.6)	0.79

CYPs: children and young persons; HIV: human immunodeficiency virus; IQR: interquartile range; NA: not available; PEP: post-exposure prophylaxis

^a CYPs eligible for HIV PEP were defined as CYPs presenting within 72 hours since exposure with a penetrating sexual assault encounter

(genital-genital, genital-anal, genital-oral), and fulfilling the following: (1) known HIV-positive assailant; (2) unknown HIV-status assailant aged >18 years; (3) assailant with multiple sexual partners or multiple assailants during the assault; (4) assailant who is a known intravenous drug user; or (5) male assailant known to have sex with men. This was adapted from guidelines on PEP by the Centres for Disease Control and Prevention (CDC) and World Health Organization (WHO).

^b CYPs ineligible for HIV PEP were defined as CYPs presenting >72 hours since exposure with known HIV-negative assailant, protected intercourse with condom use; as adapted from guidelines by the CDC and WHO.^c P values in bold are statistically significant. Statistical significance taken as $P < 0.05$, comparing the presence of variable between the 2 groups.^d Other exposures include penile-oral, finger-vaginal, finger-anal and/or insertion of foreign body into vaginal and/or anal orifices.

Table 2. Baseline investigations of children and young persons presenting to children's emergency with sexual assault.

Baseline investigations	Total (n=292)
Urine pregnancy test, no. (%)	
Positive	5 (1.7)
Negative	191 (65.0)
Not done (females)	85 (29.5)
Not done (males)	11 (3.8)
<i>Chlamydia trachomatis</i> PCR, no. (%)	
Positive	27 (9.2)
Negative	224 (76.7)
Not done	41 (14.0)
<i>Neisseria gonorrhoeae</i> PCR, no. (%)	
Positive	0 (0)
Negative	251 (86.0)
Not done	41 (14.0)
Vaginal panel DNA swab test for <i>Trichomonas vaginalis</i> , no. (%)	
Positive	214 (73.3)
Negative	67 (22.9)
Not done (females)	11 (3.8)
Not done (Males)	
Vaginal panel DNA swab test for <i>Gardnerella vaginalis</i> , no. (%)	
Positive	102 (34.9)
Negative	112 (38.4)
Not done (females)	67 (22.9)
Not done (males)	11 (3.8)
Syphilis screen, no. (%)	
TPPA CMIA positive	3 (1.0)
TPPA CMIA negative	243 (83.2)
VDRL positive	0 (0)
VDRL negative	3 (1.0)
Not done	46 (15.8)
Hepatitis C CMIA, no. (%)	
Positive	245 (83.9)
Negative	0 (0)
Hepatitis B serology, no. (%)	
Hepatitis B non-immune ^a	167 (67.6)
Hepatitis B immune	80 (32.3)
Hepatitis B surface antigen positive	0 (0)
HIV serology, no. (%)	
Positive	245 (83.9)
Negative	0 (0)

CMIA: chemiluminescent microparticle immunoassay;

DNA: deoxyribonucleic acid; PCR: polymerase chain reaction;

TPPA: Treponema pallidum particle agglutination;

VDRL: Venereal Disease Research Laboratory

^a Hepatitis B non-immunity is defined as hepatitis B surface antibody (HBsAb) levels <10 mIU/mL.

at follow-up, with no seroconversions occurring in this group.

Follow-up at outpatient clinical services

There were 267 (90.7%) CYPs referred to outpatient services, such as paediatric medicine/adolescent medicine service, infectious diseases service and/

or psychological medicine service (Table 3). Only 19 (47.5%) of 40 HIV PEP-eligible CYPs attended follow-up with the adolescent medicine service. Of the 37 CYPs who received HIV PEP, 31 were referred to the infectious diseases service and only 22 (71.0%) attended their follow-up.

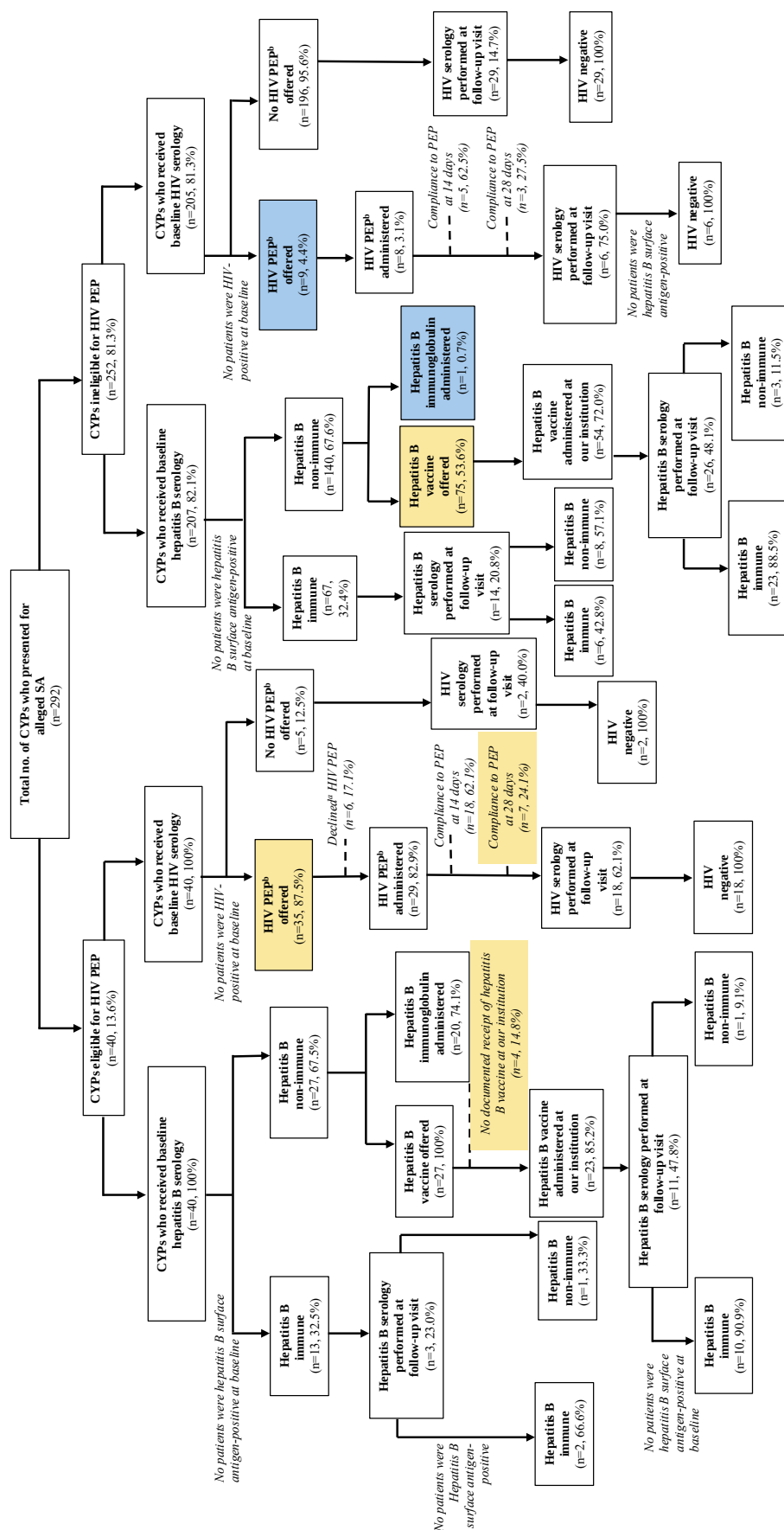
DISCUSSION

In this retrospective, single-centre study of CYPs with SA, we observed a high prevalence of HBV non-immunity in our adolescent population with suboptimal rates of booster vaccinations. While most eligible CYPs were offered HIV PEP, uptake (72%) and adherence (27.0%) were low, as were outpatient follow-up rates (57.5%). These rates were comparable to those reported in current literature.¹¹

Despite our childhood HBV immunisation programme achieving high rates of success with 95% completing a 3-dose vaccine course before 2 years of age,¹² a significant proportion (67.6%) of CYPs tested were HBV non-immune. This statistic was higher than international figures, including an audit performed in Melbourne, Australia between 2007 and 2016 that reported a 45.5% rate of non-immunity among adolescents with alleged SA.⁴ Although our rates of HBV immunity (33.4%) exceeded local adolescent HBV seroprevalence (24%),¹³ this suggests waning protection by the teenage years and warrants routine booster reviews for at-risk youths. Although an anamnestic response may still allow previously vaccinated individuals with HBsAb levels <10 mIU/mL to mount an immunological response to HBV infection after exposure,¹⁴ measurement of HBsAb levels remains the gold-standard for assessing HBV immunity and determining the need for HBV PEP.⁴ Singapore's HBsAg seroprevalence rate of 2.1%¹³ classifies Singapore as having intermediate endemicity as per WHO guidelines, indicating the need for HBV PEP for HBV non-immune SA victims. We report a proportion of HBV non-immune CYPs who were either not offered the vaccine at presentation or who were lost to follow-up with unclear receipt of HBV vaccine after referral to the outpatient clinics. These findings highlight areas for improvement in clinical care. It should be emphasised that the first medical attendance post-SA is an opportune time for prophylactic intervention. Routine HBV booster vaccinations at the initial clinical encounter should be implemented.

In our study, the majority of CYPs prescribed HIV PEP were retrospectively assessed to be eligible, and therefore PEP prescription was appropriate. However, 5 eligible CYPs were missed, stressing the need for greater clinician awareness of HIV risks and thorough history-taking. While extant literature recommends offering PEP within the first 72 hours post-assault—

Fig. 1. Hepatitis B and HIV baseline testing, post-exposure prophylaxis and follow-up serologies for children and young persons presenting to children's emergency for sexual assault.



Represents areas for practice improvement.

These CYPs who were ineligible for HIV PEP were administered PEP as a result of initial misclassification (retrospectively assessed to be ineligible).

CYPs: children and young persons; HIV: human immunodeficiency virus; PEP: post-exposure prophylaxis; SA: sexual assault

Reasons for declining HIV PEP included parental perception that perpetrator was low-risk or financial costs of HIV PEP.

All CYPs received oral dolutegravir and oral emtricitabine and tenofovir combination (Truvada; Gilead Sciences, Foster City, CA, US). Reasons for declining HIV-1 ELT included parental perception that peripartum was low-risk or financial costs of HIV-1 ELT.

CYPs were defined as CYPs receiving oral contraceptive and/or an injectable and/or an injectable combination (intra-uterine, subcutaneous, or intramuscular), and fulfilling the CYPs eligible for HIV PEP were defined as CYPs presenting within 72 hours since exposure with a penetrating sexual assault encounter (genital-genital, genital-anal, genital-oral), and fulfilling the following: (1) known HIV-positive assailant; (2) unknown HIV-status assailant and aged >18 years old; (3) assailant with multiple partners or multiple assailants; (4) assailant who is a known intravenous drug user; or (5) male assailant who has sex with male. This was adapted from guidelines on PEP by the Centres for Disease Control and Prevention and World Health Organization. Immunity to hepatitis B denotes a negative hepatitis B surface antigen, and hepatitis B surface antibody level >10 mIU/mL. Serologies were repeated at varying time points at any follow-up, with a minimum duration of 1 month post-SA.

Table 3. Follow-up outpatient visits for children and young persons presenting to children's emergency with sexual assault.

	Total (n=292)	CYPs eligible for HIV PEP ^a (n=40)	CYPs ineligible for HIV PEP ^b (n=252)	P value ^c
Referred to any outpatient health service, no. (%)	267 (90.7)	40 (100)	227 (89.7)	0.03
Attended any follow-up clinic, no. (%)	153 (57.7)	28 (70.0)	125 (54.9)	0.07
Referred to infectious diseases outpatient clinic, no. (%)	44 (15.0)	31 (77.5)	13 (5.2)	<0.01
Attended 1st follow-up clinic	32 (72.7)	22 (71.0)	10 (76.9)	0.68
Attended 2nd follow-up clinic	13 (29.5)	7 (22.6)	6 (46.1)	0.18
Did not attend any follow-up clinic	12 (27.2)	8 (25.8)	3 (23.0)	0.85
Referred to adolescent medicine clinic, no. (%)	257 (88.0)	40 (100)	217 (86.1)	0.01
Attended 1st follow-up clinic	126 (49.0)	19 (47.5)	107 (49.3)	0.83
Attended 2nd follow-up clinic	50 (19.5)	15 (37.5)	35 (16.2)	<0.01
Did not attend any follow-up clinic	130 (50.6)	21 (52.5)	109 (50.2)	0.79

CYPs: children and young persons; HIV: human immunodeficiency virus; PEP: post-exposure prophylaxis

^a CYPs eligible for HIV PEP were defined as CYPs presenting within 72 hours since exposure with a penetrating sexual assault encounter (genital-genital, genital-anal, genital-oral), and fulfilling the following: (1) known HIV-positive assailant; (2) unknown HIV-status assailant aged >18 years; (3) assailant with multiple sexual partners or multiple assailants during the assault; (4) assailant who is a known intravenous drug user; or (5) male assailant known to have sex with men This was adapted from guidelines on PEP by the Centres for Disease Control and Prevention (CDC) and World Health Organization (WHO).

^b CYPs ineligible for HIV PEP were defined as CYPs presenting >72 hours since exposure with known HIV-negative assailant, protected intercourse with condom use; as adapted from guidelines by the CDC and WHO.

^c P values in bold are statistically significant. Statistical significance taken as $P < 0.05$, comparing the presence of variable between the 2 groups.

especially for SA cases with oral, vaginal or anal penetration, with known HIV-positive assailants or assailants with high-risk behaviours—clinical application is often complicated by unclear histories,^{9,10,15,16} and the young age of victims leading to difficulty describing the degree of penetration (labial versus vaginal), uncertainty regarding condom use and ejaculation.¹⁷ This is further hampered by a lack of consensus on the administration of HIV PEP in at-risk populations who present beyond the recommended window for PEP initiation. Given concerns about drug toxicities and adherence, it is thus unsurprising that decisions around PEP are weighted and require careful, shared discussion among the victims, caregivers, and healthcare providers. A structured risk-assessment calculator that generates an objective score based on the aggregation of risk factors, may be beneficial, as evidenced by a Belgian study that reported modest improvements in HIV PEP prescription quality and reduction in overuse after piloting a computer-based decision-making programme.¹⁸

Similar to our findings, compliance with the 28-day HIV PEP regimen and follow-up remained poor across most single-centre studies.^{11,19,20} In our cohort, follow-up was suboptimal among the CYPs who were eligible for HIV PEP, who should have ideally achieved a 100% follow-up rate as they represented the cohort at heightened risk for both STIs and assault-related trauma. Factors influencing poor compliance in paediatrics are underexplored, although it has been postulated to be due to unstable living conditions.¹¹ A systematic review performed in 2019 linked PEP

adherence to improved patient health literacy on the necessity and indication of PEP, monetary support for transport to follow-up, healthcare provider support and counselling, while contextual barriers included poor social support.²⁰ In our study, those who completed PEP had at least 1 protective social factor, including access to social services, which provided social support and counselling. As such, to improve outcomes in our centre, we need to evaluate the effectiveness of our protocols in education and counselling. Strategies that support the emerging adolescent autonomy to empower and encourage personal responsibility for health management, may also be useful for improved compliance among adolescents.²¹ Mitigating the substantial financial costs and considering increased subsidy of PEP (ranging from SGD109.73–377.70 [approx. USD86–296] in Singapore despite subsidies)^{22,23} should be considered in tandem. To improve convenience, our institution has also recently embarked on efforts in providing courier of PEP to CYPs' residence.

In our cohort, follow-up was suboptimal among the CYPs eligible for HIV PEP, who should have ideally achieved a 100% follow-up rate as they represent the cohort at heightened risk for both STIs and assault-related trauma. Follow-up evaluation post-SA extends beyond PEP compliance and includes addressing other medical and psychosocial needs. We report poor outpatient follow-up rates, which are lower than those in other single-centre studies,⁸ especially in the HIV PEP-eligible group, who are at heightened risk not just for STIs but for assault-

related trauma. To improve this, recent efforts at our institution include providing teleconsultations. While international telemedicine programmes have shown promising results in improving clinical follow-up²⁴ future audits should evaluate the long-term effectiveness of these interventions.

The incidence of *Chlamydia trachomatis* (9.2%) and *Neisseria gonorrhoeae* (0%) in our cohort remains similar to Singapore's pre-COVID-19 data from 2016 to 2020 (5.6% and 0.9%, respectively).² In addition to viral STIs, there should be continued bacterial STI screening and appropriate PEP administration for eligible CYPs with SA in the paediatric population.

Established risk factors for SA among CYPs include parental divorce, history of psychiatric or behavioural issues and high-risk behaviours including smoking, alcohol use and illicit drug use.^{2,8} Our findings were congruent with this knowledge. There was an increased prevalence of high-risk behaviours in CYPs who had a high-risk SA encounter. As these high-risk behaviours can also significantly impact their health, comprehensive adolescent health counselling would benefit these CYPs by providing anticipatory care and increased visibility to community services.

The primary limitation of our study is its retrospective design, which precludes consistent data collection and led to incomplete documentation of additional considerations influencing PEP prescription decisions at initial presentation. Additionally, diagnostic miscoding could have led to under-capturing of SA cases. Nonetheless, a standardised data collection form was used to improve data reliability.

CONCLUSION

Improving HBV booster vaccination uptake, HIV PEP adherence and follow-up among CYPs presenting with SA should be prioritised. Our findings build on prior studies examining the clinical characteristics, prescribing practices of PEP and follow-up among paediatric SA victims. Prospective studies using standardised treatment protocols and risk-stratification tools will be crucial in establishing definitive PEP prescribing guidelines. Understanding barriers to PEP compliance and follow-up is key in ensuring optimal care for this vulnerable group.

Supplementary materials

Appendix S1. Overview of institutional protocol for post-sexual assault prophylaxis and follow-up.

Appendix S2. Institutional protocol for evaluation of children and young persons presenting with sexual assault.

Ethics statement

This study was performed as part of a clinical audit for quality improvement; requirement for informed consent was waived by KK Women's and Children's Hospital, SingHealth (Reference number: KKH-2023-05-00148).

Declaration

The authors declare there are no affiliations with or involvement in any organisation or entity with any financial interest in the subject matter or materials discussed in this manuscript.

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Chronic obstructive pulmonary disease 30-day readmission metric: Risk adjustment for multimorbidity and frailty

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ABSTRACT

Introduction: The 30-day readmission rate for chronic obstructive pulmonary disease (COPD) is a common performance metric but may be confounded by factors unrelated to quality of care. Our aim was to assess how sociodemographic factors, multimorbidity and frailty impact 30-day readmission risk after COPD hospitalisation, and whether risk adjustment alters interpretation of temporal trends.

Method: This is a retrospective analysis of administrative data from October 2017 to June 2023 from Changi General Hospital, Singapore. Multivariable mixed-effects logistic regression models were used to estimate unadjusted and risk-adjusted 30-day readmission odds. Covariates included age, sex, race, Charlson Comorbidity Index (CCI), Hospital Frailty Risk Score (HFRS) and year. Temporal trends in readmission risk were compared across unadjusted and adjusted models.

Results: Of the 2774 admissions, 749 (27%) resulted in 30-day readmissions. Higher CCI (CCI $\geq$ 4 versus [vs] CCI=1: adjusted odds ratio [aOR] 2.00, 95% confidence interval [CI] 1.33–2.99, $P=0.003$; CCI 2–3 vs CCI=1: aOR 1.50, 95% CI 1.15–1.96, $P=0.001$) and higher HFRS ($\geq$ 5 vs $<$ 5: aOR 1.29, 95% CI 1.01–1.65, $P=0.04$) were independently associated with increased readmission risk. While unadjusted analyses showed no significant temporal trends, the risk-adjusted model revealed a 32–35% reduction in readmission odds in 2021–2023 compared to baseline.

Conclusion: Multimorbidity and frailty significantly impact COPD readmissions. Risk adjustment revealed improvements in readmission risk not evident in unadjusted analyses, emphasising the importance of applying risk adjustments to ensure valid performance metrics.

Keywords: 30-day readmission, COPD, frailty, healthcare quality, pulmonary, respiratory medicine, risk adjustment

CLINICAL IMPACT

What is New

- Risk adjustment in hospital benchmarking enhances performance measures by accounting for case mix complexity, yet empirical evidence is lacking to support its use in the Singapore healthcare system.
- This study provides empirical data demonstrating that adjusting for clinical complexity and frailty reveals hidden improvements in 30-day readmission risk after COPD hospitalisation in Singapore.

Clinical Implications

- Incorporating risk adjustment ensures fairer evaluations of care quality, guiding policy and interventions to reduce avoidable readmissions.

and alveoli due to prolonged exposure to noxious gases and particles, such as cigarette smoke and particulate matter from air pollution.^{1,2} COPD affects approximately 292 million people globally and is the third leading cause of death worldwide.²

From a healthcare system perspective, COPD is a significant contributor to hospitalisations.^{3,4} Hospital readmissions following an initial hospitalisation for acute COPD exacerbation are common,⁵ with all-cause 30-day readmission rates reported to range between 7.3% and 38.0%.⁶

The 30-day readmission rate reflects adverse health outcomes requiring rehospitalisation within the early post-discharge period. This metric provides an opportunity to address avoidable readmissions through interventions initiated during the index admission. Examples include guideline-directed clinical management, comprehensive discharge planning, care coordination, and the provision of community support services.⁷ Consequently, the 30-day readmission rate is widely used as a quality-of-care indicator,⁸ and its public reporting is mandated in several countries.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a chronic respiratory condition defined by persistent respiratory symptoms and airflow limitation.¹ It is primarily caused by pathological changes in the airways

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In some healthcare systems, financial incentives and penalties tied to 30-day readmission rates aim to enhance accountability and encourage the delivery of safe and effective care.^{7,9} In the US, under Medicare Hospital Readmissions Reduction Program, hospitals with excess 30-day readmissions for COPD and other chronic conditions face financial penalties.¹⁰ Similarly, the UK's National Health Service does not reimburse hospitals for unplanned, avoidable readmissions within 30 days if these exceed a threshold rate.¹¹ In Denmark and Germany, index admissions and related readmissions are bundled into a single case for payment purposes, incentivising hospitals to minimise preventable readmissions.^{9,12}

One key concern is the validity of crude 30-day readmission rates as a healthcare performance metric, because readmission rates can be affected by factors unrelated to quality of care. Patients with higher medical or social vulnerabilities, such as those with multiple comorbidities or frailty, have an elevated risk of readmission.^{6,7,13} Consequently, hospitals serving a higher proportion of such patients may appear to perform worse on this metric, regardless of the quality of care provided. Without accounting for differences in patient case-mix, performance assessments may be distorted, hindering the adoption of best practices. This is especially crucial when comparing performance across different hospitals, as they may cater to populations with significantly varied risk profiles.¹⁴

To address this issue, risk adjustment methodologies have been developed to account for confounding factors, such as patient demographics, comorbidities and illness severity, when calculating readmission rates.¹⁵ By promoting fairer and more accurate comparisons of health outcomes, risk adjustment ensures that observed differences reflect variations in care quality rather than disparities in patient risk profiles.

In Singapore, limited data exist regarding the extent to which patient characteristics contribute to variability in COPD 30-day readmission rates. Additionally, it is unclear whether such variability warrants risk adjustment to ensure accurate interpretation of these rates. The 2024 Technical Manual for Healthier SG Indicators states that use of risk adjustment for condition-specific readmission rates (including COPD) is to be determined.¹⁶ With a growing emphasis on value-based care, a nuanced understanding of the factors influencing 30-day readmissions is essential for developing equitable and effective healthcare policies.

This study aimed to evaluate whether patient characteristics—including sociodemographic factors, multimorbidity and frailty—are associated with 30-day readmission risk following hospitalisation for COPD

exacerbation. Furthermore, we examined whether risk adjustment qualitatively alters the interpretation of 30-day readmission rates, particularly in the context of assessing care quality over time.

METHOD

Study design and study population

This was a retrospective cohort study. The analytic dataset was extracted from Changi General Hospital, Singapore, a 1000-bed, university-affiliated, public tertiary hospital in Singapore. The hospital manages approximately 500 admissions for acute exacerbation of COPD annually, similar to other public general hospitals in the country. The data warehouse collected clinical and administrative data from all COPD patients accessing care at the hospital, with daily data updates. Variables captured include sociodemographic factors, administrative visit details, diagnostic codes, laboratory and radiology results, and prescribed medications.

Inclusion criteria for this analysis were: all adults (>18 years) hospitalised for a primary diagnosis of COPD, identified by the International Classification of Disease (ICD-10) codes J44 and its subcodes, between 1 October 2017 and 30 June 2023.

Variables and measures

The primary outcome was 30-day readmission, defined as a binary variable indicating whether there was an all-cause readmission within 30 days of an index COPD admission. The 30-day readmission rate was defined as the proportion of index admissions for COPD (J44 diagnostic code), which were followed by an all-cause readmission within 30 days, expressed as a percentage (%).

Covariates of interest included age, sex, race, the Charlson Comorbidity Index (CCI), the Hospital Frailty Risk Score and calendar year. Age was categorised as ≤59, 60–69, 70–79 and ≥80 years. Sex was categorised as male or female. Self-reported race was categorised as Chinese, Malay, Indian or others. The CCI is a validated composite measure of comorbidity burden or multimorbidity, encompassing 17 different diagnostic domains, including cardiovascular, respiratory, liver, metabolic and malignant conditions.¹⁷ Each domain contributes a weighted score to the index. In this study, the CCI was computed based on ICD-10 codes recorded within the previous year of the index admission, and categorised into 1, 2–3, or ≥4 for analysis. The HFRS is a summed weighted score based on >100 ICD-10 codes indicative of frailty,¹⁸ and was parameterised as a categorical variable <5 or ≥5. Calendar year was categorised into bins: 2017–2018, 2019, 2020, 2021

and 2022–23. Data were pooled for October 2017 to December 2018 and January 2022 to June 2023 due to availability of <1 year of data in 2017 and 2023.

Statistical analysis

Data were expressed as mean $\pm$ standard deviation for continuous variables, and number (%) for categorical variables.

To assess the risk of 30-day readmission, we modelled the log-odds of 30-day readmission using mixed-effects logistic regression, with a random intercept to account for within-patient clustering of admissions. The intraclass correlation (ICC) and likelihood ratio test comparing a null mixed-effects versus (vs) a null standard logistic model were used to assess significant clustering. An ICC > 0.05 and a likelihood ratio test *P* value of < 0.05 were taken as evidence for significant clustering.

Unadjusted and adjusted fixed effects estimates for covariates were computed. Odds ratios with confidence intervals that did not include 1 were interpreted as evidence of statistically significant association with 30-day readmission.

To evaluate temporal trends, we examined the odds ratio (OR) for each year bin, with OR of < 1 indicating lower risk of readmission compared to the baseline epoch (2017–2018). We evaluated whether applying risk adjustment, compared to unadjusted analyses, qualitatively altered the interpretation of temporal trends in 30-day readmission risk.

As sensitivity analyses, we included the additional covariate of ward class in regression modelling as a pragmatic proxy for socioeconomic status.

Statistical analyses and regression models were performed in R with the lme4 package.

Ethics

This study was classified as a service evaluation and deemed not to require ethical review by the SingHealth Centralised Institutional Review Board (2018/2698) as per applicable ethical and regulatory standards.

RESULTS

Study population and index admissions

During the study period, a total of 2906 index admissions for COPD were identified. Among these, 132 index admissions were excluded due to in-hospital mortality during the same admission, resulting in 2774 index admissions available for analysis of 30-day readmission. Complete data on covariates were available for all 2774 entries. These admissions corresponded to 1119 unique patients.

Characteristics of patients at index admission are summarised in Table 1. An increasing age trend was observed with ascending CCI and HFRS categories. Additionally, admissions with higher CCI categories were associated with correspondingly elevated HFRS categories, demonstrating a positive relationship between these indices. The most prevalent CCI conditions were diabetes with (11.2%) and without (20.8%) complications, moderate-to-severe chronic kidney disease (13.7%), congestive heart failure (8.1%) and myocardial infarction (6.6%). The most prevalent HFRS conditions were Alzheimer's disease (7.1%), delirium (3.5%) and tendency to fall (1.8%).

30-day readmissions

Out of the 2774 index admissions, 749 (27%) were readmitted within 30 days. Crude readmission rates each annum were 31% (2017–2018), 28% (2019), 30% (2020), 22% (2021) and 21% (2022–2023). Significant clustering of admissions among individuals was observed, evidenced by the ICC of 0.28, and likelihood ratio test *P* value of < 0.001 when comparing the null mixed-effects model to the null standard logistic regression model. Among the 1119 unique patients, 795 (71.0%) had zero 30-day readmissions, 191 (17.6%) had one 30-day readmission, and 133 (11.1%) had two or more 30-day readmissions over the study period.

Stratified analyses showed that 30-day readmission rates were 24.2%, 31.2% and 34.0% for CCI of 1, 2–3 and ≥ 4 , respectively. Similarly, readmission rates were 25.5% and 30.4% for HFRS < 5 and HFRS ≥ 5 , respectively. In the fully risk-adjusted model (Table 2), a CCI of 2–3 (adjusted odds ratio [aOR]: 1.50, 95% confidence interval [CI] 1.15–1.96, *P* = 0.003) and ≥ 4 (aOR: 2.00, 95% CI 1.33–2.99, *P* = 0.001) were associated with significantly higher odds of 30-day readmission, compared to the reference category of CCI = 1. Similarly, an HFRS score of ≥ 5 was significantly associated with increased odds of 30-day readmission compared to < 5 (aOR: 1.29, 95% CI 1.01–1.65, *P* = 0.04). Patient age, sex and race were not significantly associated with 30-day readmission.

In the CCI and HFRS graphs (left and middle panels), bar plots represent percentages (left axes) and dot-line plots represent means (right axes). Crude 30-day readmission rates were modelled with locally estimated scatterplot smoothing (right panel).

Temporal trends

There was an increasing proportion of patients with higher CCI and HFRS scores over time (Fig. 1, left and middle panels). Despite the rising multimorbidity and frailty burden, an apparent decline in 30-day

Table 1. Baseline characteristics at index admission for primary diagnosis of chronic obstructive pulmonary disease.

	Overall	Charlson Comorbidity Index			Hospital Frailty Risk Score	
		1	2 or 3	≥4	<5	≥5
Number	2774	1760	764	250	1933	841
Age at index admission, years						
59 and below	275 (9.9%)	201 (11.4%)	50 (6.5%)	24 (9.6%)	239 (12.4%)	36 (4.3%)
60–69	802 (28.9%)	551 (31.3%)	188 (24.6%)	63 (25.2%)	626 (32.4%)	176 (20.9%)
70–79	1004 (36.2%)	667 (37.9%)	274 (35.9%)	63 (25.2%)	712 (36.8%)	292 (34.7%)
80 and above	693 (25.0%)	341 (19.4%)	252 (33.0%)	100 (40.0%)	356 (18.4%)	337 (40.1%)
Mean ± SD	72.9 ± 10.2	71.7 ± 9.78	75.2 ± 10.1	74.9 ± 11.3	71.3 ± 9.72	76.8 ± 10.1
Sex						
Female	229 (8.3%)	121 (6.9%)	75 (9.8%)	33 (13.2%)	123 (6.4%)	106 (12.6%)
Male	2545 (91.7%)	1639 (93.1%)	689 (90.2%)	217 (86.8%)	1810 (93.6%)	735 (87.4%)
Race						
Chinese	1467 (52.9%)	947 (53.8%)	392 (51.3%)	128 (51.2%)	984 (50.9%)	483 (57.4%)
Indian	269 (9.7%)	153 (8.7%)	99 (13.0%)	17 (6.8%)	188 (9.7%)	81 (9.6%)
Malay	705 (25.4%)	469 (26.6%)	179 (23.4%)	57 (22.8%)	514 (26.6%)	191 (22.7%)
Others	333 (12.0%)	191 (10.9%)	94 (12.3%)	48 (19.2%)	247 (12.8%)	86 (10.2%)
Charlson Comorbidity Index ^a						
1	1760 (63.4%)	-	-	-	1425 (73.7%)	335 (39.8%)
2–3	764 (27.5%)	-	-	-	422 (21.8%)	342 (40.7%)
≥4	250 (9.0%)	-	-	-	86 (4.4%)	164 (19.5%)
Hospital Frailty Risk Score						
<5	1933 (69.7%)	1425 (81.0%)	422 (55.2%)	86 (34.4%)	-	-
≥5	841 (30.3%)	335 (19.0%)	342 (44.8%)	164 (65.6%)	-	-

SD: standard deviation

^a The Charlson Comorbidity Index is computed from 17 different domains of diagnostic codes, each with a different assigned weight.^b The Hospital Frailty Risk Score is computed from summed weighted scores of >100 diagnostic codes.

Data are presented as mean ± standard deviation or no. (%).

readmission rate was observed visually (Fig. 1, right panel). However, unadjusted analyses (Table 1) showed no significant reduction in the odds of readmission over time. In contrast, the fully risk-adjusted analyses (Table 1) revealed a significantly reduced risk of 30-day readmission in 2021 (aOR: 0.65, 95% CI: 0.46–0.94, $P=0.02$) and 2022–2023 (aOR: 0.68, 95% CI: 0.49–0.93, $P=0.02$) compared to the baseline period. These findings correspond to a 32–35% reduction in the risk-adjusted odds of

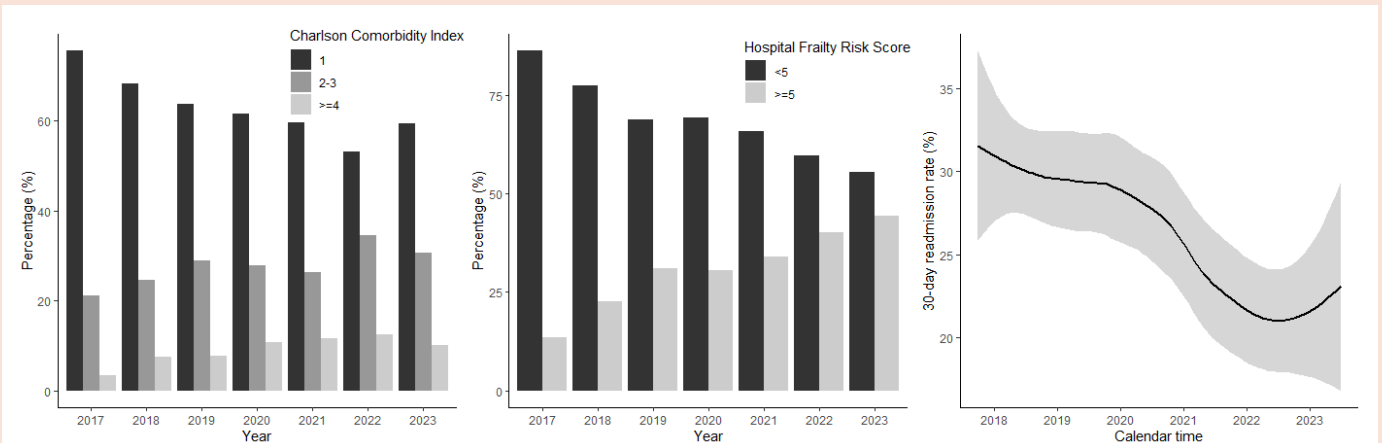
30-day readmission, indicating that risk-adjustment unmasked improvements in this quality metric over time.

In sensitivity analyses with additional adjustment for ward class (Supplementary Table S1), ward class was not significantly associated with 30-day readmission risk. Associations of CCI and HFRS with readmission remained significant, and the reduced readmission risk in 2021 and 2022–2023 was maintained.

Table 2. Unadjusted and risk-adjusted models.

Variable	No risk-adjustment			Risk-adjusted	
	Unadjusted OR (95% CI)	P value		Adjusted OR (95% CI)	P value
Age					
59 and below	1 [Reference]			1 [Reference]	
60–69	0.91 (0.59–1.40)	0.66		0.93 (0.60–1.42)	0.73
70–79	1.09 (0.70–1.70)	0.70		1.09 (0.70–1.71)	0.70
80 and above	1.21 (0.77–1.92)	0.41		1.11 (0.69–1.80)	0.67
Sex					
Female	1 [Reference]			1 [Reference]	
Male	1.14 (0.72–1.81)	0.56		1.27 (0.80–2.03)	0.31
Race					
Chinese	1 [Reference]			1 [Reference]	
Malay	1.12 (0.81–1.55)	0.36		1.15 (0.83–1.59)	0.41
Indian	1.24 (0.78–1.97)	0.48		1.19 (0.75–1.89)	0.45
Others	1.13 (0.73–1.76)	0.58		1.13 (0.72–1.75)	0.60
Charlson Comorbidity Index					
1	1 [Reference]			1 [Reference]	
2–3	1.56 (1.21–2.03)	0.008		1.50 (1.15–1.96)	0.003
≥4	2.15 (1.46–3.17)	<0.001		2.00 (1.33–2.99)	0.001
Hospital Frailty Risk Score					
<5	1 [Reference]			1 [Reference]	
≥5	1.42 (1.13–1.78)	0.002		1.29 (1.01–1.65)	0.04
Year					
2017–18	1 [Reference]			1 [Reference]	
2019	0.88 (0.66–1.18)	0.40		0.84 (0.63–1.12)	0.24
2020	0.97 (0.70–1.33)	0.84		0.88 (0.64–1.22)	0.45
2021	0.74 (0.52–1.05)	0.09		0.65 (0.46–0.94)	0.02
2022–23	0.78 (0.57–1.07)	0.12		0.68 (0.49–0.93)	0.02

Fig. 1. Temporal trends for Charlson Comorbidity Index (CCI), Human Frailty Risk Score (HFRS) and 30-day readmission rates with 95% confidence intervals.



In the CCI and HFRS graphs (left and middle panels), bar plots represent percentages (left axes) and dot-line plots represent means (right axes). Crude 30-day readmission rates were modelled with locally estimated scatterplot smoothing (right panel).

DISCUSSION

To better understand and interpret the 30-day readmission rate as a healthcare quality measure, this study investigated variations in COPD 30-day readmission risk attributable to case mix factors including demographics, multimorbidity and frailty. These variables reflect the intrinsic risk of the patient population managed by the hospital, distinct from the quality of care that the metric is intended to measure. Our analysis demonstrated an increasing trend of comorbidity burden and frailty from 2017 to 2023, reflecting an ageing patient population with

escalating levels of multimorbidity and functional impairment. Compared to a CCI of 1, a CCI score of 2–3 was associated with a 50% higher odds of 30-day readmission, while a CCI of ≥4 was associated with a 100% higher odds. Similarly, HFRS ≥5 was associated with 29% increase in readmission odds compared to HFRS <5. Although unadjusted 30-day readmission risk showed no statistically significant improvement over time, risk-adjusted analyses revealed a statistically significant 32–35% reduction in readmission odds during the later years of the study, highlighting improvements in performance over the study

period. These findings underscore the importance of risk adjustments in ensuring fair and meaningful interpretation of healthcare quality indicators.

Risk-adjusted readmission rates derived through regression modelling of administrative claims from Medicare and Medicaid hospitals were first publicly reported in the US in 2009 for a limited number of conditions.¹⁹ In subsequent years, risk-adjusted readmission rates were expanded to a range of other chronic conditions, including COPD,²⁰ and used to determine value-based payments to hospitals under the Hospital Readmissions Reduction Program.¹⁰ The US risk-adjustment methodology applies demographic variables and specific comorbidities in the previous 12 months as covariates in the statistical model.¹⁰ Risk-adjusted readmission rates were expressed as the ratio of a hospital's predicted performance relative to the national expected average for the same case mix, which is in turn multiplied by the observed national readmission rate,¹⁰ hence providing a metric for benchmarking. Internationally, the practice of risk adjustment varies: Germany and the UK do not adjust for risk, while Australia stratifies by hospital peer group rather than using regression modelling.⁷ While the core concept of risk adjustment is good practice and relevant to Singapore's healthcare system, direct adoption US risk-adjusted models without modification may be inappropriate due to differences in systems and populations. To our knowledge, our study is the first to provide empirical support for risk-adjusted benchmarking in Singapore, identifying key factors influencing performance assessment which should be incorporated in risk adjustment in our setting. Unlike US models that adjust for specific comorbidities, we used validated indices of comorbidity and frailty captured from administrative visit data, offering a simpler and more intuitive approach. Furthermore, while US studies typically assess the impact of risk adjustment on hospital rankings at a single time point,^{21–23} our study tracked changing multimorbidity and frailty levels over time, revealing otherwise unrecognised longitudinal trends in readmission risk. Our findings highlight that, beyond hospital rankings, risk adjustment has a role in longitudinal assessment of healthcare performance.

We examined all-cause 30-day readmissions following COPD admissions, reporting an average of 27% over 7 years, decreasing from 31% in 2017–2018 to 21% in 2022–2023. The all-cause readmission rate was used because any unplanned readmission is undesirable for patients, and inferring quality of care from only the documented reason for readmission is difficult.²⁰ Comparisons with published data require caution due to substantial variability in COPD readmission definitions.⁵ Many studies define readmission based on only COPD- or respiratory-related diagnoses, yielding lower readmission rates.²⁴ Others use different

denominators, such as unique patients versus total admissions.⁵ Additional methodological differences include handling of inter-hospital transfers, episode consolidations due to billing practices, discharges against advice, and eligibility of consecutive admissions as new index events.²⁰ To our knowledge, only one published study from Singapore²⁵ has reported COPD 30-day readmission rates, documenting an incidence rate of 0.12 per person-year in 2008–2009 among patients enrolled in a chronic disease management programme. However, direct comparison with our study is limited by differences in outcome definition (COPD-specific versus all-cause readmissions) and methodological approach (incidence rate versus proportion of readmissions per index admission). In 2022, crude 30-day readmission rates following COPD admission from 3 local hospitals ranged between 24–32% (unpublished data), but it is not known whether risk adjustment would lead to narrowing of this range of variability. Internationally, a meta-analysis reported 30-day all-cause readmission rates ranging between 7.3% and 38.0%, but these estimates are likely biased, because included studies considered readmissions due only to COPD, or used highly selected clinical cohorts (for example, excluding patients >65 years, or including patients on specific treatments).²⁶ In addition, the meta-analysis did not account for different methodologies used to compute readmission rates. Thus, standardisation of readmission definition and risk adjustment methodology is needed for meaningful benchmarking.

Our study was not designed to evaluate the causal factors underlying readmission rate improvements. Outcome indicators such as the readmission rates, while providing an indication of quality of care,⁸ do not inherently reveal which aspects of care influenced outcome.²⁷ Specific care processes (e.g. guideline-based treatment, patient education) and administrative factors (e.g. staffing ratios, medication subsidies) are better assessed through process and structural indicators.²⁷ A comprehensive quality improvement programme should generally include a mix of outcome, process and structural indicators.²⁷ Within this context, outcome indicators provide broad measures of the net effectiveness of healthcare, capturing both measured and unmeasured care processes and structural factors affecting patient outcomes.¹⁹ The additional value of outcome measures is that they are directly relevant to patient experience, for example, readmission rates are disruptive and costly to patients.²⁸ The challenge lies in ensuring that operationalisation of outcome indicators (like the readmission rate) accurately captures quality of care, while accounting for factors beyond clinical control or hospital jurisdiction, such as intrinsic clinical complexity²⁹ and social determinants.

Several factors, both unrelated and related to quality of care, may have contributed to the observed

decline in readmission risk. Coding practices, such as coding more comorbidities, could artificially lower readmission risk.³⁰ Additionally, secular trends, including global declines in COPD admissions during the COVID-19 pandemic,³¹ could have influenced readmission rates. However, our study found no significant decrease in readmission risk in 2020 despite the stringent public health measures implemented that year, nor a rebound in readmission risk in 2022 when restrictions were eased, suggesting that pandemic-related factors were not the primary drivers of observed trends. Temporal improvements in readmission risk may also reflect enhancements in care quality driven by targeted clinical and population health interventions implemented at our hospital. For example, COPD-specific quality indicators—including 30-day readmission rates, mortality rates and length of stay—are routinely tracked using a dashboard. Process outcomes, such as disease education, inhaler technique, smoking cessation, pulmonary rehabilitation uptake and vaccinations, are also monitored on this dashboard and shared with stakeholders, with a clear chain of accountability. Multidisciplinary teams support the implementation of quality improvement initiatives, including adherence to best-practice guidelines through integrated clinical pathways within electronic health records. Specific quality improvement projects that have been undertaken at our hospital include interventions to increase the prescribing of inpatient influenza vaccination, and a multidisciplinary health management unit (comprising clinicians, allied health practitioners, case managers, social workers and community partners) that meets monthly to identify high-risk patients for discussion and provide clinical, behavioural and social management plans with the aim of preventing readmissions.

This report comes at a pivotal time for the Singapore healthcare system, which is transitioning from a fee-for-service to a value-driven care model that holds hospitals increasingly accountable for quality of care. Quality measures are integral to enhancing healthcare value and effectiveness, but their development, measurement and benchmarking require meticulous consideration. Failure to account for confounding by case mix may lead to biased conclusions and hinder the intended goal of improved population health outcomes. An example is the Hospital Readmissions Reduction Program in the US that initially used incomplete risk-adjustment in the reporting and adjudication of 30-day readmission rates by failing to include social risk, leading to the unintended consequence of penalising hospitals serving disadvantaged populations, thereby potentially widening disparities of health.³²

To address this problem, risk adjustment is a best-practice approach to enable accurate assessment of

performance, by applying statistical methods such as stratification, standardisation or regression modelling as in this study.¹⁵ Risk-adjusted metrics facilitate meaningful benchmarking across healthcare institutions, encouraging active collaboration and adoption of best practices. In addition, by adjusting for factors outside a provider's control, risk-adjusted metrics focus on aspects of care that can be influenced or improved, enhancing accountability for quality. Policymakers can also use risk-adjusted data to make informed decisions about resource allocation and payment incentives in value-based care models.

This study has several limitations. First, while we demonstrated that risk adjustment can substantively alter the qualitative interpretation of the 30-day readmission metric, data from other hospitals in Singapore were not available for us to evaluate how risk adjustment affects interhospital comparisons. This single-centre study may also not be generalisable to other centres or countries.

Second, our study used summary indices of multimorbidity and frailty, the CCI and HFRS, instead of individual comorbidities. While incorporating individual comorbidities as covariates could better delineate their specific causal associations with readmission risk—an approach suited for identifying novel risk factors—our study had a different primary objective of providing empirical support to justify risk adjustment of performance metrics in Singapore. Each individual comorbidity likely exerts only a minor influence on readmission risk, and including numerous comorbidities as covariates would have compromised model parsimony. Besides enhancing model parsimony, using summary measures also enabled us to capture the constructs of clinical complexity and frailty, which are more relevant than individual conditions in the context of risk adjustment.

Third, we did not adjust for COPD-specific disease parameters, such as the frequent exacerbator phenotype, chronic hypoxia or chronic hypercapnia. Administrative datasets used for computing hospital-wide quality indicators often lack granular clinical data, which can pose a significant burden for hospitals to systematically collect. The alternative of computing quality indicators from clinical registries may also not be feasible, as clinical registries may not include the whole population of interest, and notably disease parameters may not be systematically collected in routine practice. Moreover, adjusting for disease-specific parameters could obscure quality-of-care differences, because these factors are potentially modifiable through interventions. For example, recurrent exacerbations can be prevented by optimising pharmacotherapy, enrolling into pulmonary rehabilitation and smoking cessation. Moreover, provision of long-term oxygen therapy and domiciliary

non-invasive ventilation are evidence-based treatments for chronic hypoxia and chronic hypercapnia, respectively. In other words, clinical factors may represent treatable traits with identifiable and actionable interventions, and may be proxy indicators for process outcomes.

Fourth, a major limitation was lack of data for social risk adjustment—for example, poverty, transport barriers, food insecurity, housing instability and caregiver availability. This reflects broader systemic gaps in capturing the social determinants of health by hospitals and healthcare systems worldwide.³³ The optimal social screening tools and domains for risk adjustment remain unclear,³³ and some studies have demonstrated that social risk adjustment has minimal impact on readmission rates, potentially serving as a proxy for unmeasured clinical complexity.²¹ Furthermore, stratifying hospitals by social risk peer groups may obscure disparities in care by limiting comparisons to hospitals serving similarly disadvantaged populations.³⁴ This approach risks overlooking genuine quality-of-care differences that may emerge when comparing hospitals across different social strata. Well-designed studies are needed to determine which social risk factors should be included in risk adjustment and to assess their impact before social risk adjustment can be implemented in Singapore's healthcare performance metrics.

CONCLUSION

Multimorbidity and frailty were associated with higher odds of 30-day readmission following an index admission for COPD. Risk adjustment revealed significant improvements in performance over time that were not evident in unadjusted analyses. These findings underscore the importance of applying risk adjustments to ensure the validity and fairness of quality metrics.

Supplementary material

Table S1. STROBE statement: Checklist of items that should be included in reports of cohort studies.

Ethics statement

This study was approved by SingHealth Centralised Institutional Review Board (2018/2698).

Declaration

All the authors have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript.

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Regulating, implementing and evaluating AI in Singapore healthcare: AI governance roundtable's view

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ABSTRACT

Introduction: An interdisciplinary panel, comprising professionals from medicine, AI and data science, law and ethics, and patient advocacy, convened to discuss key principles on regulation, implementation and evaluation of AI models in healthcare for Singapore.

Method: The panel considered 14 statements split across 4 themes: "The Role and Scope of Regulatory Entities," "Regulatory Processes," "Pre-Approval Evaluation of AI Models" and "Medical AI in Practice". Moderated by a thematic representative, the panel deliberated on each statement and modified it until a majority agreement threshold is met. The roundtable meeting was convened in Singapore on 1 July 2024. While the statements reflect local perspectives, they may serve as a reference for other countries navigating similar challenges in AI governance in healthcare.

Results: Balanced testing approaches, differentiated regulatory standards for autonomous and assistive AI, and context-sensitive requirements are essential in regulating AI models in healthcare. A hybrid approach—integrating global standards with local needs to ensure AI complements human decision-making and enhances clinical expertise—was recommended. Additionally, the need for patient involvement at multiple levels was underscored. There are active ongoing efforts towards development and refinement of AI governance guidelines and frameworks balancing between regulation and freedom. The statements defined therein provide guidance on how prevailing values and viewpoints can streamline AI implementation into healthcare.

Conclusion: This roundtable discussion is among the first in Singapore to develop a structured set of statements tailored for the regulation, implementation and evaluation of AI models in healthcare, drawing on interdisciplinary expertise from medicine, AI, data science, law, ethics and patient advocacy.

Keywords: artificial intelligence, deliberation, ethics, governance, regulation

CLINICAL IMPACT

What is New

- This roundtable discussion is among the first in Singapore to develop a structured set of statements for regulation, implementation and evaluation of AI models in healthcare.

Clinical Implications

- The panel advocates context-specific testing approaches to balance between patient safety and innovation.
- This panel recommends selectively adopting international standards, to fit regulations to suit Singapore's needs; and engaging patients actively at multiple levels as key stakeholder in AI governance and regulation.

INTRODUCTION

Artificial Intelligence (AI) can transform healthcare by enhancing operational efficiency, improving diagnostics and prognostics, personalising and guiding treatment.¹ These advances promise better patient outcomes and more effective resource allocation. However, implementing AI into healthcare also comes with significant risks, including algorithm bias,² concerns on patient privacy and autonomy,³ cognitive uncertainty in using AI for clinical decision-making,⁴ and unpredictable affectations on the doctor-patient relationship.⁵ These risks highlight the need for robust AI governance and regulation to ensure that AI technologies are safe, ethical and transparent.

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Effective governance regulations can safeguard patient trust, ensure accountability and mitigate unintended consequences. This ensures that healthcare systems are able to harness the benefits of AI responsibly.

In Singapore, regulatory oversight of AI in healthcare currently relies on voluntary compliance to published guidelines.⁶ Several such guidelines exist, including the Artificial Intelligence in Healthcare Guidelines (AIHGle) developed by Singapore's Ministry of Health with the Health Sciences Authority (HSA) and the Integrated Health Information Systems.⁷ The HSA's regulatory guidelines on AI Medical Devices (AI-MD)⁸ was aimed at outlining good practices for AI developers and users.⁶ The AI Governance Testing Framework and Toolkit,⁹ which comprises 11 key AI ethics principles, is aligned with Singapore's Model AI Governance Framework¹⁰ and other international AI frameworks. In 2024, Singapore issued the Model AI Governance Framework for Generative AI (GenAI). This GenAI framework proposes 9 dimensions that comprises "a systematic and balanced approach to address concerns related to GenAI while continuing to facilitate innovation."¹¹

In Europe, the European Union (EU) Artificial Intelligence Act tiers AI according to risk; defines obligations and liabilities of stakeholders and users (notably, obligations fall on developers for high-risk AI systems); and demands technical documentation, outlines how to use the AI, and provides a summary on training data.¹² The Act also requires model evaluations, adversarial testing, post-deployment tracking (incident reporting) and cybersecurity protections. Finally, the EU Artificial Intelligence Act bans certain AI practices, including real-time biometric identification and social scoring. The approach taken in the US is more diffused, with state legislatures passing AI bills rapidly, setting differing thresholds, coverage and subject matter. There is no federal equivalent of the same scope as the EU Artificial Intelligence Act. The regulatory landscape is also rapidly evolving in China. A proposed AI law has been drafted (Artificial Intelligence Law of the People's Republic of China) in May 2024, and is circulated for inputs amongst scholars. While there is some initial criticism that the Chinese AI law favours industry over individual protection, its circulation to academia presents unprecedented and exciting opportunity for academic and public inputs to shape practice. Internationally, the World Health Organization (WHO) is actively collaborating with member states to develop comprehensive guidance on governance, ethical standards and regulations. These efforts aim to address emerging opportunities and challenges, mitigate risks, protect public health, and build trust in the use of AI in healthcare.

Differences in AI governance rules could create tensions and present practical challenges for real-

world compliance. Currently, there is a lack of common approaches or resolution on what needs to be regulated. To gain holistic perspective, bringing key opinion leaders and stakeholders together to deliberate on critical issues and reach consensus can help provide insights that in turn, informs on actionable policies.

METHOD

This roundtable aimed to deliberate and establish consensus on key issues on AI regulation in healthcare. The roundtable panel comprised of 17 experts in medicine, AI, data science, law, ethics and patient advocacy (Table 1 and Supplementary Table S1). Panellists were selected based on their prior involvement in related initiatives, including those led by the Ministry of Health's Centre of Regulatory Excellence (MOH-CoRE) and AI Singapore. Additional participants were invited through referrals, chosen for the significance and influence of their roles in the national implementation and deployment of medical AI.

Fourteen statements, representing the themes of "The Role and Scope of Regulatory Entities," "Regulatory Processes," "Pre-Approval Evaluation of AI Models" and "Medical AI in Practice" (Table 2) were developed by the working group after a deep read on 71 framework documents published worldwide. Each theme was introduced by a moderator. Panellists deliberated on each statement, with the moderator actively refining and moderating the statements, taking into account the various viewpoints presented. Once discussions converged, panel members would cast their votes. Statements were passed if more than 80% of panellists agreed. Otherwise, discussions were resumed, the statements refined, and then put to a second vote. Regulatory agency observers were present throughout and provided input or guidance where needed.

All published statements have been reviewed by panellists and observers.

RESULTS

Fourteen AI governance statements were drafted, categorised into 4 key themes, in a 1-day roundtable conducted on 1 July 2024 in Singapore. All statements achieved full consensus with at least 80% agreement among panel members. Participant profiles are summarised in Table 1. The finalised statements, observations and interpretations are outlined below.

Role and scope of regulatory entities

Statement 1: Singapore's existing healthcare regulatory framework should be supplemented by regulatory guidance for AI that is periodically updated.

Table 1. AI governance roundtable members.

Name	Institution	Expertise
Andrew Prah	Wee Kim Wee School of Communication and Information, Nanyang Technological University	Communication and human-computer interaction
Clive Tan	Tan Tock Seng Hospital Saw Swee Hock School of Public Health, National University of Singapore	Digital health, population health and universal health coverage
Wilson Goh	Lee Kong Chian School of Medicine, Nanyang Technological University	Informatics, statistics, AI
Cher Heng Tan	National Healthcare Group (NHG)	Radiology, clinical innovation, translation and implementation.
Joseph Sung	Lee Kong Chian School of Medicine, Nanyang Technological University	AI in medicine, ethics, gastroenterology
Meng Ling Feng	Saw Swee Hock School of Public Health, National University of Singapore	Big data analytics, AI
Keng Hui Lim	Science & Engineering Research Council, Agency for Science, Technology and Research (A*STAR)	High performance computing, computational modelling and simulation
Nan Liu	Duke-NUS Medical School	AI, AI ethics
Kee Yuan Ngiam	National University Health System, Singapore	Innovations in surgery, AI in healthcare
Luke Ong	College of Computing and Data Science, Nanyang Technological University	Computation, programming languages, verification, logic and algorithms
Julian Savulescu	Centre for Biomedical Ethics, Yong Loo Lin School of Medicine, National University of Singapore	Ethics
Ai Ling Sim-Devadas	Office of Patient Engagement,	Patient engagement and advocacy
Nidhi Swarup	Crohn's & Colitis Society of Singapore	Patient engagement and advocacy
Andy Ta	Data aNalytics & AI (DNA), Synapse	Data analytics and AI
Daniel Ting	Singapore National Eye Centre	AI in healthcare
Eric Wong	National Healthcare Group	Digital health and data governance
Chiang Yin Wong	Academy of Medicine, Singapore	Public health
Zee Kin Yeong	Singapore Academy of Law	AI law

To accommodate the dynamic and rapidly evolving nature of AI technologies, regulatory frameworks must be robust yet adaptive. The panel emphasised that, rather than creating an entirely new framework for each technological paradigm shift in AI, it is more practical to build upon existing healthcare regulatory structure. By incorporating regular, targeted updates to AI regulatory guidelines, the approach ensures that policies remain aligned with technological advancements and address emerging or anticipated risks in a timely and relevant manner.

The panel emphasised the need to balance regulatory oversight with fostering innovation. While overly strict regulations could create opportunity costs, particularly for AI companies, the panel stressed that patient well-being must remain the top priority. To this end, they proposed the development of a

regularly updated “code of conduct” to act as a moral compass, guiding ethical AI practices even as technology continues to evolve. Additionally, the panel highlighted the importance of involving diverse stakeholders and experts in the development of regulations. This collaborative approach ensures that guidelines are both inclusive and practical, increasing the likelihood of acceptance and implementation in real-world healthcare settings.

Statement 2: The regulatory and governance framework for AI development and application in healthcare should be built on sound ethical principles (including the need to innovate) and is important to develop and maintain trust between users (healthcare providers and patients) and developers.

Table 2. Summaries of all 14 consensus statements.

Theme	Statement
The role and scope of regulatory entities	Singapore's existing healthcare regulatory framework should be supplemented by regulatory guidance for AI that is periodically updated.
	The regulatory and governance framework for AI development and application in healthcare should be built on sound ethical principles (including the need to innovate) and is important to develop and maintain trust between users (healthcare providers and patients) and developers.
	To support and enhance Singapore's ambition to be an AI hub and SMART Nation, establishing a centre of excellence dedicated to the regulation, governance and responsible use of AI in healthcare is essential.
Regulatory processes for medical AI	The regulatory approval for medical AI should be based on a thorough assessment of risks and benefits. Clinically relevant outcomes should be monitored regularly.
	Regulatory approval of AI products should not mandate full explainability of the models. However, their development and usage must be transparent.
	The process of AI development and application in healthcare should involve relevant stakeholders including clinicians, scientists and patients.
	Specific regulatory criteria should be established for both "locked" and "continuous-learning" models.
Pre-approval evaluation of AI models	The clinical safety and efficacy evaluation of medical AI should be rigorous and a condition for regulatory approval. While randomised controlled trials are a conventional standard, alternative study designs may also be appropriate
	Approval requirements should be based on the intended clinical use, considering the associated risks and benefits, regardless of whether the AI is designed for diagnosis or treatment.
	While it is necessary to safeguard safety and efficacy, the regulatory process should seek to promote innovation and the adoption of AI as a healthcare product or service.
	To adopt AI for clinical use, developers should adhere to prevailing national guidelines and industry standards to ensure data security and privacy.
Medical AI in practice	Clinical decisions should not rely solely on AI recommendations. Human input and discretion must always be considered the final authority in patient management.
	The use of AI in clinical tools and services should be communicated to providers and recipients in accordance with the prevailing medical standard of care.
	A clear regulatory pathway for AI products should mandate continuous post-market surveillance and routine real-world performance monitoring.

Panellists maintained that ethical considerations, while important, should not stifle the imperative to innovate. The need for innovation, to progress society and improve overall well-being, should also be seen as a moral imperative unto itself. Regulations should not only safeguard against exigent and anticipatable risks, but also ensure the advancement of AI technologies that can ultimately save lives. The panel agreed that trust between healthcare providers and patients is paramount and should not be compromised due to AI implementation. Just as critical is the trust between the AI developers and end-users, which has to be formed for smooth AI adoption. This statement highlights a fundamental position that all panellists unanimously agreed with—that the humanistic aspect of the practice of medicine needs to be first and foremost maintained when incorporating AI into patient care.

Statement 3 To support and enhance Singapore's ambition to be an AI Hub and SMART Nation, establishing a centre of excellence dedicated to the regulation, governance, and responsible use of AI in healthcare is essential.

The panel agreed that a centralised platform would be highly effective in coordinating and addressing the complex challenges of AI regulation, governance, and application in healthcare. Such a platform could foster collaboration among regulatory bodies, healthcare providers and technology developers. To ensure responsible AI integration, the platform must incorporate a "responsible use" dimension, embedding ethical standards and societal values into its initiatives. Key priorities for the centre should include the dissemination of findings, offer continuous learning opportunities to keep stakeholders—such as users, developers and implementers—up to date on

advancements in AI regulation and implementation. Additionally, the platform should provide guidance on AI ethics, facilitate collaborative spaces for interdisciplinary research, and act as an advisory body for policymakers to promote informed and ethical decision-making.

Regulatory processes for medical AI

Statement 4: The regulatory approval for medical AI should be based on a thorough assessment of risks and benefits. Clinically relevant outcomes should be monitored regularly.

The panel recommended prioritising benefits over outcomes for a more effective counterbalance to risks in AI deployment. They also highlighted the necessity of continuous monitoring of clinically relevant outcomes,¹³ acknowledging the dynamic nature of risks and benefits over time. To obtain initial approval, the AI model must demonstrate its ability to meet its defined objectives, particularly in improving patient outcomes. Additionally, the panel stressed the importance of identifying anticipated risks and providing probability estimates for these risks prior to implementation. The panel further underscored the need for follow-up work to enhance specificity and granularity, particularly in clearly defining and categorising risks and benefits, to ensure more precise evaluations and informed decision-making.

Statement 5: Regulatory approval of AI products should not mandate full explainability of the models. However, their development and usage must be transparent.

The panel concurred that requiring full explainability prior to regulatory approval is neither practical nor sustainable, as it risks hindering innovation and limiting the potential benefits of AI. Similarly, mandating evidence from full randomised controlled trials for regulatory approval was deemed unnecessary. The level of explainability required depends significantly on the efforts of developers and adopters to ensure transparency across data processing, model training, validation and the collection of real-world evidence. Although standardised requirements for explainability are currently lacking, developers should aim to provide thorough and well-documented supporting materials to facilitate the review process. Regulators, on the other hand, should prioritise the development of standardised frameworks and processes as AI testing and validation methodologies continue to mature, enabling a more structured and effective evaluation of AI systems.

Statement 6: The process of AI development and application in healthcare should involve relevant stakeholders including clinicians, scientists and patients.

The panel unanimously agreed that multi-stakeholder engagement should encompass the AI lifecycle from development, implementation to post-deployment monitoring. Panellists emphasised that stakeholder engagement should be a continuous process, ensuring that AI systems remain effective, safe and aligned with end-users' needs. Ongoing involvement fosters transparency and trust by enabling open discussions about the benefits and risks of AI. By involving stakeholders directly impacted by AI applications, developers and regulators can better address concerns, leading to more ethical and practical AI systems. Additionally, the panel highlighted the importance of aligning with international bodies and adhering to their established best practices.

Statement 7: Specific regulatory criteria should be established for both "locked" and "continuous-learning" models.

Continuous-learning models are a powerful category of AI algorithms that keep learning from new data over time. Due to this quality, such models dynamically update their parameters using real-time data during deployment,¹⁴ whereas locked models have static parameters that are updated only during scheduled offline maintenance. The panel highlighted that regulating continuous-learning models is particularly challenging due to their evolving nature, which makes traditional one-time validation insufficient. These models require distinct regulatory criteria, including ongoing monitoring and transparent documentation, to ensure safety and efficacy.

In contrast, locked models, preferred by developers, allow for stable longitudinal validation and simpler regulatory approval processes. Observers noted that Singapore updated its policy for continuous-learning medical devices in 2020 to address these challenges. However, no applications for such models have been submitted or reviewed to date, suggesting either industry hesitation or difficulty in meeting the regulatory requirements. The panel emphasised the need for clearer guidance to encourage safe adoption of continuous-learning models while maintaining high standards of accountability (that the AI systems work as intended while also establishing processes for appeals, corrections and overrides when patients or clinicians question AI decisions) and transparency (the degree to which a model's decision-making, rules can be made available for human access, interrogation and understanding).

Pre-approval evaluation of AI models

Statement 8: The clinical safety and efficacy evaluation of medical AI should be rigorous and a condition for regulatory approval. While randomised controlled trials are a conventional standard, alternative study designs may also be appropriate.¹⁵

The panel emphasised the importance of rigorously evaluating AI for clinical safety and efficacy, but acknowledged that evaluation processes must be tailored to the specific clinical context. While randomised controlled trials (RCTs) are the gold standard in drug discovery, their application to AI models faces significant challenges, such as patient recruitment, high costs, and unforeseeable risks to real patients. The panel recommended exploring alternative evaluation approaches that are more suited to AI, including performance benchmarking against prior works (similar to meta-analyses) and demonstrating benefits through real-world evidence compared against existing standards of care. Ideally, these evaluations should be prospective and supplemented with rigorous post-market surveillance to identify “unintended outcomes and biases.”¹⁶

The panel further highlighted the value of sandbox environments as viable alternatives. Sandboxes are virtual simulation environments that enable testing of AI-specific parameters, and are particularly beneficial for uncommon clinical conditions with limited data. In many cases, sandbox testing may better simulate real-world applications, offering a more practical evaluation framework. In the UK, the Medicines and Healthcare Products Regulatory Agency’s “Software and AI as a Medical Device Change Programme—Roadmap” was also discussed as a potential reference model. The roadmap proposes an “airlock process” for Software as a Medical Device (SaMD), which involves heightened monitoring and clearly defined entry and exit criteria, ensuring safer and more effective AI deployment in clinical practice.

Statement 9: Approval requirements should be based on the intended clinical use, considering the associated risks and benefits, regardless of whether the AI is designed for diagnosis or treatment.

The panel concluded that approval requirements for medical AI should be guided by the intended clinical use and risk-benefit ratio, acknowledging that risks vary depending on the tool, context and application. A nuanced approach to risk assessment is essential, particularly in evaluating the degree of influence AI has on clinical decision-making. The panel emphasised that factors, such as whether the AI is fully assistive or automated, patient-facing or physician-facing, should shape regulatory requirements, rather than a blanket definition of safety and efficacy. Furthermore, the purpose of the AI—whether for diagnosis or treatment—does not inherently define its risk level and should not solely dictate regulatory standards.

This stance aligns with frameworks such as the UK’s National Institute of Health and Care Excellence’s Evidence Standards Framework for Digital Health Technologies, which recommends higher levels of evidence (e.g. RCTs) for tools managing medical care,

and lower levels for preventative or self-management tools. Similarly, Australia’s Therapeutic Goods Association assesses SaMD based on risk profiles, categorising “recommendation” tools as higher risk than “information-only” tools. The panel also noted that some AI applications may pose minimal risks yet fail to deliver meaningful benefits, underscoring the importance of emphasising value and utility in AI development.

Statement 10: While it is necessary to safeguard safety and efficacy, the regulatory process should seek to promote innovation and the adoption of AI as a healthcare product or service.

The panel agreed that regulatory processes should foster innovation rather than hinder AI adoption with overly stringent safeguards. Maintaining safety and efficacy is not mutually exclusive and should be important criteria during AI evaluation. Broader regulatory considerations should incorporate principles of trustworthy AI, as outlined in the US National Institute of Standards and Technology’s “Artificial Intelligence Risk Management Framework (AI RMF 1.0),” which includes security, explainability, privacy, fairness, validity, reliability, accountability, and transparency. International frameworks, such as the Blueprint for an AI Bill of Rights (2022) in the US, highlight the need for robust protections while promoting innovation to ensure AI improves lives without causing harm.

Statement 11: To adopt AI for clinical use, developers should adhere to prevailing national guidelines and industry standards to ensure data security and privacy.

The panel emphasised the importance of data security and privacy for regulatory approval. However, they noted that relying solely on single prescriptions, such as the Ministry of Health, Singapore’s HealthTech Instruction Manual—which governs data management within public healthcare entities in Singapore—might be too restrictive and could inadvertently exclude broader applications of medical AI across the other parts of the healthcare sector. Other complementary guidelines, such as AIGHle or Cybersecurity Agency of Singapore’s healthcare cybersecurity framework (launched in December 2023), cover key aspects, such as software updates, malware protection, data backup and cyber hygiene. While the panel emphasised that users should adhere to prevailing national guidelines and industry standards, they recognised that this is a rapidly evolving space, which may see the various policies and guidelines converging over time. Some members raised concern that Singapore’s public healthcare stringent data privacy standards could inadvertently hinder the AI development and adoption.

Medical AI in practice

Statement 12: Clinical decisions should not rely solely on AI recommendations. Human input and discretion must always be considered the final authority in patient management.

The panel unanimously agreed, emphasising that human involvement in clinical decision-making is essential, regardless of technological advancements.^{17,18} While AI can enhance healthcare by improving affordability, accuracy and efficiency, human values must remain central to medical practice. Clinicians play a crucial role in building patient trust and ensuring human autonomy, even when AI is integrated. Patient advocacy representatives stressed that the role and responsibility of doctors should not be diminished. Ultimately, clinicians must oversee and take responsibility for AI use, including interpreting AI outputs and integrating them into clinical procedures.

Statement 13: The use of AI in clinical tools and services should be communicated to providers and recipients in accordance with the prevailing medical standard of care.

The statement emphasised the importance of transparency and consent in the use of AI in clinical settings. Panellists debated the necessity of obtaining explicit patient consent for every instance of AI use, but recognised its impracticality for routine tools, such as automated ECG interpretations. The statement recommends aligning AI communication with the prevailing medical standard of care, reserving explicit consent for scenarios where AI significantly impacts clinical decisions or involves sensitive patient data, while general consent suffices for routine use.

Clinician acknowledgment was also highlighted, stressing the need for healthcare providers to understand AI tools to effectively integrate them into clinical judgment and maintain accountability. The panellists acknowledged challenges, such as reduced patient interaction time, and underscored the importance of personalised communication tailored to patient needs. Transparency and flexibility were deemed essential for fostering trust and ensuring ethical AI adoption. Further discussions were encouraged to clarify how AI-related information should be communicated to patients.

Statement 14: A clear regulatory pathway for AI products should mandate continuous post-market surveillance and routine real-world performance monitoring.

The panel highlighted that building trust in AI requires robust tools and structures, recognising that trust can fluctuate due to various factors. Unlike drugs or

some other technologies where constant monitoring is not standard practice, AI's broader capabilities and roles make post-market surveillance essential.^{19,20} The panel also noted a lack of clarity around who should be responsible for monitoring, emphasising the need for defined accountability. On AI performance, the panel agreed that while improvement over time is not guaranteed, AI must consistently perform as intended and meet the standards for which it was approved. Establishing a minimum standard for AI performance in healthcare is crucial for ensuring reliability and safety. They stressed the importance of collaboration between healthcare providers and AI developers to maintain accountability. While current practices often rely on consensus among doctors, the panel emphasised that manufacturers and suppliers must also share ongoing responsibility for AI performance and safety.

DISCUSSION

In summary, the panel advocates for a balanced approach to AI testing and regulation in healthcare, emphasising safety, efficacy and ethical considerations.

Key recommendations include:

- **Balanced testing:** Standardised testing protocols are crucial to detect errors and biases while allowing for innovation.
- **Differentiated standards:** Autonomous AI systems require stricter regulation than assistive AI systems.
- **Risk-based evaluation:** AI systems for high-risk conditions should undergo more rigorous testing than those for low-risk applications.
- **Global and local standards:** A hybrid approach combining global standards with local needs ensures a balance between safety and innovation.
- **Human oversight:** AI should primarily serve as an assistive technology to support human decision-making.
- **Patient involvement:** Involving patients in the development process ensures human-centred and patient-friendly technologies.
- **Continuous monitoring:** Ongoing monitoring is essential to maintain the safety and efficacy of AI systems.

Limitations and further considerations

Methodologically, our approach shares several conceptual similarities with the Delphi method, although we are cautious about presenting it as a full or traditional Delphi implementation. In line with Delphi principles, our process involved the formulation of an initial problem statement by facilitators, the assembly of an expert panel, and iterative rounds of discussion and refinement aimed at reaching a shared understanding or convergence of opinion.

However, we do not claim full adherence to the Delphi protocol, particularly in terms of anonymity, multiple structured rounds and quantitative consensus metrics, which are typically associated with formal Delphi studies. Rather, we view our approach as a structured expert elicitation exercise designed to capture an early snapshot of expert perspectives within a rapidly evolving field. Our objective was to surface potential areas of convergence among a curated group of thought leaders, researchers and practitioners working at the intersection of medical AI, healthcare delivery and policy. In a domain characterised by high uncertainty and rapid technological advancement, we believe such early insights are valuable. They not only help frame emerging challenges and opportunities but also serve as a directional compass for subsequent research, collaboration and policy considerations. By documenting and presenting these perspectives, we aim to stimulate further dialogue, refine shared goals, and contribute to the strategic alignment of efforts within the broader medical AI community.

The statements discussed cover various aspects of AI regulation, but there may be other important areas that were not fully addressed. For instance, procedural considerations related to the regulatory process itself need more attention. This includes the role of government in shaping and enforcing these regulations, as well as the specifics of comparing international guidelines and standards. For product-specific areas, such as AI healthcare tools, the influence of standards from bodies like International Organization for Standardization and International Electrotechnical Commission should also be considered, as they play a significant role in defining the regulatory landscape.

Ethical, social and legal concerns deserve particular focus as they play a crucial role in AI regulation.^{21,22} These issues may require more in-depth discussions and could benefit from exploration in a separate, dedicated forum. The current discourse does not fully address the ethical nuances that arise in AI healthcare applications. Therefore, we intend to address this in a follow-up meeting in second half of 2025.

Greater emphasis is needed on the practical aspects of implementation. Action-oriented meetings and procedural discussions are essential to develop a clear path from concept to the real-world implementation of AI systems in healthcare. A Singapore-focused approach, which could involve the development of instruments and guidelines for clinical translation,²³ is necessary to ensure alignment with local needs and regulations. However, comparisons with international standards should also be made to ensure global relevance and the adoption of best practices. This comprehensive approach will support the safe, ethical and effective deployment of AI technologies.

Finally, there is the impact on medicine, and affectations on doctor-patient relationships.²⁴ While AI can transform healthcare, we may risk losing quality engagements with patients. It therefore becomes even more important to think about how to balance technological expertise with humanistic care, especially in areas of doctor training and education.²⁵

Reflections

This was one of the first roundtable discussions on AI regulation in the healthcare sector in Singapore. The panel deliberated on 14 statements across 4 key themes: regulatory bodies, regulatory processes, model evaluation, and the impact on medical practice. While the panel brought together a diverse group of participants from academia, public sectors, healthcare, and regulatory bodies, the structured process enabled respectful and productive dialogue, resulting in the finalised statements. Given the breadth of topics, the discussion spanned a full day (9 am to 5 pm), and time constraints meant that not all statements received equal attention. As an early-stage effort, we focused on pressing issues first. Future sessions will be designed to explore specific sub-topics in greater depth and detail, such as affectations on doctor-patient relationship, and ethics.

CONCLUSION

This roundtable captured opinions of experts to uncover practicable insights for medical AI regulation. The 14 statements highlighted the complexity of AI governance in healthcare, emphasising the need for adaptable regulatory frameworks that balance innovation with patient safety and treatment efficacy. As AI evolves, governance models must remain flexible while upholding ethical and clinical standards. The process underscored the value of multi-disciplinary collaboration among clinicians, patient advocates, AI developers, ethicists, and legal experts to ensure policies address real-world challenges. The discussions revealed both areas of agreement and emerging challenges, providing actionable insights to guide AI governance strategies. These insights provide valuable recommendations for policymakers, healthcare providers, and developers to foster innovation, build trust, and safeguard patient protection.

Ethics statement

Ethical approval was not required for this study because there was no personal consent required and no patient data were collected.

Declaration

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Bayesian meta-analysis in the 21st century: Fad or future of evidence synthesis?

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ABSTRACT

Meta-analyses are pivotal in evidence-based medicine. They synthesise findings from multiple studies to inform clinical practice. Traditionally, frequentist statistical methods have dominated this field. However, growing recognition of their limitations in interpreting uncertainty and integrating prior knowledge has led to increased interest in Bayesian methods. We compared the Bayesian and frequentist approaches to meta-analysis, assessed their respective strengths and limitations, and evaluated how each technique influences the interpretation of clinical trial data, particularly when evidence is ambiguous. A narrative review was conducted to understand and compare key aspects of frequentist and Bayesian statistics. Real-world clinical examples were used to illustrate the differences between how each statistical paradigm interprets the same dataset. Frequentist methods were assessed based on null hypothesis testing and *P* values, while Bayesian methods were evaluated for their use of prior distributions and posterior probabilities. We demonstrated how statistical significance of the obtained result may differ based on whether a frequentist or Bayesian statistical analysis was employed. In most cases, Bayesian methods enabled increased intuitiveness and flexibility of interpretations by incorporating uncertainty and pre-existing evidence. While frequentist methods remain standard for simpler univariate analyses, the Bayesian approach offers a more holistic framework for complex meta-analyses, as it aligns more closely with practical clinical decision-making. This places Bayesian inference a valuable tool in the future of evidence synthesis.

Keywords: Bayesian, biostatistics, frequentist, meta-analysis, statistics

INTRODUCTION

Evidence-based medicine is the cornerstone of modern clinical decision-making, but not all evidence is practice-changing. To aid clinicians, there is an accepted hierarchy to classify published evidence, often described as the evidence pyramid. Weaker study designs are found at the bottom of the pyramid,

with more robust study methods towards the top (Fig. 1).^{1,2} Systematic reviews and meta-analyses synthesise existing evidence and sit at the top of the pyramid, significantly influencing education, future research and clinical care delivery.

A meta-analysis is a statistical tool for compiling results from multiple scientific studies seeking to answer the same research question. This is essential because the results of one study may not apply under different circumstances.^{3,4} Combining studies through a meta-analysis helps to draw nuanced conclusions as it allows researchers to estimate the mean effect size across different populations while performing subgroup analyses. Meta-analyses also provide an assessment of the reliability of results.^{5,6}

There are 2 primary approaches to statistics in meta-analyses: the frequentist and Bayesian methods. They are differentiated by their interpretation of uncertainty, which refers to the degree of inherent variability in a measured value.⁶ Until recently, the reporting of meta-analyses was largely dominated by frequentist statistics. However, with the emergence of platform trials and a growing recognition of the limitations of arbitrary significance thresholds, Bayesian methods have gained traction.³ Moreover, the Bayesian approach is viewed as more intuitive and aligns better with cumulative science.⁷ How do the 2 approaches differ, and what are the implications for the future of meta-analyses?

An overview of frequentist statistics

Frequentist statistical inference has long been the preferred method for clinical trials and meta-analyses. This approach assumes that a fixed null hypothesis is true, following which long-term probabilities are calculated using only the data obtained (i.e. assessing how probable the dataset is given the null hypothesis). Therefore, any uncertainty in a frequentist analysis arises solely from sampling error. This can be understood by considering the outcome of flipping a coin indefinitely. The null hypothesis posits that the

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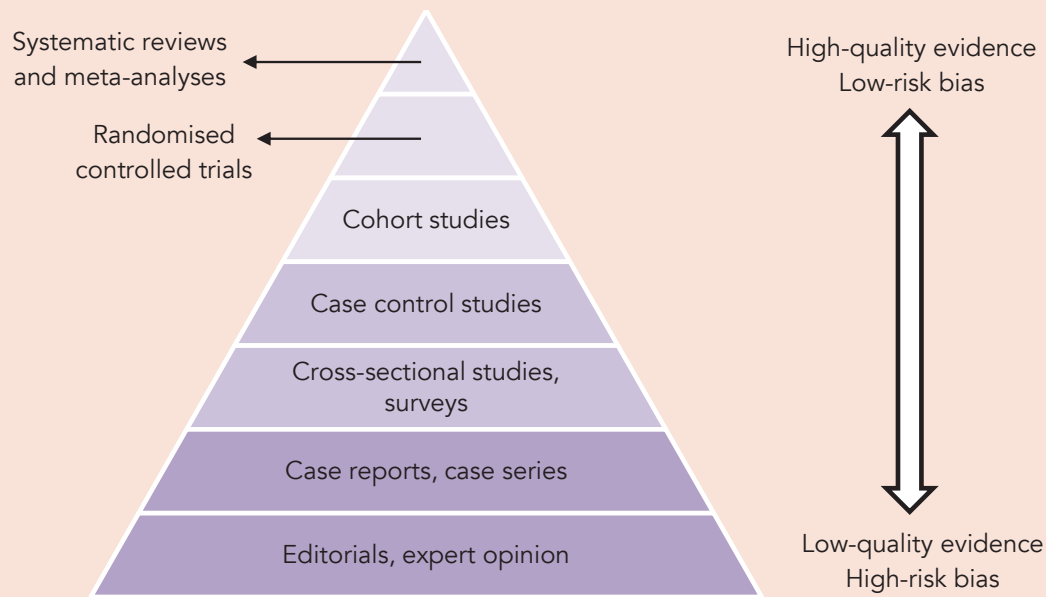
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Fig. 1. The evidence pyramid.



outcome would be heads half the time (all else being equal). Flipping the coin a few times may yield a different observation by chance (e.g. all heads). If this pattern persists in the long run, it represents a departure from the expected data, leading to the rejection of the null hypothesis.⁸ The researcher concludes that other factors must be responsible for the disparity between the observed and expected results.⁹

In a frequentist analysis, the probability of obtaining another dataset as extreme as the one collected is known as the *P* value. *P* values inform researchers of the likelihood of observing a specific dataset and help assess the compatibility of the obtained data with the null hypothesis. They do not quantify the probability of the null hypothesis itself or measure the magnitude of the treatment effect.¹⁰ A *P* value of less than 0.05 is typically regarded as an acceptable threshold for significance, allowing for the rejection of the null hypothesis. This arises from the fact that there is less than a 5% probability that the observed result is due to chance alone. However, this standard is essentially arbitrary, yet it is considered reasonable by most researchers. Challenges arise when a *P* value is very close to 0.05, as considerable doubt arises regarding the significance of the result. This may lead to a type 1 error, which occurs when the researcher erroneously rejects the null hypothesis.¹¹ The *P* value of 0.05 merely indicates the threshold at which this is deemed acceptable; it does not eliminate the risk of drawing an incorrect conclusion. In such instances, prior

knowledge becomes crucial, although frequentist inference does not provide pathways to leverage previous studies.^{12,13} The Bayesian approach addresses these shortcomings.

An overview of Bayesian statistics

The Bayesian method of statistical inference treats parameters and hypotheses as probability distributions, while the data remain fixed. This sharply contrasts with the frequentist approach, where probabilities are assigned to the observed data, and the null hypothesis is fixed and assumed to be true. Bayesian statistics is founded on Bayes' theorem, which details a method for updating probabilities using current data to build upon previous knowledge. Prior knowledge informs the prior distribution, which summarises what is already known about the subject. It can be derived from expert opinion, historical data or a combination of both. The probability of an outcome after completing a Bayesian analysis is referred to as the posterior probability (or post-test distribution). It encapsulates all the knowledge researchers have about a topic based on previous observations and the most recent experimental data.⁹

Knowledge of prior information can influence the outcome, even when all other conditions remain unchanged.⁹ A real-life example of this would be in the treatment of acute respiratory distress syndrome (ARDS).¹⁴ In 2018, the results of the extracorporeal membrane oxygenation (ECMO) to rescue lung injury in severe ARDS (EOLIA) trial were interpreted using

frequentist statistics. Subsequent interpretation of the same results using Bayesian methods yielded different outcomes.¹⁵ This emphasised how using varying pre-test probabilities in Bayesian analyses of clinical trial data can provide important information for study interpretation. This is particularly so when evidence from the trial is close to the significance threshold and it is uncertain whether current clinical practice should be changed.¹⁵

The EOLIA international clinical trial randomly assigned patients with very severe ARDS to receive immediate venovenous ECMO on diagnosis (ECMO group) or continued conventional treatment (control group), with crossover to ECMO made available for patients in the control group who had refractory hypoxaemia. The primary outcome was 60-day mortality. The trial found that 44 of 124 patients in the ECMO group and 57 of 125 patients in the control group had died. Using a frequentist statistical analysis, this is reflected as a relative risk (RR) of 0.76, 95% confidence interval (CI) of 0.55–1.04, and a *P* value of 0.09. Hence, the authors concluded that there was no significant difference in the 60-day mortality of ARDS patients treated with ECMO versus those treated with conventional mechanical ventilation that included ECMO as a rescue therapy.¹⁴

However, the results of the EOLIA trial were subsequently re-interpreted in a Bayesian analysis.¹⁵ This was because the clinically important point estimate of the absolute risk difference (11%), the

near statistical significance of the effect, and the wide divergence of pre-existing views regarding the benefits of ECMO had made interpretation of the trial controversial.¹⁵ This new study aimed to demonstrate the potential utility of Bayesian analyses by estimating the posterior probability, under various assumptions, that early ECMO was associated with reduced mortality in patients with very severe ARDS. Statistical prior distributions were developed to represent diverse levels of support for ECMO in treating lung injury in patients with severe ARDS.¹⁵ For each of the priors, the corresponding RR, credible interval (CrI) and absolute risk reduction (ARR) were estimated using Bayesian analysis. This means that the post-hoc analysis estimated the posterior probabilities, for which ECMO treatment had exceeded a range of potential values for the minimum, clinically important treatment effect (i.e. $RR < 1$, $RR < 0.9$, $RR < 0.8$, $RR < 0.67$ and $ARR \geq 2\%$, $ARR \geq 4\%$, $ARR \geq 6\%$, $ARR \geq 8\%$, $ARR \geq 10\%$ and $ARR \geq 20\%$). The results of the Bayesian inference are summarised in Table 1.

Overall, the RR of 60-day mortality in patients who received early ECMO treatment compared to conventional mechanical ventilation varied based on the prior that was used in the analysis. The more strongly the pre-test probabilities suggest that early ECMO intervention is lifesaving in severe ARDS, the higher the likelihood that the same results will strongly favour ECMO over mechanical ventilation, and vice versa. If insufficient data are available on a

Table 1. Bayesian analysis of the results of the EOLIA trial.

Prior belief	Assumed median RR	Probability of treatment effect equal to or greater than specified threshold			
		RR<1	RR<0.9	RR<0.8	RR<0.7
Non-informative (Equivalent to no prior data)	1.0	50%	50%	49%	49%
Strongly enthusiastic towards ECMO (Equivalent to previous RCT enrolling 100 patients finding a 33% RR reduction)	0.67	95%	89%	77%	58%
Moderately enthusiastic towards ECMO (Equivalent to previous RCT enrolling 264 patients finding a 22% RR reduction)	0.78	95%	83%	57%	24%
Sceptical towards ECMO (Equivalent to previous RCT enrolling 100 patients finding a 0% RR reduction)	1.0	50%	33%	18%	7%
Strongly sceptical towards ECMO (Equivalent to previous RCT enrolling 264 patients finding a 0% RR reduction)	1.0	50%	24%	7%	1%
Prior informed by previous studies	0.71	99%	48%	Not stated	Not stated

ECMO: extracorporeal membrane oxygenation; EOLIA: extracorporeal membrane oxygenation to rescue lung injury in severe acute respiratory distress syndrome; RCT: randomised controlled trial; RR: relative risk

topic, then an unbiased, non-informative prior with an assumed median RR can be used, and the outcome is driven more by the new experimental data than prior beliefs. Most notably, when the prior was informed by previous studies that contained the latest experimental data on using ECMO for ARDS as of 2018, the results were convincing and conclusive that early ECMO was superior to mechanical ventilation in treating severe ARDS (RR 0.71, 95% CrI 0.55–0.94).¹⁵ This contrasts with the results of the frequentist analysis with the same results.

Bayesian analysis of clinical trial data may provide useful information in interpreting uncertain evidence. It can provide information about the posterior probability of mortality benefit under a broad set of assumptions that can be reflective of the diverse clinical scenarios and patient populations to which trial results will be applied. Incorporating prior knowledge enables researchers to evaluate how new information alters their overall understanding of a treatment. Hence, a Bayesian analysis can refine the interpretation of an outcome and guide changes in clinical practices.⁹

Comparing the Bayesian and frequentist methods

Fundamentally, frequentist statistics aim to determine how probable the observed dataset is, given that the null hypothesis is true, and provide information on our confidence in the accuracy of the obtained result. In contrast, the Bayesian method assigns probabilities to parameters and hypotheses, enabling researchers to assess the likelihood that a treatment is superior. A key advantage of the Bayesian approach is that it mirrors the nature of clinical decision-making, which is generally grounded in probability. Consequently, it is more intuitive than frequentist inference, which reports the probability of obtaining a specific dataset under the assumption that the treatments are equal.⁹

Interpreting the frequentist 95% CI is similarly less intuitive than the Bayesian 95% CrI, as it merely reflects the long-run probability of accurately estimating a parameter rather than the actual value of interest. Reporting the frequentist 95% CIs alongside the *P* value provides insights on the size and direction of an effect, with the width of the CI indicating precision.^{16,17} It informs researchers that 95% of these computed CIs would include the true value of interest if the experiment was repeated infinitely, therefore quantifying the uncertainty surrounding effect estimates.¹⁸ In contrast, the Bayesian 95% CrI indicates that there is a 95% probability that the true value of interest lies within the CrI. The interval is fixed, while the parameter of interest is treated as the random variable. It is common for the frequentist 95% CI to be misinterpreted as conveying this meaning. However, the 95% CI and the 95% CrI

are fundamentally different means of quantifying uncertainty and may be used to estimate statistical significance when they exclude null values but should not be confused between each other.¹⁸ Only the Bayesian CrI offers a direct probability statement about the actual value of interest, allowing for instinctive understanding.

Frequentist methods are more beneficial in simple univariate analyses due to their straightforward nature, whereas Bayesian methods offer versatility in more sophisticated analyses involving complex models.¹⁹ Frequentist methods are the standard for conventional univariate meta-analysis, which assesses each pair of interventions for each outcome separately. These analyses primarily concentrate on understanding the characteristics of a single variable, reducing the necessity to incorporate prior information. Frequentist statistics are also more effortlessly integrated into various software packages, making their results simpler to interpret.^{20,21} However, Bayesian methods enable more effective modelling of complicated variance-covariance structures in multivariate meta-analysis when comparing multiple outcomes. Improved computing technology has led to more programmes offering user-friendly functions for conducting Bayesian meta-analyses, thus contributing to the increasing simplicity of calculating otherwise intricate posterior probabilities and facilitating Bayesian inference.²²

Additionally, as frequentist analyses rely on conclusions drawn solely from the collected data, the conclusion remains fixed irrespective of pre-existing knowledge.⁹ In contrast, the Bayesian method integrates prior knowledge. If robust priors are available from earlier evidence, the new study data must be compelling enough to shift the posterior probability in a different direction. This illustrates how clinicians interpret new evidence in practice, and this makes Bayesian analysis more useful to inform guideline panels, guide reimbursement decisions and assist in health technology assessments.

If there is insufficient prior knowledge on the topic, an uninformative prior or multiple priors may be employed. In such instances, statistical inference is driven more by the acquired data than by prior knowledge, making it easier to overturn preconceived beliefs.⁹ In this situation, the outcomes of a Bayesian inference will not vary substantially from frequentist methods. To obtain balanced and representative results, it is pivotal to use a widely accepted prior that is informed by objective and thorough experimental data. Hence, a key limitation of using Bayesian analysis is that the difficulty of determining an accurate prior, especially when there is a paucity of pre-existing data, leaves more opportunity for the outcomes to be influenced by biased pre-test probabilities.

Finally, Bayesian meta-analyses facilitate the propagation of uncertainty in the heterogeneity parameter. In random effects models, heterogeneity is a critical parameter that reflects the variability in treatment effects across studies but can be challenging to estimate when the number of studies is limited. In frequentist methods, heterogeneity is assumed to be fixed at a certain value, which can lead to biased conclusions. In contrast, Bayesian methods treat heterogeneity as a random variable with its own distribution. Furthermore, the risk of bias is incorporated with greater accuracy. This enables the full uncertainty in the heterogeneity parameter to be carried forward throughout the analysis, resulting in more realistic conclusions.¹⁸

CONCLUSION

The choice between frequentist and Bayesian inference depends on numerous factors. Frequentist statistics ascertain whether the observed result is attributable to chance, making it a logical selection for univariate analyses. Conversely, the Bayesian approach more intuitively captures the complex interpretation of new study data by the clinician making decisions at the bedside. Consequently, it may be more suitable for a complex, multivariate meta-analysis, where the goal is to determine whether new evidence alters current beliefs.

Ethics statement

Not applicable.

Declaration

The authors declare they have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript. This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors. No generative artificial intelligence technologies were used.

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Validation of clinical frailty scale scoring tools for older adults attending the emergency department of a tertiary hospital in Singapore

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Dear Editor,

Frailty increases vulnerability to dependency and death.¹ With Singapore's ageing population, early frailty identification in the emergency department (ED) is critical yet constrained by time and resources. Clinical Frailty Score (CFS) is a validated 9-point tool used for frailty identification, with scores ≥ 5 indicating frailty (Supplementary materials Appendix S1).² In Singapore, the CFS algorithm (CFS-A) (Supplementary materials Appendix S2) showed comparable performance against the gold-standard Frailty Index (FI)³ in hospitalised older persons and predicted outcomes, such as mortality and institutionalisation.⁴ However, there is currently no validated frailty tool for the ED in Singapore.

To address this issue, we developed 2 novel scoring tools: CFS-Fast (Supplementary materials Appendix S3), a simple visual aid; and CFS-Self (Supplementary materials Appendix S4), a self- or proxy-administered version. We aimed to validate these tools, alongside CFS-A, by comparing agreement, diagnostic and predictive performance against FI. In a prior pilot,⁵ CFS-Fast (formerly CFS-ED) and CFS-Self showed moderate agreement with the CFS-A, prompting refinements and renaming to CFS-Fast.

We conducted a prospective observational study at Tan Tock Seng Hospital ED, a tertiary care hospital with 120,000 ED visits annually. Patients aged ≥ 65 years presenting on weekdays from 10am to 5pm were enrolled. Patients who were critically ill, previously enrolled or lacked mental capacity without an accompanying legally acceptable representative (LAR) were excluded. Research assistants obtained written informed consent.

Triage nurses scored CFS-Fast; patients or caregivers scored CFS-Self; and non-study team geriatric-trained staff scored CFS-A, with all raters blinded. Trained research assistants conducted interviews and accessed records to complete a baseline data collection form; and performed telephonic follow ups at 1-, 3- and

6-months to record outcomes including mortality, hospitalisations, ED re-attendances and falls.

Based on sensitivity and specificity estimates of 50% and 90%, respectively, and an 80% frailty prevalence, we aimed to recruit 210 participants. Agreement between the 3 tools and FI was assessed using weighted kappa statistics. Predictive performances were compared with FI for the abovementioned adverse health outcomes. Area under the receiver operating characteristic curves were compared against FI to determine their diagnostic performance, sensitivity, specificity, predictive values and optimal cut-off scores. Frailty was defined as CFS scores ≥ 5 or FI ratio ≥ 0.25 .

Outcomes at 1, 3 and 6 months were analysed using univariate analysis to compare the level of agreement of adverse health outcomes; and multivariate analysis using logistic regression, adjusting for a priori confounders (age, gender and comorbidities), to determine the predictive ability of each tool in predicting adverse outcomes. To account for multiple hypothesis testing across multiple outcomes, the odds ratio (OR) of adverse outcomes were reported with 99% confidence intervals (CI).

A total of 210 patients were enrolled (Supplementary materials Appendix S5). CFS-A identified 106 (50.7%) as frail, compared to 48 (22.7%) by CFS-Fast and CFS-Self. Agreement on frail classification with FI was moderate for CFS-Self (kappa 0.58, 95% confidence interval [CI] 0.45–0.72), and fair for CFS-A (kappa 0.28, 95% CI 0.16–0.40) and CFS-Fast (kappa 0.35, 95% CI 0.22–0.49). CFS-Self had the highest area under the curve [AUC] at 0.78 (95% CI 0.71–0.84), followed by CFS-A (0.68, 95% CI 0.61–0.75) and CFS-Fast (0.67, 95% CI 0.60–0.74) (Fig. 1). CFS-A exhibited the highest sensitivity (76.8%, 95% CI 65.7–87.8%) and the lowest positive predictive value (40.6%, 95% CI 31.2–49.9%).

Over the study period, 3 (1.4%) participants died. At 3 months, 25 (11.9%) were hospitalised while 33

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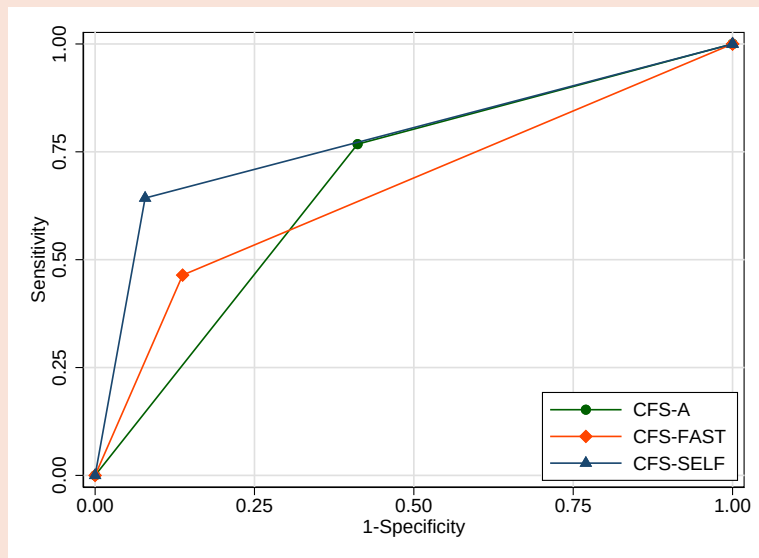
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Fig. 1. Comparison of receiver operating characteristic curves of frailty tools.



CFS-A: Clinical Frailty Score algorithm

(15.7%) re-attended the ED. FI-identified frail patients were more likely to be hospitalised (odds ratio [OR] 3.69, 99% CI 1.09–12.45) or re-attend (OR 4.23 99% CI 1.42–12.59). Patients identified as frail by CFS-A were more likely to be hospitalised (OR 4.04, 99% CI 1.01–16.16), and patients identified as frail by CFS-Self were more likely to re-attend (OR 3.61, 99% CI 1.15–11.34). At 6 months, 36 (17.1%) had been hospitalised, 43 (20.5%) had re-attended and 14 (6.7%) had fallen. FI-identified frail patients were more likely to re-attend or fall.

Adjusting frailty threshold to CFS ≥ 6 , CFS-A agreement with FI improved (kappa 0.41, 95% CI 0.28–0.54), but sensitivity reduced from 76.8% to 46.4% (95% CI 33.4–59.5%). No improvements in sensitivity, AUC or agreement were observed for CFS-Fast and CFS-Self.

To the authors' knowledge, this is the first local study validating CFS scoring tools for ED use. Only CFS-Self reliably identified frailty, showing the most promise as a front-door diagnostic tool. Self-scoring tools, given their speed and practicality, are best suited for the time-constrained ED. The variable performance of the tools may stem from challenges in clinician-administered assessments, which are often conducted under time constraints with limited information. Conversely, self or proxy assessments may offer more accurate and consistent evaluations of premorbid function, reducing inter-rater variability. Our findings align with previous studies showing moderate interrater agreement between patient- and clinician-reported CFS.^{6,7} Self-scoring frailty tools should be further explored for

use in the ED or primary healthcare institutions. Early risk stratification incorporating frailty screening could be cost-effective, reducing ED utilisation, hospitalisations and improving patient outcomes.⁸ Further, CFS-Self was translated into Singapore's 4 major languages, improving accessibility and feasibility in our multilingual population.

This prospective observational study had several strengths. Data collection over 6 months minimised recall bias and improved the accuracy of outcome assessment. Importantly, the tools were tested in a real-world setting, ensuring their validity and effectiveness in clinical use. Longitudinal follow-up strengthened the assessment of predictive validity. However, convenience sampling and exclusion of patients lacking mental capacity without an accompanying LAR, would potentially introduce bias. These patients are likely more frail, resulting in an underestimation of frailty prevalence in our sample. Future research should seek to include a more representative sample, including patients who lack mental capacity to improve generalisability.

In conclusion, CFS-Self demonstrated the strongest agreement with FI, good diagnostic accuracy, and predictive ability for adverse outcomes. Its self-administered nature is practical for frailty screening in time-constrained ED settings, though further validation is needed.

Supplementary materials

Appendix S1. Clinical Frailty Scale.

Appendix S2. CFS algorithm (CFS-A).

Appendix S3. CFS-Fast.

Appendix S4. CFS-Self.

Appendix S5. Baseline characteristics of surveyed patients.

Ethics statement

Ethics approval was granted by the National Healthcare Group Domain Specific Review Board (2022/00127).

Declaration

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Keywords: emergency medicine, frailty, risk, screening, self-administered

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Virtual reality-based cognitive training for MCI in the elderly: A feasibility randomised pilot study

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Dear Editor,

Mild cognitive impairment (MCI) is an at-risk state for progression to dementia where cognitive functions are objectively impaired but functional abilities remain preserved. Current prevalence of MCI among Singaporean Chinese older adults aged 60 and above stands at 12.5%, but this estimate is projected to rise with population ageing.¹ Significant efforts are taken to delay the conversion of MCI to dementia, given the tremendous healthcare and socioeconomic costs associated with disability and dependency in dementia. With the lack of disease-modifying pharmacotherapy to treat neurocognitive disorders, recent attention has been placed on non-pharmacological interventions including computerised cognitive training to prevent cognitive decline in MCI.²

Cognitive training involves guided repetitive practice of standardised tasks designed to target specific cognitive skills or processes, with the aim of improving cognition via reinforcement of neural pathways and neuroplastic mechanisms.³ Virtual reality (VR) technology presents as a novel application for cognitive training where its wrap-around display screens offer a multisensory and immersive environment that enhances ecological validity over that of traditional computerised interfaces.⁴ VR cognitive training (VRCT) used in the context of rehabilitation for traumatic brain injury, stroke and Parkinson's disease has brought about changes in brain structural and functional connectivity.⁵ A recent systematic review of VRCT on MCI found only 4 randomised controlled studies comparing VRCT to traditional cognitive interventions, with the majority utilising only cognitive screening measures to assess for cognition; and only 1 study had investigated the effectiveness of fully immersive VRCT.⁶ Immersion levels, training modality and the cultural theme of computerised environment are important training design factors as they moderate cognitive outcomes.⁷ This study seeks to contribute

to the dearth in literature on immersive VR training by examining the feasibility and therapeutic efficacy of a fully immersive multi-domain VRCT programme on the attention, memory and executive function of older adults with MCI.

This cross-sectional pilot study employed a randomised controlled design with participants recruited from an outpatient memory clinic in Changi General Hospital, Singapore. Participants were aged between 65 and 85 years, had a diagnosis of MCI by a clinician in accordance with Petersen's criteria, and Mini Mental Status Examination ≥ 23 . Exclusion criteria included severe visual or auditory impairment, major psychiatric disorders and serious medical illnesses. The study was approved by the SingHealth Centralised Institutional Review Board (2020/2239).

Randomly generated intervention allocations sealed in opaque envelopes were provided by a biostatistician to psychologists conducting the interventions. Participants who were assigned to the VRCT intervention group underwent hourly VRCT sessions over a 10-week period conducted in outpatient settings. The VR experiences were administered through a head-mounted Oculus Go Screen V7 (Meta Platforms, Inc, Menlo Park, CA, US) with a 5.5-inch display that weighed 468 grams. The software application used was MindGym (DancingMind Pte Ltd, Singapore) that features visual stimuli reflecting familiar localised environments. The present VRCT programme included applications that involved tasks of memory retention, escaping mazes, listening conversations and interference control. Participants who were assigned to the active control group were reviewed monthly and provided treatment-as-usual, which included weekly homework tasks from a cognitive stimulation booklet.

Feasibility of the VRCT programme was assessed across 4 domains: acceptability based on perceived ease of use and usefulness of VRCT, safety, adherence

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to VRCT sessions and preliminary efficacy. Comprehensive neuropsychological battery was administered by blinded assessors pre- and post-intervention to evaluate the cognitive outcomes of interest, including the Montreal cognitive assessment (MoCA), the frontal assessment battery (FAB), and the repeatable battery for the assessment of neuropsychological status (RBANS).

Data were analysed using SPSS Statistics software version 26.0 (IBM Corp, Armonk, NY, US). Continuous variables were presented as mean and standard deviation or median and interquartile range where appropriate, while categorical variables were presented as frequencies and percentages. A 1-way analysis of variance was conducted to assess the between-group difference of the intervention's effect over time for each outcome measurement. The significance level was established at $P < 0.05$. Cohen's d effect size (ES) was reported alongside the P values. Thresholds of 0.2 for small, 0.5 for moderate and 0.8 for large effects were employed as guiding benchmarks.

Of 33 participants who were screened for eligibility, 11 were randomly allocated to the VRCT group and 11

to the control group. Participants in the VRCT group were older and had poorer MoCA baseline scores. All participants in the VRCT group completed the full 10 weekly sessions with no dropouts. Two controls withdrew from the study due to concerns of visiting the hospital amid COVID-19. No adverse events related to VR usage such as dizziness, headache or fatigue were reported. Most participants reported high levels of comfort while using the interface. About 91% of participants found the VRCT programme useful in enhancing their subjective memory and attention. The VRCT participants exhibited significant favourable changes in the RBANS figure copy ($P = 0.01$) and FAB go/no-go ($P = 0.04$) subdomains over time as compared to the control group (Table 1). While not statistically significant, moderate to large ES favouring the VRCT group were observed in RBANS list recall ($ES = 0.7$) and RBANS figure recall ($ES = 0.8$) over time. Conversely, moderate to large ES favouring the control group was found for RBANS list learning ($ES = 0.6$).

To our knowledge, this is the first fully immersive VRCT programme conducted for older adults with MCI in Singapore. Our study supports the safety

Table 1. Changes in cognitive outcomes between groups at baseline and after 10 weeks.

		Baseline		Post	Mean difference (between groups)	Cohen's d	Between groups
		n	Mean (SD)	Mean (SD)	Mean (95% CI)		P value
MoCA	VR	11	20.8 (3.6)	20.3 (3.7)	-0.7 (-3.5 to 2.2)	0.2	0.64
	CG	9	23.4 (2.9)	23.6 (1.3)			
RBANS							
Figure copy	VR	11	16.7 (2.5)	18.0 (1.5)	3.2 (0.7–5.6)	1.2	0.01 ^a
	CG	9	18.6 (1.2)	16.7 (3.0)			
List recall	VR	11	0.4 (0.9)	1.4 (1.7)	1.1 (-0.4 to 2.6)	0.7	0.14
	CG	9	3.1 (3.1)	3.0 (3.3)			
Figure recall	VR	11	5.5 (3.2)	7.4 (3.9)	2.4 (-0.4 to 5.1)	0.8	0.09
	CG	9	7.2 (6.2)	6.8 (5.3)			
FAB	VR	11	14.4 (2.2)	15.8 (1.7)	0.6 (-1.0 to 2.1)	0.3	0.45
	CG	9	15.8 (1.6)	16.7 (1.2)			
Conflicting instructions	VR	11	2.6 (0.9)	3.0 (0.0)	0.3 (-0.4 to 0.9)	0.3	0.45
	CG	9	2.9 (0.3)	3.0 (0.0)			
Go/no-go	VR	11	2.3 (0.8)	2.6 (0.7)	0.6 (0.04–1.1)	1.0	0.04 ^a
	CG	9	2.9 (0.3)	2.7 (0.5)			

CG: control group; CI: confidence interval; FAB: frontal assessment battery; MoCA: Montreal cognitive assessment; RBANS: repeatable battery for the assessment of neuropsychological status; SD: standard deviation; VR: Virtual reality group

Mean difference (between groups): Change over time in VR – change over time in CG.

^a Significant at the $P < 0.05$ level.

and tolerability of VRCT. Factors that facilitated its acceptability included gradation of training duration and task difficulty that prevented side effects of VR usage and enabled older participants to gain familiarity and confidence in the VR system. Consistent adherence and satisfaction throughout the 10 weekly programme were indicative of sustained motivation and enjoyment levels, key in ensuring longer-term intervention adherence among participants.⁸ Improvements in verbal memory, visual memory and aspects of executive function (specifically response inhibition) were found for the VRCT intervention group. Repetitive practice on prescribed VRCT tasks appeared to have contributed to near transfer effects on immediate neuropsychological testing.² No improvement in attention was found and may be due to insufficient training frequency and intensity to bring about potential benefits.⁹

Due to the study's small sample size and lack of a priori power analysis, which limits statistical validity, our findings need to be interpreted with caution. Larger multicentre randomised controlled trials with higher training frequency and longer follow-up are needed to verify the maintenance of intervention effects on cognitive outcomes. We are unable to explain mechanistic changes in cognitive outcomes due to the lack of pathophysiological markers to understand how VRCT may counter neurodegeneration. To enhance the scalability of VRCT, future studies can also examine the utility of this programme in group-based community settings to meet the cognitive care needs of an ageing population.

Ethics statement

This study was approved by the SingHealth Centralised Institutional Review Board (2020/2239).

Declaration

The authors declare no conflict of interest and have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript.

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This work was supported by the Changi General Hospital Innovation Grant COCHFNN1904. We thank DancingMind Pte Ltd for the help in developing the virtual reality cognitive training programme for patients with mild cognitive impairment.

Keywords: *cognitive impairment, cognitive rehabilitation, cognitive stimulation, cognitive training, dementia, mild cognitive impairment, virtual reality*

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A novel opioid-sparing method for post-laparotomy pain management in gynaecologic oncology patients

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Dear Editor,

Midline laparotomy incisions often result in significant postoperative pain due to nociceptive stimulation of the skin, musculo-fascial layers and peritoneum. This pain can lead to tachycardia, tachypnoea, decreased intestinal motility, and stress responses such as hyperglycaemia and increased cortisol production.¹ Poor pain control contributes to prolonged hospitalisation, increased emergency visits, readmissions and reduced patient satisfaction.²

Opioids remain the cornerstone of postoperative pain management but are associated with side effects like respiratory depression, nausea, vomiting, urinary retention and paralytic ileus.³ These complications can prolong recovery, increase patient discomfort and raise healthcare costs due to delayed discharge and increased nursing care.⁴

To mitigate these challenges, multimodal analgesia—combining opioids, non-opioid drugs, and nerve blocks—has gained popularity. While single-dose nerve blocks provide limited relief, continuous local anaesthetic infusion via wound catheters has shown efficacy in multiple surgical disciplines. A systematic review of over 2000 patients demonstrated reduced pain scores and opioid use across various surgical disciplines, with decreased postoperative nausea, improved satisfaction and shorter hospital stays.⁵ In gynaecologic oncology, few studies with small cohorts have found continuous wound infusion to be effective for postoperative pain relief, with decreased opioid requirements following benign gynaecological procedures.⁶

We conducted a study to investigate whether the use of elastomeric pumps infusing peri-wound ropivacaine via preperitoneally inserted catheters helps reduce postoperative patient-controlled analgesia (PCA) opioid requirements in patients who had undergone midline laparotomy. Secondary objectives studied included evaluating opioid-related side effects, postoperative recovery parameters and

catheter-related complications. Ethics approval was granted by National Healthcare Group Domain Specific Review Board (DSRB 2019/00355).

A retrospective review was conducted on women undergoing gynaecologic oncologic surgeries via midline laparotomies at National University Hospital in Singapore from February 2017 to February 2022. Two groups were compared: 119 patients with only intravenous (IV) PCA before the introduction of preperitoneal wound catheters (PPWC) (pre-2017) and 133 patients receiving PPWC with or without PCA (2018 onwards). Ropivacaine was chosen as the local anaesthetic due to its greater safety margin, and reduced cardiac and central nervous system toxicity compared to bupivacaine.⁷ The amount and side effects of opioid usage, daily pain score, duration to ambulation, oral intake and bowel output were compared. Data analysis was performed using software R version 4.4.2 (R Foundation for Statistical Computing, Vienna, Austria).

The PPWC setup consisted of 2 Baxter Infusor (Baxter Healthcare Corporation, Illinois, US) elastomeric pumps connected to 20-gauge epidural catheters. Catheters were inserted preperitoneally on both sides of the midline incision before rectus sheath closure, using Tuohy needles placed laterally and directed towards the anterior superior iliac spine. A ropivacaine bolus (3 mg/kg, diluted to 20 mL per side) was administered, followed by continuous infusion at 5, 7 or 12 mL/hour based on clinical needs. The system remained in place until infusion completion, with top-ups if necessary. Routine oral painkillers were prescribed per pain team's and surgeon's discretion. PPWC removal involved gentle traction on the catheters.

Overall, we observed no significant differences in age, weight, ethnicity, type of surgery or cancer diagnosis between PCA and PPWC groups (Table 1). Ovarian cancer was the most common diagnosis, with hysterectomy and pelvic lymph node dissection being

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the most frequent procedure. The most common anaesthesia used in both groups were morphine, followed by fentanyl then oxycodone. All opioid dosages were converted into morphine equivalents based on World Health Organization guidelines.⁸

Mean PCA usage duration was shorter in the PPWC compared to the PCA group (1.8 versus [vs] 2.7 days). The PPWC group had a mean catheter use of 3.4 days with a 7 mL/hour infusion rate. All historical patients received IV PCA, whereas 17.3% of PPWC patients did not, and opioid consumption among PCA users was comparable between both groups in terms of milligrams per kilogram of body weight each day after surgery for the first 72 hours postoperatively. In spite of that, pain scores at rest and during movement were similar, confirming PPWC's non-inferiority to PCA. No catheter-related complications were reported.

A multivariate regression model confirmed that those with PPWC required lower opioid doses, similar to existing literature. Older patients required more

opioids, consistent with previous studies reporting prolonged pain and opioid needs in this population, likely due to prolonged tissue damage, slower wound healing, hyperalgesia and inflammation in older individuals.⁹ This finding suggests that older patients may benefit from combining IV PCA and PPWC for improved pain control.

In terms of postoperative recovery, there were no significant differences in time to ambulation and bowel function. Opioid-related side effects such as nausea, vomiting and ileus were also similar (27–31%). This is likely due to Enhanced Recovery After Surgery protocol applied to all our gynaecology oncology patients. Routine post-laparotomy care included routine antiemetic medications, and ambulatory and chest physiotherapy, standardising the time to ambulation. However, PPWC patients had longer times to oral intake (1.78 vs 1.40 days; $P=0.002$) and hospital stays (5.74 vs 4.89 days; $P=0.01$). Further analysis is necessary to clarify these findings. Possible

Table 1. Demographics of patients who received PPWC versus PCA only.

Demographics	PPWC (n=133)	PCA only (n=119)	P value
Median age (range), years	60 (28–90)	56 (25–84)	0.14
Median weight (range), kg	59 (35–126)	59 (30–93)	0.70
Ethnicity, no. (%)			
Chinese	88 (66.2)	71 (59.7)	0.30
Malay	17 (12.8)	19 (16.0)	
Indian	10 (0.08)	5 (0.04)	
Others	18 (0.14)	24 (20.2)	
Diagnosis, no. (%)			
Ovarian cancer	95 (71.4)	81 (68.1)	0.18
Endometrial cancer	23 (12.3)	19 (16.0)	
Cervical cancer	3 (0.02)	10 (0.08)	
Others	12 (0.09)	9 (0.08)	
Type of surgery, no. (%)			
THBSO +/- PLND	105 (78.9)	102 (85.7)	0.32
THBSO + PLND + bowel resection	21 (15.8)	14 (11.8)	
THBSO + PLND + other organ resection	7 (0.05)	3 (0.03)	
Mean duration of surgery (range), hour	3.9 (1.92–8.73)	3.3 (1.3–9.8)	1.2×10^{-5}
Previous abdominal surgery, no. (%)	31 (23.3)	25 (21.0)	0.77

PCA: patient-controlled analgesia; PLND: pelvic lymph node dissection; PPWC: preperitoneal wound catheters; THBSO: total abdominal hysterectomy and bilateral salpingo-oophorectomy
P values were obtained with chi-square test for all variables.

selection bias exists, as surgeons might have used PPWC in more complex surgeries or adopted more conservative postoperative care for such cases.

To our knowledge, our study is the first local investigation of PPWC for local anaesthesia infusion in gynaecologic oncology cases, describing its unique system. The PPWC system is a continuous wound instillation system, providing uninterrupted analgesia compared to single-dose injections or PCA systems, which deliver local anaesthesia only on demand. The PPWC setup is easy to use and portable. The Baxter Infusor elastomeric pumps are disposable, allow for adjustable infusion rates and have a capacity of 300 mL, and are thus not only lightweight but sufficient for approximately 2 days, covering the peak postoperative pain period. Removal is simple, and complications were minimal. Accurate preperitoneal catheter placement is ensured before closing the rectus sheath, which allows for effective analgesia by blocking afferent nerve transmission, which is potentially superior to subcutaneous placement.¹⁰ However, our study limitations include its retrospective design, potential selection bias and uniform infusion rates not reflecting individualised pain needs.

In conclusion, PPWC is a novel, effective method for postoperative pain relief in gynaecologic oncology patients undergoing midline laparotomy. It reduces opioid use, and is also safe, cost-effective and easy to administer. Prospective studies comparing PPWC to IV PCA are recommended to validate these findings.

Ethics statement

Ethics approval was granted by National Healthcare Group Domain Specific Review Board (DSRB 2019/00355).

Declaration

The authors declare they have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript.

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Keywords: anaesthesiology, gynaecology oncology, laparotomy, obstetrics and gynaecology, postoperative pain

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"Epidemiology of paediatric intensive care unit admissions, deaths and organ donation candidacy: A single-centre audit": Correspondence

Jonathan Tze Liang Choo¹ FRCPCH, Amanda XY Yap¹ MRCPCH, Danielle EH Choo², Mei Yoke Chan³ FRCPCH

Dear Editor,

Cardiac transplantation is an option for children with end-stage heart failure, but around the world there has been an issue with inadequate organ availability. Effective donor management is crucial to the successful recovery of organs for cardiac transplantation. The recent paper by Low et al.¹ demonstrates that while there are potential donors (who may be identified during admission to the intensive care unit), there remains a gap between the number of potential donors and the actual number of organs donated. The authors, and indeed also the authors of the corresponding editorial,² call for an independent group of medical professionals to support end-of-life decision-making for children with terminal disease. We agree with this recommendation. Here, we articulate the practical ethics underpinning donor stewardship and consider how families with a child close to death may be better supported in the grieving process while given the opportunity to consider donating their child's organs (specifically the heart) to save another child's life.

While there are many ethical issues that have been considered at the end-of-life, 2 principles are fundamental to the care of the potential donor: the principles of autonomy and justice.

The principle of respect for a person's autonomy remains a central principle in medical ethics.³ Parents of a child should be allowed a choice in each important aspect of their child's care. Indeed, the preferences and choices of older children should also be considered. Therefore, it remains important to respect the care preferences of the family and the child as the child reaches his or her end-of-life. In medically appropriate cases, the family should be given the choice of whether they would like to consider organ donation.

Justice is the principle that promotes the fair and equitable use of resources.⁴ Organs are a scarce resource. Each year, it is expected that 1 child (less than 16 years of age) would require a ventricular assist device or cardiac transplantation at our centre as a life-extending procedure. While there are important

considerations and requirements to be fulfilled for each heart transplant recipient, given that there are potential donors, it would be an opportunity lost should the family not be given the opportunity to decide on whether they wish to donate their child's organs in the event of death.

Donation of organs from adult donors is legislated under the Human Organ Transplantation Act (HOTA).⁵ Through this Act, individuals above the age of 21 may actively refrain from organ donation as an "opt out" approach. Organ donation in children, in Singapore falls under the Medical (Therapy, Education and Research) Act, or MTERA. Under this Act, explicit informed consent is required from a child's parents or legal guardians for organ donation upon the death of a child. The question is therefore, how can parents be presented a choice for or against organ donation upon the impending death of their child? A careful and sensitive approach is required, particularly in paediatrics.

The encouragement to donate may come from another person. Building on the work of Thaler and Sundstein, Wilkins et al. have termed this as "interpersonal nudging."⁶ While at face value, the term "nudge" carries a connotation of a manipulation of an individual's choice, Thaler and Sundstein define a "nudge" in a more neutral way, as "any aspect of the choice architecture that alters people's behaviour in a predictable way without forbidding any options or significantly changing their... incentives."⁷

It can be argued that the intentional identification of potential donors and the subsequent organ donation are right actions because they lead to an outcome of goodness—a life saved. This is the utilitarian approach. Some good can therefore be derived from an otherwise heartbreaking experience. However, if such actions were to result in significantly unbearable pain for the bereaved family, it would be necessary to reweigh the scales, as this approach would no longer maximise total net happiness. Overall, interpersonal nudging would be a simple articulation of the possibility of organ donation.

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Table 1. Four-box toolkit in the donation of the heart for transplantation in paediatric patients.

Medical indications • Are there medically good reasons for withdrawal of care? • Are there other reasonable options of care that the patient/family would like to explore?	Patient preferences • Has the patient indicated his or her preference towards organ donation? • Does the family/legal guardian have a preference towards or is against organ donation?
Quality of life • Does the family have adequate support in the grieving process? • Is the family able to make meaning of the impending death and potential organ donation?	Contextual issues • Legal issues in different jurisdictions. Are there legal constraints to organ donation/organ harvesting? • Religious values of the patient and the family.

There is a narrow window of opportunity of approximately 6 hours for the donor heart to be transplanted⁸; and donor parents would expectedly be under tremendous stress during this period. Every cardiac transplantation as an event is an intersection of 2 crises, one involving the donor (and family)—the “donor crisis”; and another involving the recipient (and family)—the “recipient crisis.” It would be prudent to develop a robust system to care for both these aspects of the event but here we will consider primarily the “donor crisis”.

A simple “nudge” during the “donor crisis” as part of end-of-life care would be to have an independent medical professional team articulate the possibility of organ donation in a suitable case.⁹ This team would act apart from the intensive care team and may then broach the subject from a more impartial perspective. In our view, ideally palliative care specialists may fulfil the leadership role, working together with a transplant coordinator from the National Organ Transplant Unit (NOTU), as part of their holistic end-of-life care for these children (considering that the act of organ donation is a part of the grieving process). Alternatively, medical doctors with adequate training in intensive care, palliative care and bioethics may also be suitable. Social workers and clinical psychologists would also be expected to be important members of this interdisciplinary team. We have included the four-box toolkit¹⁰ (Table 1) to clarify the practical ethical framework of approaching potential donor families.

Ethical donor stewardship is an important aspect of managing the crisis of a paediatric cardiac transplant. In the Singapore context, an interdisciplinary team led by a paediatrician or palliative care specialist independent of the intensive care team would be well-placed to broach the subject of organ donation to the family, allowing the expression of parental autonomy, yet ensuring that the opportunity for the recovery of the organ is not lost, such that suitable children with end-stage cardiac failure may receive the heart they need.

Ethics statement

Not applicable.

Declaration

All the authors have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript.

Keywords: cardiology, heart failure, mortality, paediatrics, palliative medicine

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Authors’ reply

Dear Editor,

We appreciate the opportunity to respond to the letter titled “Epidemiology of paediatric intensive care unit admissions, deaths and organ donation candidacy: A single-centre audit”: Correspondence, which highlights the ethical dilemma for healthcare teams caring for a potential paediatric organ donor—the duality of autonomy (for the donor family) versus (vs) justice (for the potential recipients of organs). Here, we further elaborate on sociocultural and logistical challenges faced by the medical teams when raising the topic of organ donation, discuss the role of a neutral third-party and emphasise the need to better understand families’ attitudes towards organ donation to guide future advocacy work.

Emerging social science research highlights how decision-making differs when one decides for another person as compared with himself or herself.¹ In relation to paediatric organ donation, risks may be assessed differently because parents feel a greater weight of responsibility for the outcomes for their child.² This is evidenced by a local study on organ donation decisions for next-of-kin vs self, which showed that survey participants were less willing to donate their relatives’ organs than their own, highlighting 2 key factors—fears about organ donation and religion—predicting congruency between decisions for family vs self.³ In addition, the effect of culture on organ donation has been extensively discussed by various groups over the years (albeit mainly in the adult population) and remains one of the barriers to increasing organ transplant uptake in Singapore.^{4,5} In our audit, 8 paediatric aged patients were identified who met the criteria for organ

donation (Table 1).⁶ Of these, 2 organ donors make up the 6 paediatric deceased organ donations that occurred in our hospital over the past 10 years. By extrapolating the findings on attitudes of organ donation in Singapore,⁵ we postulate that parents struggle with the guilt of not only having failed to protect their child, but also not allowing their child the dignity of dying whole, on top of making complex medical decisions. We suggest that a study assessing current attitudes towards paediatric organ donation among parents may guide future advocacy work.

We identified logistical challenges towards holistic discussions on organ donation in our cohort. Based on our data, time was often short, with potential organ donors having a median length of intensive care unit stay of 4 (4, 8.5) days.⁶ In addition, majority of patients in our cohort who qualified as potential organ donors were admitted for unexpected/accidental causes such as drowning and traumatic brain injury (Table 1). As such, raising the topic of organ donation in such high stress, emotionally charged environment may be perceived as insensitive and refusal of the medical team to enact further life saving measures. Physicians may thus find themselves straining to practice the principles of autonomy and justice as raised by the authors of the letter.

As discussed in the original publication, a neutral third-party who is well versed in end-of-life care and organ donation would be best to identify the candidate donor and to facilitate the conversation on organ donation.⁶ We agree that it may be during these discussions, that interpersonal nudging may be used. Interpersonal nudging uses social and psychological insights to subtly influence another person’s behaviour by creating an environment or situation where a desired choice is more likely.⁷ However, contrary to

Table 1. Characteristics of potential organ donors in the cohort.

Patient	Age (year)	Sex	Race	Comorbidity	Cause of death	Organ/tissue donated
1	15	Female	Chinese	None	Hypoxic ischaemic encephalopathy	No
2	11	Male	Malay	None	Drowning	No
3	4	Female	Chinese	None	Viral encephalitis	No
4	<1	Female	Chinese	Global developmental delay	Hypoxic ischaemic encephalopathy	No
5	11	Male	Chinese	None	Intracranial haemorrhage	No
6	5	Female	Chinese	None	Drowning	No
7	6	Male	Japanese	None	Traumatic brain injury	Yes
8	2	Female	Malay	None	Drowning	Yes

the letter, we disagree that this needs to necessarily be led by a medical specialist (e.g. palliative care specialist). Indeed, involvement of a palliative care provider can positively contribute to the care of these patients and families by supporting families through their grief, navigating difficult or sensitive communications, and assisting with end-of-life decision-making that is congruent with the patient/families' goals of care.⁸⁻¹⁰ However, the role of a neutral third party may be fulfilled just as well by a trained nurse or medical social worker. In Singapore, the donor coordinator (DC) from NOTU serves this role well. Their early involvement in end-of-life conversations with families, even before the diagnosis of brain death is confirmed, can help prepare families for the possible discussion on organ donation. It is found that familiarity with the professional who formally asked for donation consent was important in achieving a favourable donation decision.² Hence, early involvement by the DC is vital. In further discussions, the DC takes the role of helping families to navigate the medical and non-medical nuances of organ donation, thereby giving the managing physician space to focus on their primary responsibilities of care to the patient. This also enables organ donation to be conducted in a timely, appropriate and dignified manner, with family members informed and supported.

Despite the enactment of MTERA and HOTA in 1972 and 1987 respectively, Singapore has one of the lowest organ donation rates in developed nations, with many groups calling for further advocacy and community engagement.⁵ In response, the NOTU embarks on efforts to promote greater awareness of organ donation and transplantation. For example, the Live On Festival encourages youths to explore and express their perspectives on the topic through art and writing. This programme incorporates the values of responsibility, compassion and empathy by offering insights into the emotive and delicate aspects of organ donation and transplantation. In a survey from the US, education, donation attitudes and beliefs, and knowledge of brain death were significantly associated with donation decision.² The finding that parents who consented to organ donation were more likely to have received information about organ donation/transplantation within the last 6 months than were non-donors, makes a strong case to increase efforts in community awareness and education programmes.

In conclusion, attitudes towards paediatric organ donation remain relatively unexplored and are a key barrier to improving organ donation rates. Understanding how social and cultural factors influence parents' decisions on organ donation will help tailor future

advocacy work and guide policy changes. Establishing the role of a neutral, third-party interdisciplinary team who can, in the limited time, support and guide families through the patients' end-of-life journey will enable the primary physician to focus on medical issues while increasing the likelihood of a favourable organ donation decision.

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