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Adopting a healthy lifestyle in early childhood is critical, as it forms the foundation for future well-being.

A Singapore consensus statement developed for infants, toddlers and preschoolers provides a 24-hour activity guide with recommendations for good metabolic health through regular physical activity, limiting sedentary behaviour, adequate sleep and positive eating habits.

Illustration by Xinyu Li

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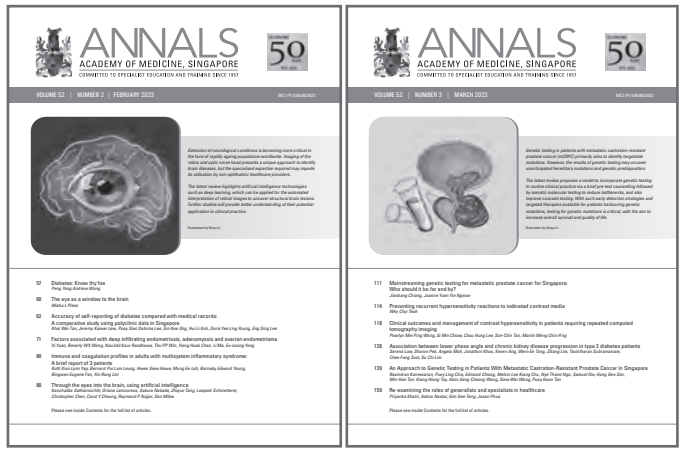

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EDITORIAL

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Proactive steps to population health: Starting early, starting right

Daniel Chan [1,2] *MRCPCH (UK)*

The global burden of non-communicable diseases is rising, with continued projected increases in the prevalence of metabolic syndrome (MetS) in the future. This epidemic, albeit of a metabolic nature, poses broad socioeconomic and healthcare burdens worldwide. Population health improvement and optimisation of healthcare are important to address these burdens. Modelling health systems to be more health-centric—in addition to being disease-centric—is key , focusing on preventive care initiatives, which avert the development of metabolic diseases in the community at large.

Origins and clustering of risk factors for the development of MetS as an adult begin in infancy and early childhood—formative periods of life, which are susceptible to environmental influences, shaping lifelong cardiometabolic health. This forms the basis of the Developmental Origins of Health and Disease hypothesis. Epigenetics have a potential role in the mediation between an obesogenic environmental influence, and an individual's subsequent metabolic health trajectory.[1] Advances in microbiome research, especially those related to gut dysbiosis, have also demonstrated influences in metabolic health.[1] Given that early epigenetic programming may determine a person's lifelong health, it is therefore crucial that primary prevention and population health efforts begin from early childhood, with the ultimate aim of a population growing and ageing healthily.

Through birth cohort studies, risk factors that adversely impact a child's neurocognitive and metabolic health have been determined, thereby identifying components of an obesogenic environment. Caloric intake and rapidity of weight gain during infancy have been shown to direct ly influence body mass index throughout childhood.[2] In turn, childhood obesity tracks into adulthood as well, with a significant correlation with body mass index demonstrated at 50 years of age.[3] Optimal weaning and introduction of a healthy balanced diet to a child are thus pivotal in determining subsequent metabolic health, with appetitive traits and taste preferences as an adult shown to be ingrained from an early age.[4]

Holistic considerations should also include the formation of healthy habits and lifestyle from a young age. Physical activity during infancy and early childhood may not be a domain frequently prioritised by caregivers and healthcare providers. However , it has been shown to have a positive impact on a child's body composition (particularly muscle mass and bone mineralis ation), cardiometabolic health and neurocognitive development,[5] with its bene fits continuing into adulthood. Furthermore, with the increasing widespread use of digital devices, it is also critical to understand its adverse impact on a child' s neurodevelopment. Exposure to screen time in early childhood has been shown to impair attentive and executive functions, with neuroimaging evidence of whi te matter changes and electroencephalographic alterations.[6] Apart from its deleterious effects on neurodevelopment, longer screen time also correlates with poorer quality and duration of sleep, with increased odds of developing childhood obesity as well.[7] Overall, a person's long-term metabolic health seems to be an outcome of multiple compounding effects, with an accumulation of predisposing or protective cardiometabolic factors from early childhood.

In this issue of the *Annals*, Loo et al. [8] present recommendations on daily physical activities, lifestyle and dietary habits in children aged 0 to <7 years old. A systematic review of the literature was performed, with an amalgamation of the latest available evidence, and synthesis of consensus sta tements by workgroup members, comprising physicians and allied health professionals. For ease of reference, these statements were categorised into three age groups: 0 to <1 year , 1 to <3 years, and 3 to <7 years old. These recommendations fulfil the clinical purpose of improved developmental, physical and neurocognitive health in children aged <7 years old, with the aim of reducing the incidence of non-communicable diseases in their later years. The "Consensus statement on Singapore integrated 24-hour activity guide for early childhood" represents the first step in the distillation of up-to-date literature and expert opinions, which should serve as subsequent guidance for an evidence-based approach to population health

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management. The Healthier SG initiative was announced by the Ministry for Health in March 2022, [9] with an important emphasis on community engagement and preventive care to reduce the economic and healthcare burden of non-communicable diseases among other chronic illnesses. This is a paradigm shift, with an increased focus towards efforts in health promotion in addition to management of patients and diseases.

However, future challenges remain in the implementational and translational aspects of delivering preventive medicine. With clear scientific findings, prospective data and expert opinions, the next integral step would be engaging the community and delivering this information in an accessible and sustainable manner. A key component in achieving this would be to enlist stakeholders, forming community partnerships and championing the use of digital platforms and innovation to educate the general public. Digital applications, online forums and social media are some available avenues to allow this information to be accessed by parents, children's caregivers, as well as healthcare providers.

Models of care also need to be modified and updated accordingly, with a "guided" delivery of anticipatory guidance that is less episodic, random and physician dependent. Primary care providers are well placed under the Healthier SG model, with well-baby visits for developmental screening and vaccinations, and the assignment of a regular family doctor enabling continuity of care, forming strong patient-doctor relationships and partnerships in preventive medicine. Population health is not only defined by improving health outcomes in a particular group of individuals, but also includes the distribution of these outcomes within this group. [10] Therefore, it is also important to consider the social determinants of child health, and how preventive healthcare can be delivered in a robust yet accessible and active manner such that those with disadvantaged or marginalised circumstances can still receive and apply this knowledge effectively in their children's lives. It is important that recommendations from this consensus guidelines can pervade different aspects of a child's life. This includes considerations in pre-school educational systems, incorporating physical activity, outdoor exposure and play, nutritional understanding of the diet provided in pre-school centres, and how screen viewing may sometimes be used as a tool for educational purposes.

In conclusion, given that lifelong cardiometabolic health is potentially determined by the accrual of protective or predisposing factors during infancy and early childhood, it is critical to optimise environmental factors during this vulnerable window. Adopting a life-course approach could yield dividends in population health management and address the burgeoning tide of non-communicable diseases. Following the compilation of evidence and expert opinions in the consensus guidelines, future efforts should be directed towards the application of implementation sciences to facilitate its uptake in the community, and integrating health economics to ensure its accessibility and efficacy as well.

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ORIGINAL ARTICLE

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Comparison of existing methods of low-density lipoprotein cholesterol estimation in patients with type 2 diabetes mellitus

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ABSTRACT

Introduction: Elevated low-density lipoprotein cholesterol (LDL-C) is an important risk factor for atherosclerotic cardiovascular disease (ASCVD). Direct LDL-C measurement is not widely performed. LDL-C is routinely calc ulated using the Friedewald equat ion (FLDL), which is inaccurate at high triglyceride (TG) or low LDL-C levels. We aimed to compare this routine method with other estimation methods in patients with type 2 diabetes mellitus (T2DM), who typically have elevated TG levels and ASCVD risk.

Method: We performed a retrospective cohort study on T2DM patients from a multi-institutional diabetes registry in Singapore from 2013 to 2020. LDL-C values estimated by the equations: FLDL, Martin/Hopkins (MLDL) and Sampson (SLDL) were compared using measures of agreement and correlation. Subgroup analysis comparing estimated LDL-C with directly measured LDL-C (DLDL) was conducted in patients from a single institution. Estimated LDL-C was considered discordant if LDL-C was <1.8mmol/L for the index equation and ≥1.8mmol/L for the comparator.

Results: A total of 154,877 patients were included in the final analysis, and 11,475 patients in the subgroup analysis. All 3 equations demonst rated strong overal l correlation and goodness-of-fit . Discordance was 4.21% for FLDL-SLDL and 6.55% for FLDL-MLDL. In the subgroup analysis, discordance was 21.57% for DLDL-FLDL, 17.31% for DLDL-SLDL and 14.44% for DLDL-MLDL. All discordance rates increased at TG levels >4.5mmol/L.

Conclusion: We demonstrated strong correlations between newer methods of LDL-C estimation, FLDL, and DLDL. At higher TG concentrations, no equation performed well. The Martin/Hopkins equation had the least discordance with DLDL, and may minimise misclassification compared with the FLDL and SLDL.

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Keywords: Cardiovascular risk, diabetes mellitus, low-density lipoprotein, triglycerides

INTRODUCTION

Elevated low-density lipoprotein cholesterol (LDL-C) levels are a major risk factor for the development of atherosclerotic cardiovascular disease (AS CVD). A reduction in LDL-C levels has been shown to significantly reduce the risk of incident ASCVD[1] and all-cause mortality.[2] LDL-C levels are hence key treatment targets in the prevention of ASCVD, with a target of <1.8mmol/L for patients with high cardiovascular risk.[3,4]

Accurate LDL-C measurement is important to guide treatment decisions. The established reference

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CLINICAL IMPACT

What is New

- Current methods of low-density lipoprotein cholesterol (LDL-C) estimation may underestimate LDL-C, especially at higher triglyceride levels.

Clinical Implications

- Such underestimations can lead to undertreatment in patients at high risk of atherosclerotic cardiovascular disease.
- Use of the Martin/Hopkins equation has the potential to minimise the clinical discordance in estimation values compared with the conventional Friedewald equation.

method for measuring LDL-C is the beta-quantification method,[5] which requires ultracentrifugation followed by polyanion precipitation of high-density lipoprotein cholesterol (HDL-C) and other lipoproteins. This process is time-consuming, costly, and requires equipment not readily available in all routine laboratories.

Clinical laboratories therefore typically estimate LDL-C levels using the Friedewald equation (FLDL): LDL-C = total cholesterol (TC) – HDL-C – triglycerides (TG)/2.2, with all units in mmol/L. [6] This has been widely adopted both in clinical practice and in research studies.[5] However, the FLDL has been reported to underestimate LDL-C levels, particularly when LDL-C levels are very low (<1.0mmol/L) [7] or TG levels are elevated.[8] Moreover, the equation cannot be used when there is significant hypertriglyceridaemia (TG ≥4.5mmol/L) as the assumption of a factor of 5 in the TG:very low-density lipoprotein (V LDL) ratio is no longer valid.[6]

To overcome these limitations, Martin et al. developed an estimation method using an adjustable factor based on strata-specific median TG:VLDLC ratios instead of a fixed ratio.[9] The Martin/Hopkins equation (MLDL) has been reported to be more accurate than the FLDL at lower LDL-C levels, [10] but can overestimate LDL-C levels when TG is high (>2.8mmol/L). [11] Sampson et al. therefore developed a novel equation based on a population with a high frequency of hypertriglyceridaemia.[12] The Sampson equation (SLDL) is validated in patients with TG levels up to 9.0mmol/L and has been reported to be more accurate than both FLDL and MLDL in patients with TG levels >2.8mmol/L.[11] In fact, some have reported that the SLDL may still be accurate even with TG levels >9.0mmol/L. [13] However, not all reports have described concordant findings, with a recent study in a large East Asian population reporting that the MLDL had the greatest accuracy across all TG levels.[14]

Patients with diabetes are an important population with high cardiovascular risk in whom appropriate lipid-lowering therapy is crucial. These patients also typically have elevated TG levels when compared to patients without diabetes .[15] Moreover, patients of Asian ethnicities appear to have higher TG levels when compared to their Caucasian counterparts .[16] Underestimation of LDL -C levels when using the conventional FLDL may lead to undertreatment and worse cardiovascular outcomes in this group of patients. We hence compared the correlation and agreement in LDL-C estimated by the FLDL, MLDL and SLDL in a multiethnic Asian population of patients with type 2 diabetes mellitus (T2DM), and to determine if these differences would have any clinical significance in determining intensification of lipid lowering therapy. We also explored the relationship of all 3 equations with directly measured LDL-C (DLDL).

METHOD

Study design and population

We conducted a retrospective cohort study using data from the SingHealth Diabetes Registry (SDR), a multi-institutional diabetes registry in Singapore. It incorporates data from the largest healthcare cluster in Singapore, providing healthcare services to approximately 50% of the national population via a total of 20 healthcare institutions. The structure and data collection for the SDR have been described previously.[17] This study included patients ≥18 years of age with T2DM, enrolled between 2013 and 2020. The following data were collected for all patients: demographics (age, sex and ethnicity), weight and body mass index, smoking status, history of hypertension, peripheral vascular disease, ischaemic heart disease and previous ischaemic stroke, current lipid-lowering medications and lipid test results (TC, TG and HDL-C). Patients with any missing demographics or with negative estimated LDL-C values using any of the 3 methods were excluded from analysis. Only the latest lipid test result for each unique patient was included in the analysis.

To determine the accuracy of estimation methods against DLDL, subgroup analysis was also performed on patients from a single institution within the SDR, which had started performing routine DLDL

measurements via a homogenous enzymatic colorimetric assay using the cobas c702 (Roche Diagnostics, Basel, Switzerland) platform from 22 July 2017. [18] In addition to the earlier-mentioned data, DLDL values were also collected for this subset of the population. Patients with lipid test results recorded prior to this date or with missing data, including DLDL measurements, were excluded from this subgroup analysis.

This study utilised anonymised data from the SDR and was granted a waiver for the need to obtain informed consent by the SingHealth Centralised Institutional Review Board.

LDL-C estimation equations

LDL-C values were estimated in mmol/L, using the Friedewald, Martin/Hopkins, and Sampson equations:

Friedewald:	FLDL = Non-HDLC – TG/2.2
Martin/Hopkins:	MLDL = Non-HDLC – TG/AF
Sampson:	SLDL = TC/0.948 – HDLC/0.971 – (TG/3.74 + TG x Non-HDLC/24.1 – TG^2 /79.36) – 0.244

where non-HDL-C is defined as TC-HDLC, and is the adjustable factor based on the strata-specific median TG:VLDL ratios obtained from the 180-cell table by Martin et al. (converted to mmol/L).[9]

Statistical analysis

The baseline characteristics of the population were described with continuous variables expressed as means and standard deviations, and categorical variables reported as numbers and proportions. LDL-C and other lipid values were reported as medians and interquartile range (IQR) (25^{th}–75^{th} percentile) as their distributions were notably right-skewed.

The distribution of estimated LDL-C values by all 3 equations was described using box and whisker plots stratified by TG values. Overall and strata-specific median estimated LDL-C values were compared with using Mann-Whitney U tests. TG strata were defined firstly at >1.7mmol/L[3], being a commonly used treatment threshold in consensus guidelines, and >4.5mmol/L, the traditional upper bound of TG for the FLDL. Ordinary least squares regression was performed to measure the correlation of FLDL versus SLDL, and FLDL vs MLDL, and the results were evaluated using R^2, root-mean-square-error (RMSE), and the correlation coefficient (r). Goodness-of-fit between observed values and the regression models was also evaluated using R^2. Agreement between each of the 3 equations was assessed using Bland-Altman plots.

To determine the clinical significance of differences in estimated LDL-C values, concordance and discordance between the estimated LDL-C values were evaluated categorically within TG strata using a LDL-C threshold of <1.8mmol/L, a common treatment target for patients at high cardiovascular risk.[3] Patients with diabetes mellitus are typically considered at minimum to have high, if not very high, cardiovascular risk. LDL-C values using 2 different equations were considered concordant if both estimates were either ≥1.8mmol/L or <1.8mmol/L. As the hypothesis was that FLDL tended to underestimate LDL-C, discordance was defined as an LDL-C value of <1.8mmol/L on the FLDL (reference equation) and an LDL-C value of ≥1.8mmol/L on either the SLDL or MLDL, respectively (comparator equations). Discordance was defined unidirectionally since the FLDL or DLDL would typically be conventionally used to make treatment decisions at present. The same methods were used for the subgroup analysis evaluating the correlation of the DLDL with FLDL, SLDL and MLDL. All analyses were performed using Python 3.8 (Python Software Foundation, Delaware, US).

RESULTS

Patient characteristics

A total of 154,877 patients were included in the final analysis, as described in Fig. 1. The baseline characteristics of the study population are summarised in Table 1. Of note, most patients were already on lipid-lowering therapy at the time of inclusion into the study, with statin therapy being the most common therapeutic modality.

Among the original cohort of 154,877 patients, 11,475 patients had DLDL measurements available and were included in the subgroup analysis. Characteristics of patients included in the subgroup analysis were mainly similar to that of the overall sample, apart from a slightly higher rate of prevalent ischaemic heart disease, ischaemic stroke or transient ischaemic attack, and overall cardiovascular disease. Additionally, there was a slightly higher proportion of patients of Malay ethnicity due to the demographic distribution in the local area of the single institution from which patients were recruited. These are shown in Table 1.

Differences between LDL-C estimated by all 3 equations

Bland-Altman plots did not demonstrate significant agreement, as would be expected between 3 equations derived using different models or coefficients (Supplementary Fig. S1). All 3 equations were closely correlated by linear regression regardless of TG strata. However, as expected, a slightly poorer fit was observed

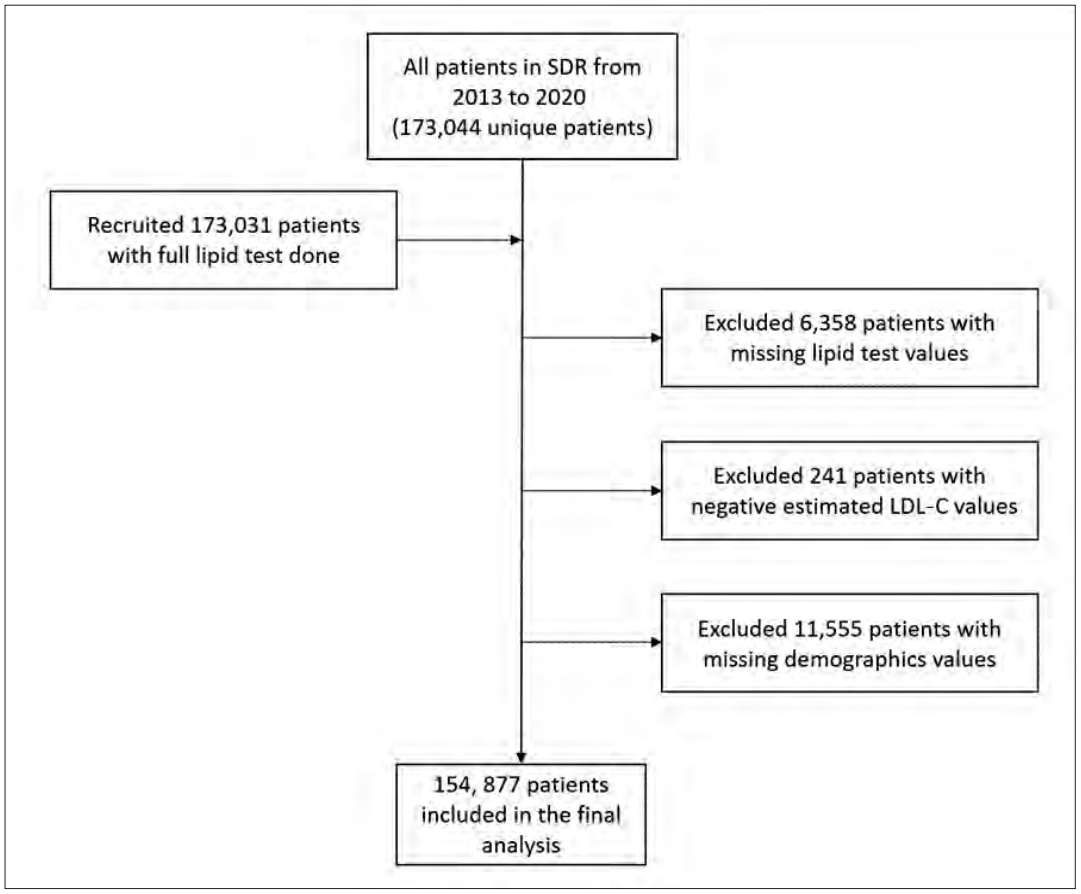

Fig. 1. Flow diagram of participants in the study.
LDL-C: low-density lipoprotein cholesterol; SDR: SingHealth Diabetes Registry

towards higher TG values (RMSE 0.534 and 1.006 for SLDL and MLDL, res pectively). While both the SLDL (R^2=0.990 and r=0.995, P<0.001) and MLDL (R^2=0.964 and r=0.982, P<0.001) demonstrated consistently high R^2 and r values above 0.9, the SLDL showed a smaller RMSE (0.1 11 vs 0.192) and hence a better fit with the FLDL, although the significance of these differences is marginal. These findings are summarised in Table 2. S LDL (median 2.12, IQR 1.68–2.64) and MLDL (median 2.14, IQR 1.72–2.67) tended to estimate higher LDL-C values than the FLDL (median 2.04, IQR 1.61–2.56), as shown in Fig. 2 and described in Supplementary Table S1. The differences between overall and TG strata-specific medians were all statistically significant (P<0.05).

Discordance rate between FLDL-SLDL and FLDL-MLDL

The discordance between FL DL-SLDL and FLDL-MLDL for all subjects w ere 4.21% and 6.55%, respectively. Discordance was relatively low at TG values of <1.7mmol/L, at 2.33% and 2.89%, respectively. However, at moderate TG values of 1.7–4.5mmol/L, these rose to 8.14% and 14.1% for FLDL-SLDL and FLDL-MLDL, respectively . The discordance rate at TG values above 4.5mmol/L was the highest at 18.81% and 37.55% for FLDL-SLDL and FLDL-MLDL, respectively, as illustrated in Fig. 3.

Comparing all 3 equations against DLDL

All 3 estimation methods were highly correlated with DLDL for low and moderate TG levels, with SLDL (R^2=0.933 and r=0.966, P<0.001) achieving s lightly better R^2 and r values than FLDL (R^2=0.917 and r=0.958, P<0.001) and MLDL (R^2=0.918 and r=0.958, P<0.001). However, correlation coef ficients were observed to diverge at higher TG levels (≥4.5mmol/L), with FLDL performing the worst against DLDL having the smallest R^2 (0.574) and r (0.758) values, and largest RMSE value (1.354). Notably , neither SLDL (R^2=0.584, r=0.764 and RM SE=1.093, P<0.001) nor MLDL (R^2=0.547, r=0.739 and RMSE=1.167, P<0.001) fared much better at this range. These findings are summarised in Table 2. Bland-Altman plots did not

Table 1. Demographic and baseline clinical characteristics of patients.

		Overall sample n=154,877	Subgroup with DLDL n=11,475
Age, median (IQR), years		67.0 (59.0–75.0)	66.0 (58.0–76.0)
Body mass index, median (IQR)		25.7 (22.9–29.1)	26.0 (22.9–29.8)
HbA1c, median (IQR)		6.9 (6.4–7.7)	7.0 (6.2–8.2)
Sex, no. (%)	Male	80,727 (52.1)	6,775 (59.0)
	Female	74,150 (47.9)	4,700 (41.0)
Ethnicity, no. (%)	Chinese	108,314 (69.9)	6,575 (57.3)
	Malay	23,493 (15.2)	2,781 (24.2)
	Indian	16,352 (10.6)	1,122 (9.8)
	Others	6,718 (4.3)	997 (8.7)
Smoking status, no. (%)	Never-smoker	126,589 (81.7)	8,706 (75.9)
	Current smoker	13,919 (9.0)	1,372 (12.0)
	Ex-smoker	3,924 (2.5)	427 (3.7)
	Unknown	10,445 (6.7)	970 (8.5)
Hypertension, no. (%)	Yes	138,608 (89.5)	10,662 (92.9)
	No	16,269 (10.5)	813 (7.1)
Cardiovascular disease,[a] no. (%)	Yes	61,650 (39.8)	7,740 (67.5)
	No	93,227 (60.2)	3,735 (32.5)
Ischaemic heart disease, no. (%)	Yes	42,472 (27.4)	5,647 (49.2)
	No	112,405 (72.6)	5,828 (50.8)
Peripheral vascular disease, no. (%)	Yes	7,925 (5.1)	1,135 (9.9)
	No	146,952 (94.9)	10,340 (90.1)
Ischaemic stroke or TIA, no. (%)	Yes	20,440 (13.2)	3,001 (26.2)
	No	134,437 (86.8)	8,474 (73.8)
Lipid-lowering therapy,[b] no. (%)	Statin	136,105 (97.7)	10,526 (98.4)
	Fibrate	13,461 (9.6)	1,025 (9.6)
	Ezetimibe	4,842 (3.5)	733 (6.9)
	PCSK9 inhibitor	27 (0)	7 (0.1)
	Others	234 (0.2)	22 (0.2)
TG strata, no. (%)	<1.7mmol/L	107,802 (69.6)	7,505 (65.4)
	1.7–4.4mmol/L	45,416 (29.3)	3,729 (32.5)
	≥4.5mmol/L	1,659 (1.1)	241 (2.1)

DLDL: directly measured low-density lipoprotein cholesterol; HbA1c: haemoglobin A1C; IQR: interquartile range; PCSK9: proprotein convertase subtilisin-kexin type 9; TG: triglyceride; TIA: transient ischaemic attack

[a] Defined as composite of ischaemic heart disease, peripheral vascular disease, a stroke or transient ischaemic attack.

[b] Patients may be on more than one lipid-lowering therapy.

Table 2. Correlations between Friedewald equation (FLDL) with Sampson equation (SLDL) and Martin/Hopkins equation (MLDL), as well as between directly measured LDL-C (DLDL) with FLDL, SLDL and MLDL.

		Overall			TG<1.7			1.7≤TG<4.5			TG≥4.5		
		FLDL	**SLDL**	**MLDL**	**FLDL**	**SLDL**	**MLDL**	**FLDL**	**SLDL**	**MLDL**	**FLDL**	**SLDL**	**MLDL**
FLDL	RMSE		0.111	0.192		0.051	0.061		0.160	0.283		SLDL	MLDL
	R^2		0.990	0.964		0.998	0.995		0.997	0.984		0.534	1.006
	r		0.995	0.982		0.999	0.997		0.998	0.992		0.987	0.977
	P value		<0.001	<0.001		<0.001	<0.001		<0.001	<0.001		0.994	0.989
DLDL	RMSE	0.516	0.437	0.424	0.390	0.356	0.369	0.628	0.505	0.437	1.354	<0.001	<0.001
	R^2	0.917	0.933	0.918	0.964	0.967	0.964	0.919	0.925	0.920	0.574	0.584	0.547
	r	0.958	0.966	0.958	0.982	0.983	0.982	0.959	0.962	0.959	0.758	0.764	0.739
	P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

LDL-C: low-density lipoprotein cholesterol; RMSE: root-mean-square-error; TG: triglycerides

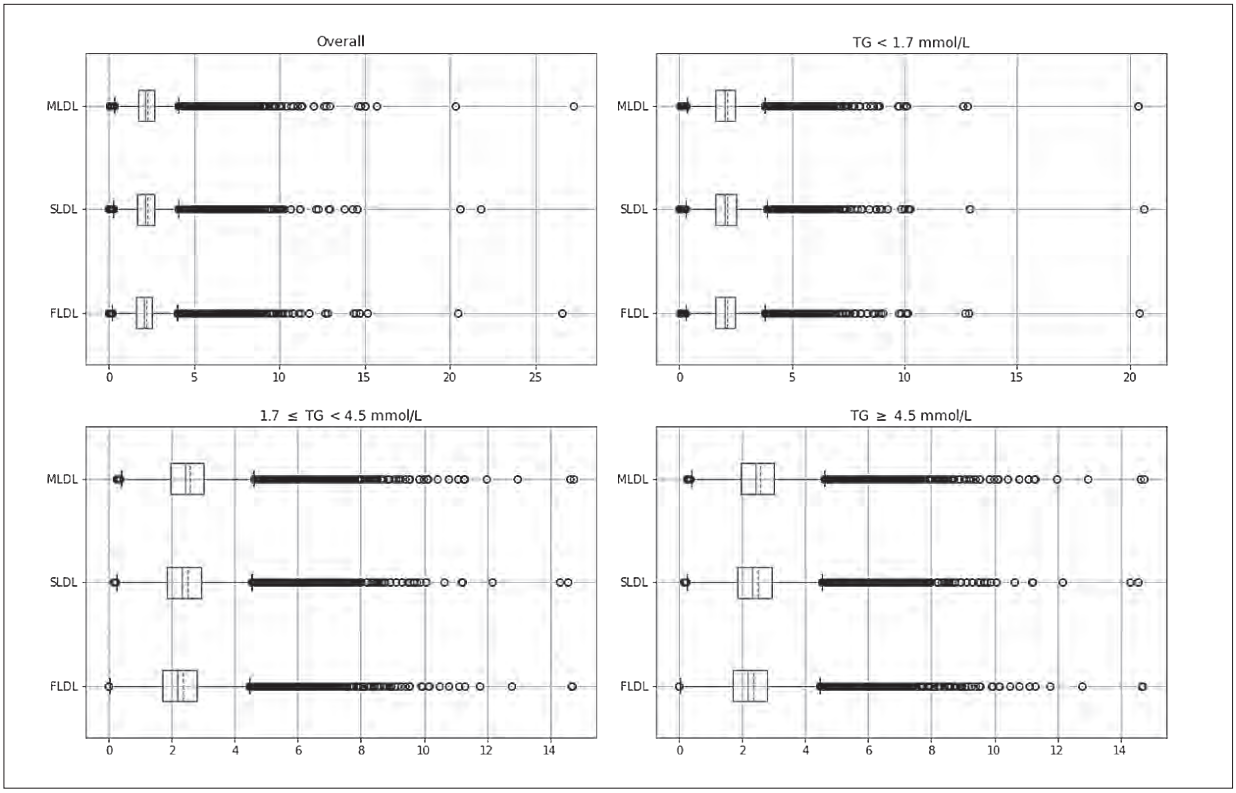

Fig. 2. Distribution of overall and triglyceride strata-specific estimated LDL-C values in the main study population.
LDL-C: low-density lipoprotein cholesterol; TG: triglycerides

demonstrate significant agreement as well.

Of note, all 3 equations tended to estimate lower LDL-C values than DLDL across TG strata, except for MLDL at TG values above 4.5mmol/L (which estimated higher LDL-C). These differences were all statistically significant. FLDL tended to estimate the lowest values regardless of TG, followed by SLDL and then MLDL. The difference in SLDL and MLDL estimated LDL-C was the most pronounced at TG levels above 4.5mmol/L. These are demonstrated in Fig. 4.

Discordance rates were somewhat higher when the DLDL was used as the comparator , with overall rates of 21.57%, 17.31% and 14.44% for the FLDL, SLDL and MLDL, respectively. Even at low TG levels of below

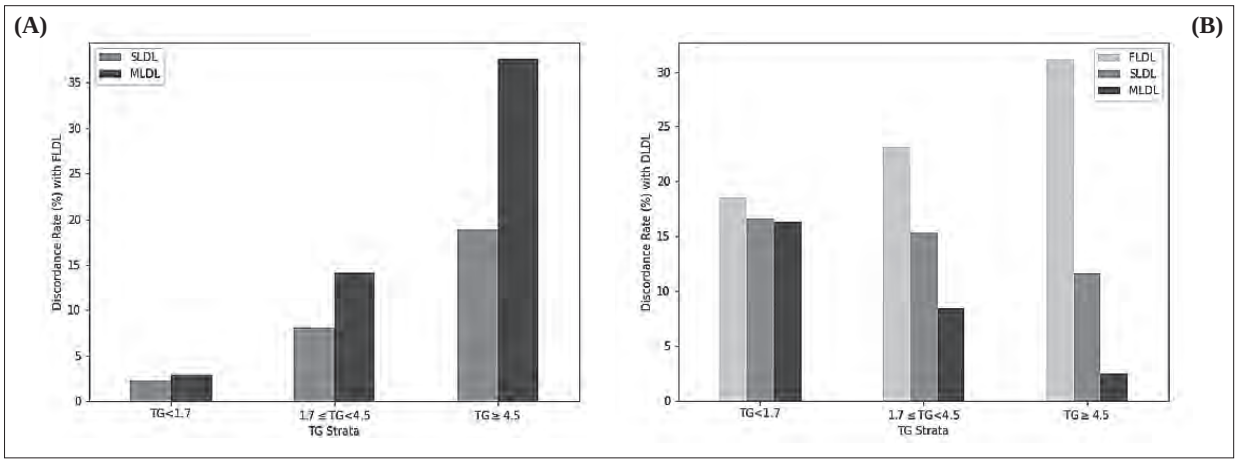

Fig. 3. (A) Discordance rates between Friedewald equation (FLDL) with Sampson equation (SLDL) and Martin/Hopkins equation (MLDL) across all triglyceride (TG) strata. (B) Discordance rates of FLDL, SLDL and MLDL with directly measured LDL-C (DLDL). Estimated low-density lipoprotein cholesterol (LDL-C) was considered discordant if LDL-C was <1.8mmol/L for the index equation and ≥1.8mmol/L for the comparator.

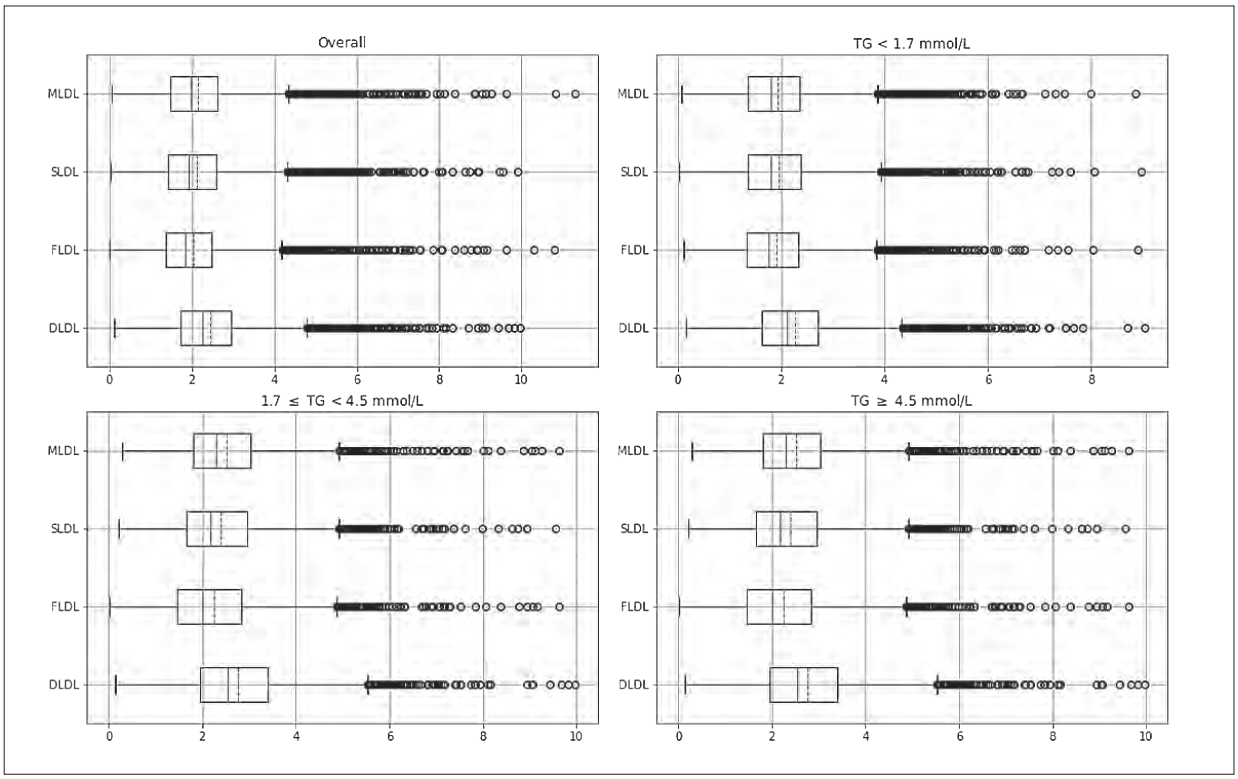

Fig. 4. Distribution of overall and triglyceride (TG) strata-specific estimated low-density lipoprotein cholesterol (LDL-C) values in the subgroup analysis. All 3 equations had lower median values than directly measured LDL-C (DLDL), with Friedewald equation (FLDL) estimating the lowest values across strata. The differences between median estimated LDL-C values and median DLDL values were all statistically significant (P<0.05).

1.7mmol/L, the discordance was still fairly substantial at 19.71%, 17.93% and 17.49%, respectively. As expected, discordance rates rose moving across the TG strata. The MLDL demonstrated the lowest discordance rates within each TG stratum, as shown in Fig. 3.

DISCUSSION

We conducted a lar ge study of 154,877 patients with T2DM, demonstrating the relationship between LDL-C values estimated by the FLDL, MLDL and SLDL. The study population is a uniquely relevant group of patients with both elevated TG levels and high

cardiovascular risk. To our knowledge, this is the first study comparing all 3 equations in this population, as well as against DLDL.

Both the SLDL and MLDL are alternative methods for estimating LDL-C in patients with T2DM, and are closely correlated with the conventional FLDL. In fact, all 3 methods also showed good correlation with DLDL. This is perhaps unsurprising as all 3 equations have the same theoretical basis—both HDL-C and TG are subtracted mathematically (albeit with varying factor coefficients) from the overall cholesterol, just as they are removed via polyanion precipitation and ultracentrifugation, respectively, in the beta-quantification method. There are differences in the correlation coefficients, with the SLDL appearing to demonstrate the best fit with both FLDL and DLDL overall, although the true magnitude of differences in both the correlation and goodness-of-fit (based on *r*, R^2 and RMSE values) between the equations is marginal.

Additionally, while the equations are closely correlated, none are equivalent to DLDL. The gold standard of LDL-C measurement should remain as beta-quantification. Commercially available homogenous enzymatic colorimetric assays (as used in our study) are an alternative to beta-quantification. These assays utilise a multistep reaction in which cholesterol esterase and oxidase produce hydrogen peroxide from solubilised LDL-C. Hydrogen peroxide reacts with selected reagents in the presence of peroxidase to produce a red-purple dye, which can be measured photometrically at the sub and main wavelengths of 700nm and 600nm, respectively. These assays are reported by the manufacturer to correlate well with beta-quantification and offer advantages including assay validity up to a maximum TG concentration of 23.0mmol/L.[18] However, these are not widely available, particularly in primary care settings. Therefore, these equations still offer a practical alternative to LDL-C measurement.

Unlike the MLDL and FLDL, the SLDL was designed to correlate better with measured LDL-C in hypertriglyceridaemic patients with TG values up to 9.0mmol/L.[19] However, this was not observed in our study. While the SLDL did correlate the best at TG values above >4.5mmol/L, with the highest correlation of 76.4%, this was firstly still much lower than its overall correlation of 96.6%, and secondly only marginally different from that reported for the MLDL (73.9%) and FLDL (75.8%). The goodness-of-fit was also similar for all 3 equations. As such, it remains uncertain which is the best method of LDL-C estimation when TG levels are high. More work including epidemiological studies and clinical intervention studies comparing different LDL-C estimation methods may be required in this group of patients.

Evaluating the discordance between the equations is important as this reflects a real-world treatment gap. Hypothetically, a patient with an estimated LDL-C of below 1.8mmol/L may not be targeted for more aggressive treatment, where in fact the true LDL-C value may be higher than 1.8mmol/L. This patient would hence be undertreated and exposed to a higher risk of poorer cardiovascular and overall outcomes. It is notable that the discordance between estimation methods can be close to 40% in patients with the highest TG values. This suggests that there may be a large unrecognised proportion of patients with diabetes who may be undertreated, especially when using the traditional Friedewald model. Lipid-lowering therapy is typically safe and effective.[3] As such, a method of LDL-C estimation that favours intensification of treatment may be preferred. Similar to previous reports,[20] the MLDL had the lowest discordance rates and hence may be considered as the most clinically favourable alternative to the traditional FLDL.

This study has several limitations. Firstly, the SDR only includes patients from 1 of the 3 healthcare clusters in Singapore. However, as previously described, the SingHealth cluster is the largest healthcare cluster in Singapore and is responsible for the medical care of approximately 50% of the national population. As such, these results can still be extrapolated to the national population at large.

Secondly, we used an LDL-C threshold of 1.8mmol/L when defining clinically relevant discordance, in keeping with international guidelines.[3,21] However, guidelines from Asian societies are heterogenous with respect to treatment targets[22] and evidence can be mixed.[23] Indeed, the local guidelines for our study population suggest a more permissive LDL-C target of <2.6mmol/L in high-risk and <2.1mmol/L in very-high-risk patients,[24] although this is currently under review. Nevertheless, while the exact value of the treatment target may be debated, it remains clear that lower lipid targets are generally beneficial even in Asian populations,[25] and we believe it is likely that there will still be substantial discordance between estimated LDL-C levels even if the LDL-C threshold used may vary slightly.

Lastly, only a subgroup of patients had direct LDL-C measurements. However, we believe this subgroup is largely similar to the overall population, apart from slight differences in ethnic profile and certain prevalent comorbidities at time of enrolment, which would not be expected to significantly affect LDL-C values.

Additionally, direct LDL measurements in the subgroup analysis were conducted using a homogenous enzymatic colorimetric assay. Significant non-selectivity errors have been reported when using this method in general, [26] although this particular laboratory has previously reported achieving satisfactory results on this assay when benchmarked on the College of American Pathologists external quality assurance programme.[18]

CONCLUSION

In a very large sample of patients with T2DM from an Asian population, we demonstrated strong correlation between newer methods of LDL-C estimation and the traditional FLDL. While the SLDL seemed to perform the best in statistical terms, the practical overall difference between the equations seems to be marginal. However, at higher TG concentrations, no one equation performed very well, suggesting further study may be required in this area. Clinically significant discordance was noted between equations and with DLDL. The use of the MLDL in this population may lead to less misclassification and undertreatment than the FLDL and SLDL.

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ORIGINAL ARTICLE

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Restaging of rectal cancer with hybrid positron emission tomography magnetic resonance imaging after preoperative chemoradiotherapy

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ABSTRACT

Introduction: This study determines the sensitivity and specificity of positron emission tomography/magnetic resonance imaging (PET/MRI) parameters in predicting treatment response in patients with localised rectal cancer who have undergone preoperative chemoradiotherapy (CRT).

Method: Patients with stage I–III adenocarcinoma of the rectum planned for preoperative CRT followed by surgery were recruited. Patients had PET/MRI scans at baseline and 6–8 weeks post-CRT. Functional MRI and PET parameters were assessed for their diagnostic accuracy for tumour regression grade (TRG). Nonparametric receiver operating characteristic analysis was employed to determine the area under the ROC curve (AUC), and the sensitivity and specificity of each quantile cut-off.

Results: A total of 31 patients were recruited, of whom 20 completed study protocol. All patients included had mid or lower rectal tumours. There were 16 patients (80%) with node-positive disease at presentation. The median time to surgery was 75.5 days (range 52–106 days). Histopathological assessment revealed 20% good responders (TRG 1/2), and the remaining 80% of patients had a poor response (TRG 3/4). When predicting good responders, the AUC values for percent maximum thickness reduction and percent apparent diffusion coefficient (ADC) change were 0.82 and 0.73, respectively. A maximum thickness reduction cut-off of ≥47% and a percent ADC change of ≥20% yielded a sensitivity and specificity of 75%/95% and 75%/73%, respectively.

Conclusion: Parameters such as percent maximum thickness reduction and percent ADC change may be useful for predicting good responders in patients undergoing preoperative CRT for rectal cancer. Larger studies are warranted to establish the utility of PET/MRI in rectal cancer staging.

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Keywords: PET/MRI, preoperative chemotherapy, rectal cancer, staging

INTRODUCTION

Neoadjuvant chemoradiotherapy (CRT) followed by surgery is the current standard of care for locally advanced rectal cancers. Randomised trials have shown that a neoadjuvant approach results in improved tumour downstaging, improved R0 resections, improved local control and increased sphincter preservation rates.[1] Reliable response assessment and restaging post-CRT add invaluable information for making optimal surgical and subsequent management decisions.

Current imaging modalities for response assessment and local restaging of rectal cancer patients post-CRT are inaccurate in this regard, particularly for T staging prediction and nodal status prediction.[2,3] This is due to an overlap in the appearance of the underlying residual tumour and post-treatment changes after CRT. A non-invasive and accurate way of assessing the treatment effect of CRT will guide surgical planning and allow for optimal selection of patients who need less extensive surgery, thereby reducing surgical morbidity.

One forerunner in the evaluation of rectal cancer burden pre- and post-CRT is hybrid positron emission tomography/magnetic resonance imaging (PET/MRI).[4,5] PET/MRI is a new imaging technology that can

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CLINICAL IMPACT

What is New

- This study evaluated the role of PET/MRI in rectal cancer restaging after chemoradiotherapy (CRT), with clearly defined and standardised protocols for MRI and PET acquisition.
- Using a percent maximum thickness reduction cut-off of ≥47% and a percent apparent diffusion coefficient (ADC) change of ≥20%, there was a sensitivity and specificity of 75%/95% and 75%/73%, respectively.
- The presence of mucinous rectal lesions can limit the role of PET/MRI due to their low fluorodeoxyglucose activity.

Clinical Implications

- MRI parameters, such as percent maximum thickness reduction and percent ADC change, may be useful for predicting good responders in patients undergoing preoperative CRT for rectal cancer.
- Future studies evaluating the role of PET/MRI in rectal cancer staging should also aim to specifically evaluate its utility in rectal cancers with a mucinous component.

overcome the shortfalls of existing imaging techniques. The MRI data acquired provide a detailed high-resolution anatomical map that can be correlated to the metabolic information from the PET scan, which has been shown to be highly sensitive for residual tumour detection. However, the diagnostic accuracy of PET/MRI in identifying good responders to preoperative CRT treatment remains unclear.

Thus, this prospective study aims to determine the diagnostic accuracy of various PET/MRI parameters in determining the treatment response of rectal cancer patients to preoperative CRT.

METHOD

Patients

This prospective study was approved by the National Healthcare Group Domain Specific Review Board B- 2014/00626 and 2015/01172. Eligible patients must be ≥18 years of age, diagnosed with cT2–4, N0–2 and M0 biopsy-proven adenocarcinoma of the rectum ≤12cm from the anal verge. Patients must have adequate renal, liver and haematological function and medically operable, with ECOG performance status 0–2. Exclusion criteria included patients with contraindications to MRI. Informed consent was obtained from all trial participants. The planned accrual was 30 patients over 2 years. The study workflow is shown in Fig. 1. All patients underwent a computed tomography (CT) of thorax/abdomen/pelvis and MRI rectum as standard workup for distant and local staging, respectively.

Radiotherapy

All patients received preoperative CRT followed by surgery. The radiotherapy regimen utilised 50.4Gy in 28 daily fractions delivered using conventional 3-dimensional conformal radiation therapy. The clinical target volume (CTV) included primary tumour and gross nodes. Elective nodal irradiation included the presacral, mesorectal, obturator and internal iliac lymph nodes. The planning target volume included the CTV with a 5mm margin.

Chemotherapy

The chemotherapy regimen was either concurrent capecitabine (at a dose of 825mg/m^2) or concurrent infusional 5 fluorouracil (at a dose of 425mg/m^2).

PET/MRI

The PET/MRI was acquired on a single machine. The MRI sequences were (1) multiplanar T2-weighted images of the pelvis; (2) diffusion-weighted images of the pelvis, including b values for intravoxel-incoherent motion analysis; (3) dynamic contrast-enhanced MRI of the pelvis; (4) magnetic resonance spectroscopy; and (5) T1-weighted (Dixon technique) and T2-weighted images of the whole body for PET data anatomic correlation and attenuation correction. PET data were acquired simultaneously with MRI, obtained 60 minutes after the injection of 18F-fluorodeoxyglucose (FDG) (300–385MBq).

Pathological assessments

Tumour response post-CRT and surgery was graded according to the tumour regression grade (TRG). TRG 1 is defined as no viable tumour cells, TRG 2 is defined as single or small groups of cancer cells, TRG 3 is defined as residual cancer outgrown by fibrosis, TRG 4 is defined as significant fibrosis outgrown by cancer, and TRG 5 is defined as no regressive changes in tumour.

Endpoints

Patients underwent PET/MRI scans at baseline and 6–8 weeks post-CRT. The scan findings were compared

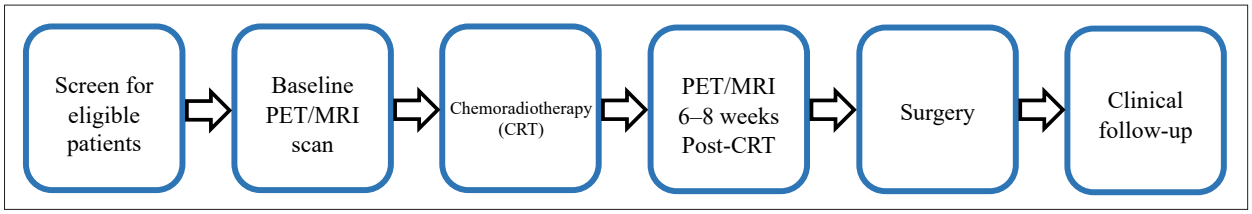

Fig. 1. Study workflow.
CRT: chemoradiotherapy; PET/MRI: positron emission tomography/magnetic resonance imaging

against the TRG on the histopathological specimen. The diagnostic accuracy of functional MRI and PET parameters was assessed based on TRG 1/2 (good responders). These parameters include percent volume reduction, percent standard uptake volume (SUV) reduction, percent SUV volume reduction, percent glycolysis reduction, percent maximum thickness reduction, percent apparent diffusion coefficient (ADC) change, post-treatment (PTx) volume, PTx SUV max, PTx SUV volume, PTx glycolysis, PTx maximum thickness and PTx ADC values. Each parameter is divided equally into 5 quantiles. Nonparametric receiver operating characteristic analysis was employed to determine the sensitivity and specificity of each quantile cut-off. An AUC value of ≥0.8 was taken to be clinically useful in predicting for response to preoperative CRT. Statistical analysis was performed with STATA version 14 (Stata Corp, College Station, TX, US).

RESULTS

Patients

From April 2015 to August 2019, 31 patients were recruited. Twenty patients completed the study protocol. Eleven did not, including one who withdrew voluntary consent, and one lost to follow-up. Nine patients did not complete their scheduled scans.

Patient and tumour characteristics are highlighted in Table 1. Eighty percent (16/20) of patients were male. Majority of patients were aged 50 years or older. Patients had mid or lower rectal tumours. Eighty percent (16/20) of patients had node-positive disease.

Surgery

The median time to surgery was 75.5 days (range 52–106 days). All patients underwent surgery post-CRT. Eighty percent (16/20) of patients had anterior resection. R0 resection was obtained in 95% (19/20) of patients. Lymphovascular invasion was present in 75% (17/20) of patients, and no patients had perineural invasion. Twenty percent of patients had a good response (TRG 1/2) to preoperative CRT. Surgical

Table 1. Patient characteristics and tumour staging.

Patient characteristics	N=20	%
Sex		
Male	16	80.0
Female	4	20.0
Age, years		
≤50	1	5.0
≥50	19	95.0
Location of tumour (cm from the anal verge)		
High (9–12cm)	0	0
Mid (5–8cm)	7	35.0
Lower (0–4cm)	13	65.0
cT		
T2	3	15.0
T3	15	75.0
T4	2	10.0
cN		
N0	4	20.0
N1	2	10.0
N1a	1	5.0
N1b	3	15.0
N2a	5	25.0
N2b	5	25.0
Combined clinical stage		
T2N0	2	10.0
T2N2	1	5.0
T3N0	1	5.0
T3N1	6	30.0
T3N2	8	40.0
T4N0	1	5.0
T4N2	1	5.0

procedures performed and pathological findings are detailed in Table 2.

Pathological response

Ten percent (2/20) of patients had a complete pathological response (TRG1). Tumour was successfully downstaged in the remaining 18 patients (2 TRG 2 and 13 TRG 3), 95% (19/20) of patients had clear margins after surgery, whereas 5% (1/20) had a positive surgical margin after surgery.

Table 2. Surgical procedures and pathological findings.

	N=20	%
Surgical procedure		
Abdominoperineal resection	4	20.0
Anterior resection	15	75.0
Low anterior resection	1	5.0
Lymphovascular invasion		
Yes	3	15.0
No	17	85.0
Perineural invasion		
Yes	0	0.0
No	20	100.0
Margin		
Positive	1	5.0
Negative	19	95.0
ypT		
T0	2	10.0
T1	2	10.0
T2	5	25.0
T3	11	55.0
T4	0	0.0
ypN		
N0	13	65.0
N1	6	30.0
N2	1	5.0
TRG		
0	2	10.0
1	2	10.0
2	13	65.0
3	3	15.0

PET/MRI in predicting tumour response

Figs. 1 and 2 illustrate how PET/MRI can help accurately predict tumour response during surgery. Fig. 1A displays the PET/MRI images of a patient with poorly differentiated low rectal carcinoma. Pretreatment sagittal T2 and fused PET/MRI images show primary tumour (SUV max=11.2) with pathological enlarged and hypermetabolic presacral node (short arrow). Fig. 1B depicts post-CRT images, showing marked tumour volume reduction with residual tumour of MRI and marked remnant metabolic uptake in the primary tumour (SUVmax=9.6) and presacral node. Preoperative clinical stage was cT3N1. Final stage was ypT3N2a. Histological response was a poor response TRG 3.

By contrast, Fig. 2A shows another patient's PET/MRI images. Pretreatment axial T2 images and fused PET/MRI images show primary tumour (SUVmax=13.4) with no suspicious nodes in the mesorectum. Fig. 2B depicts post-CRT images, showing marked tumour volume reduction with residual wall thickening posteriorly that was indeterminate for remnant tumour. However, there was no significant corresponding metabolic update (SUVmax=2.5) in the area of wall thickening. Preoperative clinical tumour state was cT3N1. Postoperative tumour stage was ypT0N0. Histological response assessment was a complete response (TRG 1).

Correlation of PET/MRI parameters with tumour response

Table 3 shows the AUC for PET and MRI parameters for the prediction of pathological response. The correlation of these parameters with TRG 3/4/5 (reference) versus 1/2 is presented in Supplementary Table S1. When predicting good responders, the AUC values for percent maximum thickness reduction and percent ADC change were 0.82 and 0.73, respectively. The AUC values for all other parameters were less than 0.6. A maximum thickness cut-off of ≥47% and a percent ADC change of ≥20% yielded a sensitivity and specificity of 75%/95% and 75%/73%, respectively.

DISCUSSION

PET/CT has conventionally been used for the staging and assessment of treatment response for rectal cancer patients treated with CRT.[6,7] However, the limited soft tissue contrast and lower anatomic detail afforded by the CT component render it less useful for providing accurate local staging information in rectal cancer. Similarly, the use of MRI for restaging post-CRT is also not ideal as changes in tumour or lymph node size on MRI have not been shown to correlate with tumour response.[5,8]

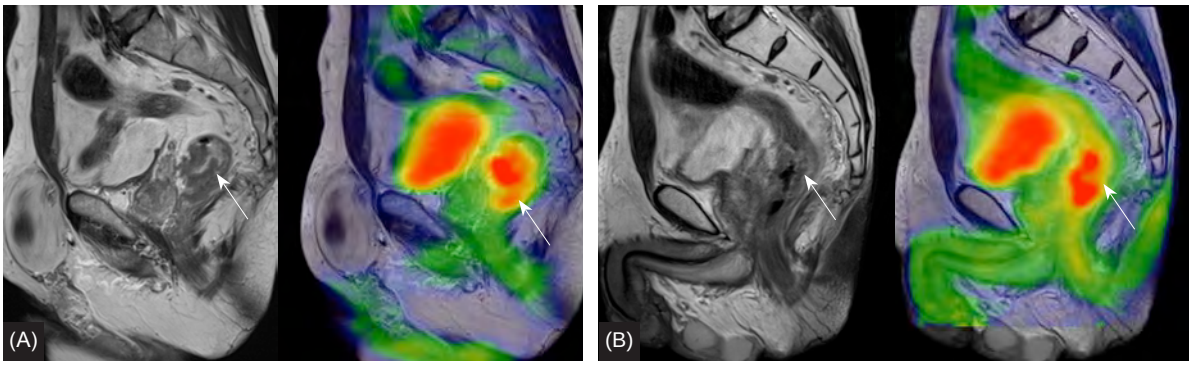

Fig. 2. Poor response to preoperative chemoradiotherapy (CRT). (A) Preoperative positron emission tomography/magnetic resonance imaging (PET/MRI). (B) Post-CRT PET/MRI. Arrows indicate the rectal tumour.

Table 3. AUC values for PET/MRI parameters with TRG 3/4/5 (ref) vs. 1/2.

	AUC
Volume reduction	0.31
SUV reduction	0.50
SUV volume reduction	0.38
Glycolysis reduction	0.44
Maximum thickness reduction	0.82
ADC change	0.73

ADC: apparent diffusion coefficient; PET/MRI: positron emission tomography/magnetic resonance imaging; SUV: standard uptake volume; TRG: tumour regression grade

In addition, the interpretation of MRI in the post-CRT setting can be more challenging due to difficulties in discriminating residual tumour from areas of radiation-induced fibrosis. A meta-analysis performed to evaluate MRI accuracy in the post-CRT setting revealed a mean overall sensitivity of only 40.3% for tumour response.[9,10] The hybrid PET/MRI approach potentially overcomes the aforementioned limitations seen in MRI and PET/CT. It also offers the added advantage of reducing ionising radiation exposure to patients.

Several studies have attempted to elucidate the utility of PET/MRI in the staging of rectal cancer patients.[5] In terms of local staging, PET/MRI has been shown in some reports to be superior to MRI alone and comparable to PET/CT.[11,12] Although the use of PET/MRI also confers an advantage in characterising distant metastasis to abdominal solid organs, such as the liver, it is known to be a poorer modality in identifying pulmonary lesions than CT.[8,11,13,14] Specific to restaging after CRT, Crimì et al. investigated the role of PET/MRI in 22 patients with locally advanced mid/low rectal cancer treated with preoperative CRT by correlating ADC maps, FDG images and histogram analysis with pathological response.[5] They found a significant correlation between the post-treatment SUV mean values and tumour regression grading. However, the interpretation of the results was limited by the relatively small sample size.

The advent of total neoadjuvant therapy for patients with locally advanced rectal cancer has led to improved pathological responses.[15,16] Patients who achieve a complete clinical response to preoperative chemotherapy and radiotherapy may be suitable candidates for the watch and wait approach, thereby allowing for organ preservation through the omission of surgery.[17] As one of the first few studies evaluating the role of PET/MRI in rectal cancer restaging, the current study demonstrates that hybrid PET/MRI data acquisition provides complementary information, which allows for more accurate evaluation of residual disease post-CRT, as shown in Figs. 2 and 3. In such cases, the combination of morphological, functional and metabolic data using PET/MRI is particularly important to enhance differentiation between viable tumour tissue that has been replaced by fibrosis. This is further demonstrated in various studies that have reported alterations made to patient treatment strategies after the analysis of PET/MRI findings.[5,11,14]

Nonetheless, only MRI parameters, such as ADC change and maximum thickness reduction, predicted for good tumour response to preoperative CRT in the current study. Using a percent maximum thickness reduction cut-off of ≥47% and a percent ADC change of ≥20%, there was a sensitivity and specificity of 75%/95% and 75%/73%, respectively. Other parameters, such as percent volume reduction, percent SUV reduction, percent SUV volume reduction, percent glycolysis reduction, PTx volume, PTx SUV max, PTx SUV volume, PTx glycolysis, PTx maximum thickness and PTx ADC values, were not useful in predicting tumour responses to preoperative CRT. These findings can be explained by the presence of mucinous rectal

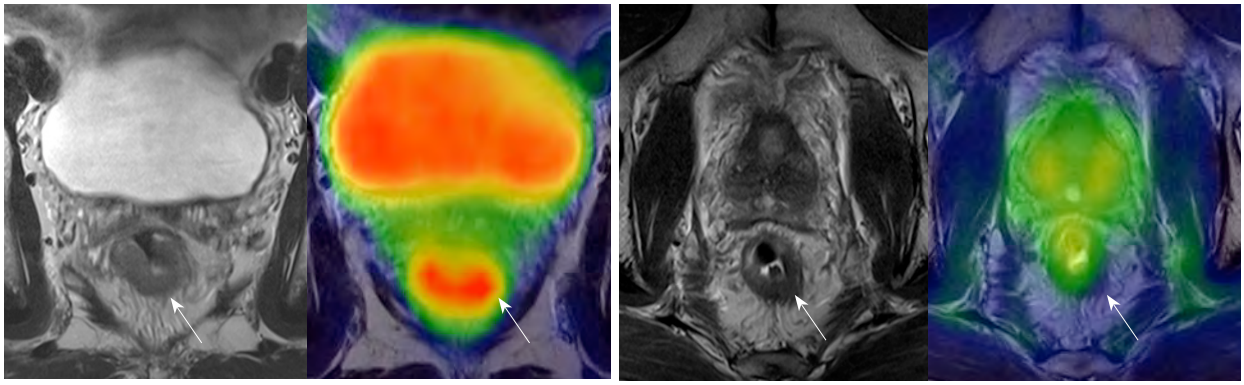

Fig 3. Good response to preoperative chemoradiotherapy (CRT). (A) Preoperative positron emission tomography/magnetic resonance imaging (PET/MRI). (B) Post-CRT PET/MRI. Arrows indicate the rectal tumour.

lesions, which can limit the role of PET/MRI due to their low FDG activity. Future studies evaluating the role of PET/MRI in rectal cancer staging should also aim to specifically evaluate its utility in rectal cancers with a mucinous component.

Although limited by the small sample size, this study is one of the first few works evaluating the role of PET/MRI in rectal cancer restaging after CRT. It is also conducted in a prospective manner with clearly defined and standardised protocols for MRI and PET acquisition. Notably, 11 of the 31 patients did not complete the study protocol, and this was likely due to the long acquisition time required for PET/MRI. Future studies should also evaluate the length of the acquisition time and the impact it has on patients undergoing PET/MRI, including the cost effectiveness of PET/MRI in rectal cancer staging.

CONCLUSION

Parameters such as percent maximum thickness reduction and percent ADC change may be useful for predicting good responders in patients undergoing preoperative CRT for rectal cancer. Larger studies are warranted to establish the utility of PET/MRI in rectal cancer staging.

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ORIGINAL ARTICLE

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Evaluation of a return to work coordination programme for injured workers in a public hospital in Singapore

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ABSTRACT

Introduction: This study evaluates the effectiveness of a hospital-based return to work (RTW) programme in facilitating injured workers to R TW earlier through personalised case management. Factors associated with programme effectiveness are also examined.

Method: This was a quasi-experimental study comparing 81 participants who underwent conventional treatment before the RTW programme with 108 participants who directly received the RTW intervention. Analyses included time to RTW and the factors associated with dropout. Stratified analysis and multivariate logistic regres sion were used to mitigate potential s election bias from the additional recruitment process for the intervention group.

Results: Participants in the intervention group returned to work 59.5 days earlier , with 84% able to RTW 6 mont hs post inj ury compared with the control (63%; $P<0.01$). Stratified analysis found the intervention to be associated with better RTW outcomes among males, younger workers, non-residents, blue-collared workers, workers from the construction, marine, manufacturing and metalworking industries, and workers having lower Work Ability score (WAS), while light-duty provision was a possible confounder. The better outcomes in the intervention group were also independent of company size and injury severity. After adjusting for the above factors, the intervention group had 2.2 times higher odds of RTW at 6 months (95% confidence interval 0.84–5.90). Lower WAS and longer delay in initial RTW assessment were associated with delayed RTW within the intervention group. Migrant workers experienced higher dropout rates, thus being identified as a vulnerable group.

Conclusion: The RTW coordination model of care is effective in facilitating RTW, with early programme referral being an important facilitator and WAS as a useful screening tool for delayed RTW.

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Keywords: Occupational medicine, occupational therapy, programme evaluation, public health, return to work coordination

INTRODUCTION

Workers who have sustained an injury at work often face difficulties returning to work, according to a study showing that over 40% of injured workers in Singapore experienced increased lethar gy at work and that about 40% had difficulties in performing work at pre-injury standards.[1] One in 4 workers also felt that certain work activities might lead to re-injury ,[1] while some had the mentality that full recovery was needed before they could return to work (RTW). Another study showed that lower self-perceived work ability was associated with a longer duration of sickness absence. [2] Nevertheless, the need for full recovery has been disproved by many studies showing that gradual RTW can be a therapeutic goal.[3,4]

RTW coordination has been shown to be useful in addressing the barriers patients face in returning to work.[5-7] A randomised controlled trial conducted in Singapore demonstrated that the injured workers who received RTW coordination returned to work 10 days earlier than workers in the control group, with a higher proportion of workers in the intervention group returning

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CLINICAL IMPACT

What is New

- This study highlights the real-world effectiveness of a return to work (RTW) programme, with comparison against a control group that underwent conventional treatment.
- Migrant workers had higher likelihood of earlier RTW and dropout rates from the RTW programme.

Clinical Implications

- Personalised case management by occupational therapists who follow through the patient's recovery journey, from medical appointments to providing updates to the employer on patient's readiness to RTW can overcome RTW barriers.
- Occupational health professionals and policymakers are integral for uptake of RTW programmes and to safeguard the rights of injured workers.

to modified jobs.[8] Notably, migrant workers were excluded from the trial.

Following this trial, the Singapore Ministry of Manpower (MOM) partnered with 7 public hospitals in Singapore to implement an RTW programme in 2017, providing case management and coordination for injured workers to help them regain their work ability and long-term employability.[9] This programme is covered under the Work Injury Compensation Act (WICA), allowing workers to file claims for work-related injuries without having to file a civil suit.[10] A team comprising RTW coordinators (RTWCs) and adminis trative staff was formed to implement the programme in each hospital. Prior to this programme, there was no standard clinical practice to facilitate the R TW of patients with work injuries, and any R TW issues were addressed by the treating physicians or therapists on an ad-hoc basis.

This study aims to evaluate the real-w orld effectiveness of the R TWC model of care in a public hospital in Singapore for patients with work injuries and to examine the factors associated with better RTW outcomes, providing useful information for programme improvement. This study included migrant workers to gain new insights into R TW issues for this group, given the substantial proportion of migrant w orkers in Singapore's workforce.

METHOD

Study design

This was a quasi-experimental study conducted in a single public hospital. Data were dichotomised into 2 periods: 1 October 2017 to 31 December 2017 before the RTW programme commenced (control group), and 1 June 2018 to 1 June 2020 after the start of the programme (intervention group). Ethics approval was given by the Institutional Review Board of the National Healthcare Group in Singapore.

Inclusion and exclusion criteria

Inclusion criteria for this study were workers who had sustained work injuries and were covered under the WICA, had been given more than 14 days of medical-certified leave post injury , and are Singaporeans, permanent residents or migrant workers with a valid work pass of more than 9 months.

Control group

The control group comprised injured workers who had received medical treatment in the hospital in the 3 months before the R TW programme. These patients had received standard care, which included routine medical and rehabilitation treatment. The study team sent an invitation to these patients before giving them a call to obtain participation consent and information about their medical and R TW status at 6 months post injury , such as time taken to RTW or whether they remained unemployed.

Intervention group

Participants in the intervention group were either recruited from an MOM-provided listing of i njured workers who had received medical treatment in the hospital, or were internally referred by the medical team (such as hand sur gery and orthopaedics). Potential participants were screened for eligibility by the administrative staff. Patients who did not meet the inclusion criteria or were uncontactable were excluded. Eligible patients who gave consent to join the R TW programme were recruited into the intervention group.

Three RTWCs provided the intervention. The RTWCs were occupational therapists with more than 5 years of clinical experience and had under gone specialised training in functional capacity evaluation and occupational assessment.

The RTW programme consisted of personalised case management through an RTWC to assist the injured worker to RTW. Upon recruit ment of a pat ient, the

RTWC conducted a vocational assessment to understand the patient's functional capacity post injury, to determine the patient's job demands and to identify enablers and challenges for RTW. The RTWC would also initiate early contact with the employer to verify the job demands and explore if modified duties were available when required. The RTWC would then attend the following medical appointment of the patient to update the doctor on the patient's job requirements and discuss the RTW plan. Subsequently, the RTWC would provide regular updates to the employer on the patient's progress and readiness to RTW. If warranted, the RTWC would conduct workplace assessments and provide recommendations for workplace accommodations.

Outcomes

Baseline data included demographics and occupational variables, injury-related information like the Injury Severity Score, time taken to RTW, RTW status at 6 months post work injury, current job scope, total duration of medical leave, whether there was any provision of light duty by the treating physician, and the assessment of work ability based on the Work Ability score (WAS), which is the first item of the Work Ability Index.[11] The WAS measures the worker's self-assessment of the current work ability as opposed to the lifetime best on a scale from 0 (cannot work at all right now) to 10 (my work ability is at its best right now).[11] The WAS has been found to have high convergent validity with the Work Ability Index and is predictive of work ability.[11-13] Six months was set as the timepoint at which the RTW status was tracked, as most participants were expected to complete the programme within this time frame. For the control group, 6 months was the only timepoint at which the participants' RTW status was known.

Statistical analyses

To evaluate the effectiveness of the programme, outcomes from the control and intervention groups were compared. Baseline data of participants who dropped out of the RTW programme were also analysed to determine the factors influencing the participants' ability to continue with the programme. Fisher's Exact test and chi-square statistics were conducted to compare categorical variables, whereas the non-parametric Mann-Whitney U test was used for continuous variables in the event of non-normality. Statistical analyses were done using Stata version 16 (StataCorp LP, College Station, US). Statistical significance was set at $P<0.05$.

To mitigate potential selection bias given that the intervention group underwent an additional recruitment process, stratified analysis was first utilised to compare the RTW outcomes between the control and intervention groups across different demographic and occupational strata. Multivariate logistic regression was then done to adjust for these factors. As our results subsequently showed multiple possible effect modifiers and one possible confounder (light-duty provision), different multivariate models were built. The first model was based on the identified effect modifiers, second model was adjusted for the potential confounder separately, and a third model was adjusted for all these factors combined. The results are expressed as odds ratios with 95% confidence intervals.

RESULTS

Participants

A total of 226 participants were recruited, with 82 in the control group and 144 in the intervention group. One participant in the control group was lost to follow-up, whereas 36 dropped out from the intervention group owing to the following reasons: not allowed to work in Singapore as work visa was converted to Special Pass by employer (n=10); chose to pursue common law compensation (n=8); not keen to adhere to RTW plan (n=7); repatriated to home country (n=4); uncontactable (n=4); family not supportive (n=2); and other personal reasons (n=1). Data from 189 participants were analysed, with 81 in the control group and 108 in the intervention group.

Comparisons of the demographics and pre-injury occupational information of the participants of the 2 groups are shown in Table 1. Specifically, both groups were comparable in terms of nationality and injury severity, with the conventional group having a lower median age at time of injury. The majority of the patients in the intervention group (92%) and control group (96%) had mild injuries, with upper limb injuries being the most common injury (58% in control group, 81% in intervention group), followed by lower limb and back injuries (28% in control group, 15% in intervention group). Participants in the intervention group had a higher proportion of blue-collar workers (Table 1), with majority classified as cleaners and labourers (47%), and plant and machine operators and assemblers (26%). The body site of injury was also similar between blue-collar and white-collar workers.

Factors associated with RTW status at 6 months

The intervention arm took a significantly shorter median duration to RTW (81.5 days) than did the conventional

treatment arm (141 days; Table 1), with a higher proportion of participants being able to RTW 6 months post injury (84%) compared with the control (63%). A higher proportion of participants in the intervention group were also able to RTW to the same pre-injury job at 6 months (64%) compared with the control group (49%, P=0.054), with this percentage increasing to 82% upon discharge from the programme. Among the participants in the intervention group who were unable to RTW at 6 months, 24% had moderate or severe injuries and 89% had undergone surgical treatment, compared with 7% and 64% in the conventional group, respectively.

The factors associated with the RTW status at 6 months are shown in Table 2. For both the control and intervention groups, a higher WAS at baseline and light-duty provision were associated with better RTW status, while age, nationality, occupation type and industry sector had differing associations between both groups. Subsequent stratified analysis found several potential effect modifiers, with intervention being associated with better RTW outcomes among males, younger workers, non-residents, blue-collar workers, workers from the construction, marine, manufacturing and metalworking industry, and workers with a lower baseline WAS (Table 3). The better RTW outcome seen in the intervention group was also independent of company size and injury severity. Light-duty provision seemed to be a possible confounder, with a smaller difference in RTW status noted between the control and intervention groups.

The above factors were subsequently used in the multivariate logistic regression, with the RTW status at 6 months post injury as the dependent variable (Table 4). After adjusting for these factors, the intervention group had 2.2 times higher odds of returning to work at 6 months compared with the conventional treatment group.

Factors associated with earlier RTW (within 80 days)

Variables associated with earlier RTW in the intervention group included non-residents, duration elapsed from injury to RTW assessment, total number of days of medical leave, total number of days of light duty and WAS at discharge (P<0.05; Table 5). A total of 55.1% of the participants who are non-residents returned to work earlier compared with the residents. Participants who returned to work later had experienced a longer delay in their RTW assessment (84.5 days), had taken more median days of medical leave (116 days) and light duty (57 days), and had a lower median WAS at discharge compared with those who returned to work earlier.

Dropouts

Of the 111 non-residents recruited in the intervention group, only 70.3% completed the intervention. Of those who dropped out of the RTW programme, 92% were migrant workers. Analyses of baseline data of participants who dropped out showed that they had a significantly lower baseline WAS of 3 compared with a median score of 8 in those who completed the intervention. They also had a significantly longer duration of medical leave (110 days) than those who completed the intervention (76.5 days; Table 6).

DISCUSSION

Effectiveness of the RTW programme

This study demonstrated that an RTW programme in a public hospital was effective in enabling participants to RTW earlier by about 60 days, with an additional 20% able to RTW at 6 months post injury compared with participants who received standard care. These are important outcomes as earlier RTW benefits both employers and workers in terms of financial goals and job sustainability.[14-16] Our results are also similar to studies showing that the RTWC model of care helps to expedite RTW.[5-7] In our study, the intervention group had a similar duration of first RTW (81 days) as other participants in another Singapore hospital (64 days); also, the proportion of patients able to RTW (84%) was similar to patients with work injuries in an overseas RTW coordination programme in Malaysia (75%).[17,18] This duration, however, is longer compared with that from a randomised controlled trial on the RTW coordination in Singapore in which participants were recruited directly from the hospital's emergency department database,[8] suggesting that later recruitment into the programme could be associated with a longer duration to RTW.

The study also showed that the RTW programme was effective for specific demographic and occupation groups, including foreigners and blue-collar workers. As of December 2022, the total foreign workforce in Singapore numbered 1.15 million, excluding domestic workers,[19] representing a substantial proportion of the blue-collar workforce in Singapore. While the previous study by Tan et al.[8] had focused on Singaporeans and permanent residents, this study was able to recruit a good proportion of migrant workers into the RTW programme.

WAS as a screening tool for RTW

Work ability is defined by the extent to which a worker's capabilities are matched by the demands at work.[20] Factors associated with poor work ability include poor musculoskeletal capacity, high mental

Table 1. Descriptive statistics of the control and intervention groups.

Variables	Conventional treatment (n=81)	Intervention treatment (n=108)	*P* value
Sex, no. (%)			
Male	72 (88.9)	96 (88.9)	1.00
Female	9 (11.1)	12 (11.1)	
Age at time of injury, median (IQR), years	32 (26–47)	36.5 (31–47)	0.01
Race, no. (%)			
Chinese	29 (35.8)	38 (35.2)	0.49
Malay	7 (8.6)	4 (4.0)	
Indian	19 (23.5)	31 (28.7)	
Other	26 (32.1)	35 (32.4)	
Nationality, no. (%)			
Non-resident	58 (71.6)	79 (73.2)	0.81
Resident	23 (28.4)	29 (26.9)	
Company size, no. (%)			
SME (≤200 employees)	48 (60.8)	65 (60.2)	0.94
Large (>200 employees)	31 (39.2)	43 (39.8)	
Occupation, no. (%)			
White and pink collar	17 (21.8)	11 (10.2)	0.03
Blue collar	61 (78.2)	97 (89.8)	
Industry sector, no. (%)			
Construction, marine, general manufacturing, metalworking	49 (60.5)	78 (72.2)	0.09
Other[a]	32 (39.5)	30 (27.8)	
Light duty given, no. (%)			
No	47 (58.0)	15 (13.9)	<0.01
Yes	34 (42.0)	93 (86.1)	
ISS score, no. (%)			
Mild injury (ISS 1–8)	78 (96.3)	99 (91.7)	0.62
Moderate injury (ISS 9–15)	3 (3.7)	5 (4.6)	
Severe injury (ISS 16–24)	0	2 (1.9)	
Critical injury (ISS ≥25)	0	2 (1.9)	
Work Ability score (baseline), median (IQR)	6 (0–8)	6 (5–7)	0.73
Average length of time taken to first RTW, median (IQR), days	141 (61–999)	81.5 (56.5–122)	<0.01
RTW category at 6 months from injury date, no. (%)			
Able to RTW[b]	51 (63.0)	91 (84.3)	<0.01
Unable to RTW	30 (37.0)	17 (15.7)	

IQR: interquartile range; ISS: Injury Severity Score; RTW: return to work; SME: small and medium enterprise

[a] Includes (in decreasing order of frequency) transport and storage; hospitality , tourism, food and beverage; cleaning and landscape; wholesale and retail trade; pharmaceutical, health and social services; chemical, oil and gas; electronic and precision; energy and utilities; aviation; and others.

[b] Categories include "same employer–same pre-injury job", "same employer–modified job", "same employer–similar job", "same employer–different job" and "different employer–different job".

Table 2. Association between return to work (RTW) status at 6 months and various demographic and occupational groups.

Variables	Proportion able to RTW at 6 months					
	All participants (n=189)		Conventional treatment (n=81)		Intervention treatment (n=108)	
	No. (%)	*P* value	No. (%)	*P* value	No. (%)	*P* value
Sex						
Male	126 (75.0)	1.00	43 (59.7)	0.14	83 (86.5)	0.09
Female	16 (76.2)		8 (88.9)		8 (66.7)	
Age at time of injury						
<35 years	64 (71.9)	0.33	24 (52.2)	0.02	40 (93.0)	0.06
≥35 years	78 (78.0)		27 (77.1)		51 (78.5)	
Race						
Chinese	55 (82.1)	0.11	23 (79.3)	<0.01	32 (84.2)	0.90
Malay	9 (81.8)		6 (85.7)		3 (75.0)	
Indian	39 (78.0)		13 (68.4)		26 (83.9)	
Other	39 (63.9)		9 (34.6)		30 (85.7)	
Nationality						
Resident	41 (78.9)	0.47	19 (82.6)	0.02	22 (75.9)	0.23
Non-resident	101 (73.7)		32 (55.2)		69 (87.3)	
Company size						
SME (≤200 employees)	88 (77.9)	0.24	33 (68.8)	0.16	55 (84.6)	0.90
Large (>200 employees)	52 (70.3)		16 (51.6)		36 (83.7)	
Occupation						
White and pink collar	21 (75.0)	0.97	16 (94.1)	<0.01	5 (45.5)	<0.01
Blue collar	119 (75.3)		33 (54.1)		86 (88.7)	
Industry sector						
Construction, marine, general manufacturing, metalworking	92 (72.4)	0.22	26 (53.1)	0.02	66 (84.6)	0.87
Other	50 (80.7)		25 (78.1)		25 (83.3)	
ISS score						
Mild injury (ISS 1–8)	136 (76.8)	0.08	50 (64.1)	0.55	86 (86.9)	0.03
Moderate, severe or critical injury (ISS ≥9)	6 (50.0)		1 (33.3)		5 (55.6)	
Light duty given						
No	36 (58.1)	<0.01	25 (53.2)	0.03	11 (73.3)	0.25
Yes	106 (83.5)		26 (76.5)		80 (86.0)	
Work Ability score (baseline)						
<7	63 (60.0)	<0.01	14 (32.6)	<0.01	49 (79.0)	0.11
≥7	79 (94.1)		37 (97.4)		42 (91.3)	

ISS: Injury Severity Score; SME: small and medium enterprise

Table 3. Stratified analysis comparing return to work (RTW) status at 6 months between the control and intervention groups across different demographic and health factors.

	No. (%) unable to RTW at 6 months	No. (%) able to RTW at 6 months	*P* value
Sex: male			
Conventional treatment	29 (40.3)	43 (59.7)	<0.01
Intervention treatment	13 (13.5)	83 (86.5)	
Sex: female			
Conventional treatment	1 (11.1)	8 (88.9)	0.34
Intervention treatment	4 (33.3)	8 (66.7)	
Age at time of injury <35 years			
Conventional treatment	22 (47.8)	24 (52.2)	<0.01
Intervention treatment	3 (7.0)	40 (93.2)	
Age at time of injury ≥35 years			
Conventional treatment	8 (22.9)	27 (77.1)	0.88
Intervention treatment	14 (21.5)	51 (78.5)	
Nationality: Resident			
Conventional treatment	4 (17.4)	19 (82.6)	0.55
Intervention treatment	7 (24.1)	22 (75.9)	
Nationality: Non-resident			
Conventional treatment	26 (44.8)	32 (55.2)	<0.01
Intervention treatment	10 (12.7)	69 (87.3)	
Company size: SME ≤200 employees			
Conventional treatment	15 (31.3)	33 (68.8)	0.05
Intervention treatment	10 (15.4)	55 (84.6)	
Company size: Large >200 employees			
Conventional treatment	15 (45.5)	18 (54.6)	0.01
Intervention treatment	7 (16.3)	36 (83.7)	
Occupation: White and pink collar			
Conventional treatment	1 (5.9)	16 (94.1)	<0.01
Intervention treatment	6 (54.6)	5 (45.5)	
Occupation: Blue collar			
Conventional treatment	29 (45.3)	35 (54.7)	<0.01
Intervention treatment	11 (11.3)	86 (88.7)	
Industry: Construction, marine, general manufacturing, metalworking			
Conventional treatment	23 (46.9)	26 (53.1)	<0.01
Intervention treatment	12 (15.4)	66 (84.6)	
Industry: Other			
Conventional treatment	7 (21.9)	25 (78.1)	0.75
Intervention treatment	5 (16.7)	25 (83.3)	

Table 3. Stratified analysis comparing return to work (RTW) status at 6 months between the control and intervention groups across different demographic and health factors. (Cont'd)

	No. (%) unable to RTW at 6 months	No. (%) able to RTW at 6 months	*P* value
ISS Score: Mild injury (ISS 1–8)			
Conventional treatment	28 (35.9)	50 (64.1)	<0.01
Intervention treatment	13 (13.1)	86 (86.9)	
ISS Score: Moderate injury and above			
Conventional treatment	2 (66.7)	1 (33.3)	1.00
Intervention treatment	4 (44.4)	5 (55.6)	
Light duty given			
Conventional treatment	8 (23.5)	26 (76.5)	0.20
Intervention treatment	13 (14.0)	80 (86.0)	
Light duty not given			
Conventional treatment	22 (46.8)	25 (53.2)	0.17
Intervention treatment	4 (26.7)	11 (73.3)	
Work Ability score (baseline) <7			
Conventional treatment	29 (67.4)	14 (32.6)	<0.01
Intervention treatment	13 (21.0)	49 (79.0)	
Work Ability score (baseline) ≥7			
Conventional treatment	1 (2.6)	37 (97.4)	0.37
Intervention treatment	4 (8.7)	42 (91.3)	
For patient profile: 1. Sex: male, and 2. Age: <35 years, and 3. Nationality: non-resident, and 4. Occupation: blue-collar worker, and 5. Industry: construction, marine, general manufacturing, metalworking, and 6. Work Ability score (baseline) <7			
Conventional treatment	17 (81.0)	4 (19.1)	<0.01
Intervention treatment	3 (13.0)	20 (87.0)	

ISS: Injury Severity Score; SME: small and medium enterprise

Table 4. Univariate and multivariate logistic regression comparing return to work (RTW) status at 6 months between the control and intervention groups.

	Able to RTW at 6 months							
	Unadjusted		Model 1[a]		Model 2[b]		Model 3[c]	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Control	1 [Reference]		1 [Reference]		1 [Reference]		1 [Reference]	
Intervention group	3.15 (1.58–6.26)	<0.01	5.21 (2.24–12.1)	<0.01	2.08 (0.96–4.49)	0.06	2.23 (0.84–5.90)	0.11

CI: confidence interval; OR: odds ratio
[a] Model 1: Adjusted for sex, age, nationality, occupation, industry, work ability (baseline).
[b] Model 2: Adjusted for light-duty provision.
[c] Model 3: Adjusted for sex, age, nationality, occupation, industry, work ability (baseline), light-duty provision.

Table 5. Factors associated with earlier return to work (RTW) (within 80 days) in the control and intervention groups.

	Proportion able to RTW within 80 days			
	Conventional treatment (n=81)		Intervention treatment (n=108)	
Variables	**No. (%) or median (IQR)**	***P* value**	**No. (%) or median (IQR)**	***P* value**
Sex, no. (%)				
Male	25 (34.7)	0.28	48 (50.0)	0.76
Female	5 (55.6)		5 (41.7)	
Age at time of injury, no. (%)				
<35 years	16 (34.8)	0.63	24 (55.8)	0.25
≥35 years	14 (40.0)		29 (44.6)	
Race, no. (%)				
Chinese	15 (51.7)	0.07	17 (44.7)	0.72
Malay	4 (57.1)		3 (75.0)	
Indian	5 (26.3)		15 (48.4)	
Other	6 (23.1)		18 (51.4)	
Nationality, no. (%)				
Resident	12 (52.2)	0.08	10 (34.5)	0.07
Non-resident	18 (31.0)		43 (54.4)	
Company size, no. (%)				
SME (≤200 employees)	19 (39.6)	0.51	36 (55.4)	0.11
Large (>200 employees)	10 (32.3)		17 (39.5)	
Industry sector, no. (%)				
Construction, marine, general manufacturing, metalworking	13 (26.5)	0.02	40 (51.3)	0.46
Other	17 (53.1)		13 (43.3)	
Occupation, no. (%)				
White and pink collar	13 (76.5)	<0.01	3 (27.3)	0.20
Blue collar	15 (24.6)		50 (51.6)	
ISS score, no. (%)				
Mild injury (ISS 1–8)	30 (38.5)	0.29	51 (51.5)	0.16
Moderate injury and above (ISS ≥9)	0 (0)		2 (22.2)	
Light duty given, no. (%)				
No	15 (31.9)	0.26	8 (53.3)	0.72
Yes	15 (44.1)		45 (48.4)	
Work Ability score (baseline), median (IQR)				
Able to RTW within 80 days	8 (7–10)	<0.01	7 (5–8)	0.12
Unable to RTW within 80 days	0 (0–7)		5 (4–7)	

Table 5. Factors associated with earlier return to work (RTW) (within 80 days) in the control and intervention groups. (Cont'd)

Variables	Proportion able to RTW within 80 days			
	Conventional treatment (n=81)		Intervention treatment (n=108)	
	No. (%) or median (IQR)	*P* value	No. (%) or median (IQR)	*P* value
Work Ability score (first RTW), median (IQR)				
Able to RTW within 80 days	NC		8 (7–9)	0.08
Unable to RTW within 80 days	NC		7 (6–9)	
Work Ability score (discharge), median (IQR)				
Able to RTW within 80 days	NC		9 (8–10)	0.01
Unable to RTW within 80 days	NC		8 (7–9)	
Duration elapsed from injury to assessment, median (IQR), days				
Able to RTW within 80 days	NC		50 (39–70)	<0.01
Unable to RTW within 80 days	NC		84.5 (60–162)	
Total no. of medical leave days, median (IQR)				
Able to RTW within 80 days	NC		55 (42–67)	<0.01
Unable to RTW within 80 days	NC		116 (90–175)	
Total no. of light-duty days, median (IQR)				
Able to RTW within 80 days	NC		32 (15–57)	0.01
Unable to RTW within 80 days	NC		57 (29–93)	

IQR: interquartile range; NC: data not collected; RTW: return to work; SME: small and medium enterprise

work demands, lack of autonomy, poor physical work environment and high physical workload.[11,20] In this study, participants with lower self-perceived work ability in the intervention group were more likely than those in the conventional treatment group to RTW at 6 months post injury, highlighting the positive impact of the RTW programme in assisting workers with poor to moderate self-reported work ability (WAS 0 to 7)[11] to the barriers in returning to work.

Studies have found self-reported work ability to be related to workers' perception of pain and physical functioning.[21,22] The recovery process is often ladened with patient's negative or uncertain expectations about recovery, requiring support by RTW practitioners to facilitate recuperation.[23] In particular, injured workers' perception of the need to attain full recovery before returning to work needs to be addressed with timely professional support in the programme.[24] Healthcare professionals thus need to consider how workers perceive their work ability to better support them in their RTW.[22] As our study also found lower WAS to be associated with higher dropout rates from the RTW programme, the WAS is potentially useful to screen for workers who are at risk for delayed RTW or dropout to benefit from early RTW assessment and intervention.[11]

Light-duty provision

Light duty, or modified work, refers to temporary or permanent work that is physically or mentally less demanding than normal job duties.[16] Current evidence has found that light duty or modified work helps to facilitate RTW for temporarily or permanently disabled workers, and injured workers who were offered modified work returned to work about twice as often as those who were not.[16] In our study, those who were given light duty in both arms had better RTW outcomes. Notably, more than half of the participants in the control group did not receive light duty upon returning to work. These participants possibly lacked awareness of potential work modification, requested for medical leave instead of light duty or only wanted to RTW when fully recovered.[25] This finding could also be attributed to the reluctance of medical practitioners to issue light duty

Table 6. Factors associated with dropouts from the return to work programme.

Variables	Completed intervention (n=108)	Dropout (n=36)	*P* value
Sex, no. (%)			
Male	96 (73.8)	34 (26.2)	0.52
Female	12 (85.7)	2 (14.3)	
Age at time of injury, no. (%)			
<35 years	43 (70.5)	18 (29.5)	0.28
≥35 years	65 (78.3)	18 (21.7)	
Race, no. (%)			
Chinese	38 (84.4)	7 (15.6)	0.02
Malay	4 (57.1)	3 (42.9)	
Indian	31 (86.1)	5 (13.9)	
Other	35 (62.5)	21 (37.5)	
Nationality, no. (%)			
Resident	29 (90.6)	3 (9.4)	0.02
Non-resident	79 (70.5)	33 (29.5)	
Company size, no. (%)			
SME (≤200 employees)	65 (72.2)	25 (27.8)	
Large company (>200 employees)	43 (79.6)	11 (20.4)	0.32
Occupation, no. (%)			
White and pink collar	11 (78.6)	3 (21.4)	1.00
Blue collar	97 (74.6)	33 (25.4)	
Industry sector, no. (%)			
Construction, marine, general manufacturing, metalworking	78 (73.6)	28 (26.4)	0.51
Other	30 (79.0)	8 (21.1)	
Light duty given, no. (%)			
No	15	NC	
Yes	93	NC	
ISS score, no. (%)			0 16
Mild injury (ISS 1–8)	99 (76.7)	30 (23.3)	
Moderate injury and above (ISS ≥9)	9 (60.0)	6 (40.0)	
Work Ability score (baseline), median (IQR)	8 (6–8)	3 (0–5)	0.00
Days elapsed from injury to assessment, median (IQR)	64 (46–116)	76 (49.5–127.5)	0.43
Total no. of medical leave days, median (IQR)	76.5 (53.5–118)	110 (84.5–155.5)	<0.01
Total no. of light-duty days, median (IQR)	43 (25–78)	36.5 (0–83.5)	0.24

IQR: interquartile range; ISS: Injury Severity Score; NC: data not collected; SME: small and medium enterprise

instead of medical leave.[26] However, the term "light duty" may be non-specific, and MOM has previously given guidance that light duties should take into account the job demands and work environment.[27] Light duties would therefore vary for different vocations, and what it entails for blue-collar workers would be different from that for white-collar workers. In an RTW programme, the RTWC thus plays an important role in working with the employer and employee to recommend appropriate job-specific modified duties. Since all injured workers are entitled to full pay while being on light duties under WICA,[28] our study thus highlights the role of the RTWC in advocating for earlier RTW with modified duties to facilitate more successful RTW outcomes.[29]

Early access to the RTW programme

Our results showed that early access to the RTW programme was vital for earlier RTW. Participants who took more than 80 days to RTW had experienced a delayed RTW assessment of 84.5 days compared with the 50 days for those taking 80 or less days to RTW. The longer duration to RTW assessment could be due to patient factors like lack of awareness on the benefits of early RTW or having perceptions of the need to attain full recovery before returning to work.[25] Healthcare factors limiting early RTW assessment include late referral by the medical team or a lack of awareness of the RTW programme. As medical practitioners are often the first point of contact to initiate patient referrals into the programme, the programme uptake is highly dependent on their knowledge of occupational rehabilitation and available RTW services. Increasing awareness and providing formal training on occupational rehabilitation can be implemented to encourage medical practitioners to introduce the RTW programme in a timely manner.[30]

Migrant workers as a vulnerable group

In this study, migrant workers had a higher likelihood of earlier RTW. It has been found that some foreign workers returned to work prematurely because of fear of repatriation or of losing one's job, especially if employers place undue stress for injured workers to RTW earlier.[31] There is therefore a need for RTWCs to work closely with employers to develop an RTW plan based on the patient's functional capacity and readiness to work, as well as to highlight the importance of injury prevention. The RTWC needs to serve as an advocate for migrant workers to ensure they RTW when medically safe.[29]

In our study, migrant workers also experienced higher dropout rates. About half of the dropouts had their work passes terminated and converted to Special Pass, or chose common law to settle their work injury compensation claims. There is currently limited legislation to protect migrant workers who are terminated from work due to work injuries, hence the need for relevant legislation to safeguard their rights.[32] The RTWC needs to educate injured workers on their rights under the WICA and keep them engaged during the RTW process. Understanding their rights would help to influence their decisions and actions during the RTW process in terms of claims management and law-related procedures.[33] The RTWC also plays an important role in educating the employers on the benefits of retaining their workers, including maintaining productivity and reducing replacement worker costs.[34] For example, the RTWC can raise concerns and mediate issues that employees may have difficulties in broaching with their employers.[29]

Strengths and limitations of the study

A particular strength of this study was the stakeholder engagement adopted throughout the process. The stakeholders were able to provide guidance in programme planning and evaluation. For example, the RTWCs were involved in the identification of programme indicators, clarification of findings and the discussion of results and recommendations. The findings were therefore relevant and contextualised within the RTW programme.

In addition, this study has provided useful data that the programme is effective for a diverse group of participants including migrant workers. The findings can be added to the current literature and benefit future policy planning.

The differential dropout caused by attrition in the intervention group could have resulted in selection bias, loss of statistical power in the data analysis, or both. This is exacerbated with the relatively small sample size, as the small number of observations for certain factors such as severe injuries and non-provision of light duties, affected the statistical power of the stratified and multivariate analyses. The initial screening that the intervention group underwent could be another selection bias, considering the injured workers who were recruited and consented to the study could have differing motivation levels or concerns in returning to work. Subsequent stratified analysis mitigated this bias to some extent by evaluating the effectiveness of the intervention within the same demographic and occupational group. On a related point, our study was not able to explore the motivational factors that workers have in returning to work, even though these factors both influence the participation in the programme as well as the time to first RTW, as was discussed for migrant workers earlier.

Exploring these factors either as a qualitative study or as part of programme evaluation would allow programme implementers to design a programme that is tar geted to the needs of the workers. Another limitation is the lack of economic analyses of the programme, and future cost-benefit analyses are required to study the programme's cost-effectiveness. This study was also limited to patients who were injured at work and may not be generalisable to other patient groups, such as patients recovering from non-work conditions like heart condition or cancer treatment.

CONCLUSION

This study supports the effectiveness of an RTWC model of care implemented in a public hospital in Singapore and provided data that the programme is effective for a diverse group of participants, including migrant workers. The findings provide useful clinical information for occupational health professionals and policymakers to finetune current work processes and enhance the uptake of and outcomes from RTW programmes. Collaborative efforts between the R TWCs and the medical team will increase programme awareness and benefit more injured workers in the long run.

Disclosure

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

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REVIEW ARTICLE

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Consensus statement on Singapore integrated 24-hour activity guide for early childhood

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ABSTRACT

Introduction: Early childhood is a critical period for growth and development. Adopting healthy lifestyle behaviours during this period forms the foundation for future well-being and offers the best protection against non-communicable diseases. Singapore studies have shown that many young children are not achieving the recommendations on physical activity, sedentary behaviour and sleep. A workgroup was set up to develop recommendations for caregivers of infants, toddlers and preschoolers (aged <7 years) on how to integrate beneficial activities within a daily 24-hour period for optimal development and metabolic health.

Method: The Grading of Recommendations Assessment, Development and Evaluation (GRADE-ADOLOPMENT approach was employed for adoption, adaption or de novo development of recommendations. International and national guidelines were used as references, and an update of the literature reviews up to September 2021 was conducted through an electronic search of PubMed, Embase and Cochrane Central Register of Controlled Trials (CENTRAL) databases.

Results: Four consensus statements were developed for each age group: infants, toddlers and preschoolers. The statements focus on achieving good metabolic health through regular physical activity, limiting sedentary behaviour, achieving adequate sleep and positive eating habits. The 13th consensus statement recognises that integration of these activities within a 24-hour period can help obtain the best results.

Conclusion: This set of recommendations guides and encourages caregivers of Singapore infants, toddlers and preschoolers to adopt beneficial lifestyle activities within each 24-hour period.

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Keywords: Eating habits, metabolic health, paediatrics, physical activity, sedentary behaviour, sleep

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CLINICAL IMPACT

What is New

- To our knowledge, this is the first Singapore guide to examine the relationship between all lifestyle activities integrated within a 24-hour period and their health outcomes for children less than 7 years of age.
- The inclusion of eating habits in the integrated guide provides a complete optimal metabolic cycle in young children.

Clinical Implications

- This guide provides updated evidence for healthcare professionals to promote beneficial lifestyle activities for all healthy infants, toddlers and preschoolers (aged <7 years) in the domains of physical activity, sedentary behaviour, and sleep and eating habits, as well as integration of these activities.

INTRODUCTION

Early childhood is a critical period for growth and development, setting the foundation for future and lifelong well-being.[1] Adopting healthy lifestyle behaviours in early childhood can potentially influence and shape behaviours later in life.[2] Frameworks have been developed, such as from the Center on the Developing Child at Harvard University, and are advocated for early childhood health promotion and disease prevention;[3] these form key strategies in reducing future non-communicable diseases (NCDs). The World Health Organization (WHO) global action plan for the prevention and control of NCDs (2013–2020) highlighted that exposure to risk factors of NCDs often starts early in life, and interventions in early childhood often offer the best protection against these diseases.[4]

The current Singapore guidelines on physical activity for children less than 7 years were updated in 2013.[5] This group of children includes infants, toddlers and preschoolers who have not started mainstream school, which commences as the child turns 7 years old in Singapore. Over recent years, there is emergent evidence surrounding physical activity, sedentary behaviour and sleep for this group of children, and how these concepts relate to one another within a 24-hour period, for better health outcomes.[6-10] This workgroup also integrated dietary choices and eating behaviours closely linked to movement behaviours in terms of, but is not limited to, optimising energy balance, which is important for obesity prevention.[11] Encapsulating all these elements, we developed the Singapore Integrated 24-hour Activity Guidelines for Early Childhood (0 to <7 years).

Supporting evidence for healthy lifestyle behaviours in early childhood

We present the updated evidence from local and international studies for health outcomes of physical activity, sedentary behaviour, sleep, and diet/eating habits in children under 7 years of age.

Physical activity

Physical activity provides many health benefits including improved motor and cognitive development, and cardiometabolic, musculoskeletal and psychosocial health.[12] Children in this age group should be encouraged to regularly participate in a variety of activities regularly; those who engage in more physical activity overall and/or at a higher intensity (i.e. moderate to vigorous or vigorous intensity) consistently enjoyed favourable health benefits.[13,14] Tummy time (i.e. prone position) appears to be positively associated with motor development for infants.[15] Outdoor play (under adult supervision) is reported to confer health benefits on preschoolers, such as reducing the risk of incident myopia.[16,17] A cross-sectional study of 78 preschoolers in Singapore, using wrist-worn accelerometers, showed that the children spent a median of 7.8 hours/day in sedentary behaviour and 0.5 hours/day in moderate- to vigorous-intensity physical activity. The same study also revealed that preschool teachers were not familiar with physical activity guidelines and that parents reported very little outdoor playtime with children after preschool.[18]

Sedentary behaviour

Excessive sedentary behaviour and screen time can have detrimental health effects on children in early childhood.[19] Prolonged sedentary screen time is adversely associated with adiposity, poor motor and cognitive development, and impaired psychosocial health.[20,21] Indeed, prolonged sitting, reclining or lying are also unfavourably associated with adiposity or motor development.[22] Studies of screen time and sedentary behaviour in the Growing Up in Singapore Towards healthy Outcomes (GUSTO) cohort, a longitudinal cohort study investigating the influence of early development on body composition and metabolic health,[23] showed that the average screen time for infants (12 months) and toddlers (2 years) was 2.0 and 2.4

hours/day, respectively.[24,25] Screen time in infants was negatively associated with later cognition (compos ite intelligence quotient [IQ] and verbal IQ), whereas for toddlers, higher screen time was associated with less physical activity and greater sedentary behaviour.[24,26]

Sleep

Sleep is essential for growth and good health in early childhood.[27] As a newborn grows, he/she regulates his/her sleep through the establishment of a circadian cycle with less daytime naps and more night-time sleep.[28] Children of different ages require dif ferent optimal sleep durations.[29] However, shorter sleep in children could be the result of increased screen time around bedtime and collectively may be associated with higher levels of adiposity, poor growth and emotional dysregulation.[30] The sleep duration of children less than 2 years of age in the GUSTO cohort was significantly associated with body length; shorter sleep duration was also associated with higher body mass index and shorter body length for those at 3 months of age.[31]

Diet and eating habits

A healthy diet provides optimal nutrition for a child's physical and cognitive development.[32] Nutritional needs and eating patterns change with each progressive stage of childhood.[33] Setting good eating habits and shaping positive eating behaviours in early childhood help form the foundation for a healthy diet, which can reduce the future risks of overweight or obesity, as well as protect against NCDs.[34] Infants in the GUST O cohort who were fed breast milk showed better gross motor skills at 2 years and better cognitive performance at both 2 and 4.5 years of age, when compared to formula-fed infants.[35] Higher intake of suga r-sweetened beverages in young children (18 months to 5 years) was associated with higher levels of adipos ity and greater ris k of overweight or obesity.[36]

Integration of activities

The GUSTO study also reviewed the adherence to 24-hour movement guidelines (Canada/Australia) in 864 children at 5.5 years old, and results showed that few children (5.5%) met all of the movement guidelines.[37] A more recent study examined the proportion of preschoolers meeting the WHO guidelines on physical activity, sedentary behaviour and sleep, and the effect on their quality of life. More than 2,000 parents of preschoolers were surveyed and only 9.6% met all of the recommendations, whereas 12.6% did not meet any of the recommendations. This study also showed that the health-related quality of life (using the Pediatric Quality of Life Inventory) increased as the preschoolers achieved more recommendations.[38] The nationally representative study in terms of ethnicity is to date the largest prevalence study in Singapore on sl eep, physical activity and sedentary behaviour among preschoolers.

Aim of consensus statement

This guidance provides a holistic approach for developing and maintaining good health among children in early childhood (i.e. <7 years) in Singapore, by integrating physical activity, sedentary behaviour, sleep, and dietary and eating habits advice. It is equally important to understand that these activities are closely related in influencing health outcomes and time-use behaviour, and to organise them within a daily 24-hour period. Incorporating healthy dietary and eating habits with movement behaviours encourage children to practise and adopt these recommended habits and behaviours at a young age, thereby conferring good health.

These recommendations are for all healthy infants (0 to <1 year), toddlers (1 to <3 years) and preschoolers (3 to <7 years), regardless of sex, cultural background or socioeconomic status. Children with special needs or medical conditions should consult a qualified medical professional for additional guidance.

METHOD

The consensus workgroup consisted of physicians (neonatologists, paediatricians—including developmental paediatricians—sports physicians and family physicians), allied health professionals (dietitians, exercise physiologists), academics, educators and res earchers from multiple institutions and organisations.

The workgroup assessed the evidence reviews conducted for the WHO Guidelines on Physical Activity, Sedentary Behaviour and Sleep for children under 5 years of age, and the 24-Hour Movement Guidelines for children less than 5 years of age from Canada, Australia and South Africa.[6-9] Relevant evidence for children aged 5 to less than 7 years from WHO Guidelines on Physical Activity and Sedentary Behaviour and the 24-Hour Movement Guidelines for Children and Youth/Young People from Canada and Australia were also reviewed.[39-41] The literature was updated to September 2021 through an electronic search of PubMed, Embase and Cochrane Central Register of Controlled Trials (CENTRAL) databases, and the keywords used included "infant", "toddler", "preschool", "physical activity", "sedentary behaviour", "sleep", "eating habits" and "diet". The update included systematic reviews, randomised control trials and cohort studies. Only results in English language were

considered. The health outcomes included cardiometabolic health, physical fitness, bone and skeletal health, adiposity, motor and cognitive development, behaviour development and psychosocial health.

The workgroup used the Grading of Recommendations Assessment, Development and Evaluation (GRADE)-ADOLOPMENT approach,[42] which builds on the GRADE Evidence to Decision (EtD) framework,[43] to provide a structured and transparent methodology for healthcare recommendations. It evaluates the strength of recommendations from associated guidelines and the quality of evidence supporting the recommendations. Regular meetings were conducted for workgroup members to present and discuss each recommendation, which was then revised based on the members' comments. A consensus was achieved when all members agreed to the revised recommendation for the Singapore paediatric population.

RESULTS

These recommendations are intended for healthcare professionals providing holistic care to infants (statements A), toddlers (statements B) and preschoolers (statements C), including education and the promotion of healthy activities that form the foundation for lifelong well-being. The full EtD framework is included as Supplementary Material.

Physical activity

(A) Infants should be physically active several times a day, where more is better. It should be in a variety of forms and be conducted within a safe and supervised environment.

(A) Activities should include non-screen-based interactive floor-based play and tummy time, for those who are not yet mobile.

(A) Tummy time should be commenced soon after birth, building up towards at least 30 minutes spread throughout the day.

(B, C) Toddlers and preschool children should accumulate 180 minutes of physical activity throughout the day within a safe environment.

(B, C) Daily outdoor play is highly encouraged, as is the involvement of caregivers participating in all forms of physical play with both groups and more activity is considered better.

(C) For preschoolers, at least 60 minutes should be of moderate to vigorous intensity and older preschoolers (5–6 years of age) should be exposed to a variety of age-appropriate activities that also promote muscle- and bone-strengthening, several times a week.

Supporting information

Physical activity in infants is associated with improved measures of adiposity, motor skill development, psychosocial, and cardiometabolic health indicators (e.g. blood pressure, lipid level and insulin resistance).[12] For infants not yet mobile, tummy time—defined as awake prone positioning on a firm surface—is positively associated with multiple developmental aspects.[6] Tummy time has positive effects on global development,[44] particularly gross motor development,[45] body mass index and prevention of brachycephaly.[46,47] Infants can start on tummy time as soon as they are brought home and build up from a few minutes towards a minimum of 30 minutes of prone activities spread throughout the day. During tummy time, the infant can be encouraged to play and should be supervised by a responsible adult caregiver.

Toddlers should engage in a spread of physical activities of at all intensities.[12] This should include activities that encourage exploration and involve movement skills such as walking, running, crawling, climbing, balancing, bending, dancing and playing with balls. The more active play the toddlers achieve, the better. Toddlers who engaged in at least an hour of moving freely each day had significantly stronger object and locomotor skills.[48] Caregivers should participate actively with toddlers during both indoor and outdoor play, as such positive interactions are associated with better developmental skills, reduced risk for obesity, and accumulate physical activity.[49,50]

Structured and unstructured play is also important for a toddler's global development and these activities can take place in all environments.[51] In childcare centres, more than half of a toddler's indoor moderate to vigorous physical activities occur in modified open-plan spaces, which are indoor areas with modifications for segregation between activities (e.g. noisy and quiet activities, or messy and clean activities) to reduce distractions, and during class transitions. Enhancing childcare structure quality and inclusion of modified open-plan spaces can promote physical activity and reduce sedentary time for toddlers.[52]

Physical activity among preschoolers is associated with multiple health benefits, especially when it is moderate to vigorous intensity.[12,53,54] Evidence supports positive improvements in motor and cognitive development,[53] physical fitness, psychosocial well-being, cardiometabolic and bone health and lower adiposity.[7,12] In addition, a strong foundation in childhood movement competence may be associated with improved participation in physical activities later in life. Therefore, preschoolers should be encouraged to participate in a

variety of activities encompassing fundamental movement skills and age-appropriate/modified sports in a safe environment.[55,56] A Singapore study found that nearly 70% of the lower primary students failed to demonstrate age-appropriate movement proficiency, indicating a critical need for physical activity interventions at the preschool age.[57] Older preschoolers, aged 5–6 years, can also improve muscle and bone strength through weight-bearing (e.g. climbing), resistance (using their own bodyweights, e.g. knee push-ups) or light-impact exercises (e.g. running and hopping). These activities may be in the form of informal play at playgrounds or as part of organised team sports such as football.

High prevalence of myopia in Singapore is a serious health concern; daily outdoor play for at least 2 hours provides respite from excessive "near-work" (e.g. reading and screen time) and helps to reduce early onset myopia.[16,17] Moreover, outdoor play allows more playtime including moderate to vigorous physical activities and confers many other learning opportunities for children, caregivers and educators,[58] while also providing parents with time to create and strengthen bonds with their children.[59]

Sedentary behaviour

(A, B, C) A daily routine for activities, sleep and meals may be useful in reducing the amount of sedentary behaviour.

(A, B) Avoid restraining infants and toddlers for more than 1 hour at a time.

(A, B) When infants or toddlers are seated, reclined or lying down, caregivers are encouraged to engage them in singing, reading, storytelling and imaginative play.

(A, B) Screen time, regardless of the type of device, is not recommended for infants and toddlers younger than 2 years of age.

(B, C) For toddlers 2 years and above and preschoolers, screen time should be limited to less than 1 hour per day.

(C) For preschool children, limit the total daily amount of sedentary behaviour, such as sitting, reclining or lying down, and take breaks during extended periods of time spent being sedentary.

Supporting information

Infants and toddlers should not be restrained (e.g. strollers and high chairs) for more than 1 hour at a time as this is associated with high levels of adiposity and less favourable motor development.[6,19] Sedentary behaviour among toddlers also includes the use of any screen device, reading, drawing, eating, travelling in a vehicle, while seating, reclining, or lying down.[60] Screen time in both groups is associated with unfavourable measures of adiposity, decreased scores on measures of psychosocial health, cognitive development, social skills, sleep duration and quality, and gross motor development.[19] Indeed, any form of screen time, including that in the background, is not recommended in infants. International guidelines consistently recommend that toddlers should not be restrained to their seats for more than 1 hour at a time, and those of less than 2 years of age should have no exposure to screens.[6-8] When infants or toddlers are sedentary, they still require supervision. Engaging in "serve and return" activities such as reading, singing, storytelling or imaginative play with a caregiver is encouraged as this has greater potential for cognitive and social development.[19,61]

For preschoolers, while sedentary behaviour—for instance during educational periods—cannot be completely eliminated, regular movement breaks, such as in the form of active play are essential to minimise adverse health effects.[62] It is also important to limit recreational screen-based sedentary behaviours such as television viewing and handheld device use. The WHO evidence-based guidelines acknowledged that among children aged 3–6 years, these appliances bore detrimental effects on their fitness, adiposity and behaviour or sleep, regardless of the type of screen device.[6,63] Indeed, in a prospective cohort studies among young children in Singapore, screen viewing was found to have an impact on movement behaviours (e.g. moderate- to vigorous-intensity physical activity and sleep) and abdominal adiposity (quantified using magnetic resonance imaging) later in life.[26,64]

Sleep

(A, B, C) For all ages, a regular routine, consistent bedtime, conducive sleep environment and, for toddlers and preschoolers, avoiding screen time before night-time sleep, will help obtain quality of sleep.

(A) Infants should achieve 14–17 hours (for 0–3 months) and 12–15 hours (for 4–11 months) of sleep daily and include regular naps to promote optimal health.

(A) Infants are recommended to sleep on their back in their own cot, in the same room as their caregivers to ensure sleep safety.

(B) Toddlers should achieve 11–14 hours of sleep daily, with regular sleep and wake-up times.

(C) Preschoolers should achieve 10–13 hours (for 3–4 years) or 9–13 hours (for 5–6 years) sleep daily. Older preschoolers may not need to nap if sufficient sleep has been obtained at night.

Supporting information

Infants spend most of their time sleeping, which can be up to 80% in newborns.[65] Good sleep improves cognitive,[66] physical[67] and social outcomes, [68] as well as reduces obesity and the risk of sudden infant death syndrome.[69] Adequate sleep improves family well-being and is an important predictor of maternal health.[70] Good sleep safety practices include infants sleeping supine in their own cot and in the same room as the caregivers.[71]

Recent literature supports that short sleep duration during toddlerhood is associated with greater risk of depressive symptoms and poorer temperament in later childhood.[72] Specifically, toddlers sleeping 10 hours or less per night had 1.5 times the odds of reporting high symptom scores (i.e. above 90th percentile) on the short-version Mood and Feelings Questionnaire at 8 years of age, as compared to toddlers sleeping 13–14 hours per night.[72] The symptoms reported included feelings of unhappiness, restlessness, frequent crying episodes and difficulty in concentration. Short sleep duration is also linked to obesogenic eating behaviours.[73,74]

Similarly, for preschoolers, achieving the number of recommended hours of sleep is associated with better health outcomes in terms of physical, psychological and cognitive w ell-being. Shorter sleep duration is associated with higher adiposity levels,[75] poorer emotional regulation,[76] more screen time, [77,78] higher risk of injuries, [79] poorer cognitive development, [80,81] increased hyperactivity-inattention,[82] reduced phys ical activity,[78,83] and poorer quality of life. A study by Sparano et al. on the relationship of sleep duration and blood pressure in young children (mean age of 6.1 years old) showed that children with 9 hours or less sleep had a higher prevalence of hypertens ion when compared to children with more than 11 hours of sleep (18.5% versus 11.6%).[84] These children were followed up prospectively for 2 years and similarly, the incidence of hypertension was highest in the former group (12.4%) and lowest in the latter group (6.0%).[84]

Although there are cultural differences in sleep duration and practices,[85] setting bedtime routines and providing a conducive sleep environment can improve sleep duration and quality.[86] A conducive sleep environment is one that is dark, quiet and of a comfortable temperature. Adaptive bedtime activities, such as storytelling or cuddling help toddlers sleep longer and have fewer parents' perceived sleep problems.[86] Consistency of this routine across weekdays and weekends reduced disruption to sleep patterns. For toddlers above 2 years and preschoolers, screen time should be avoided 1 hour before night-time sleep.[87] Screens emit blue light that suppresses endogenous melatonin production, in turn resulting in shorter sleep duration, later bedtimes and longer time to fall asleep.[88]

Diet

(A) Breastfeeding is recommended for infants. From 6 months of age, a variety of developmentally and culturally appropriate solid foods of various textures and flavours should be introduced with no added salt and sugar.

(A) A daily routine of meals consisting of appropriate portions spaced every 2–3 hours is recommended to avoid overfeeding.

(B, C) Food should not be used to soothe toddlers or be provided as a reward, and screen time should be avoided during meal times for toddlers and preschoolers.

(B) The variety of foods offered to toddlers should be progressively increased and they should wean off milk as the main source of nutrition. Healthy family meals, whole milk and water should be offered, while establishing a structured routine for meal and snack times.

(C) For preschoolers, healthy eating habits should be developed as a family, with caregivers as role models. Sugar-sweetened beverage consumption should be limited, and develop structured meal and snack times in appropriate portions to support growth and development.

(C) Preschoolers should be helped to recognise hunger and satiety cues.

Supporting information

It is recommended that infants are exclusively breastfed for at least the first 6 months of life; this provides adequate nutritional requirements and maternal antibodies to support their health, growth and development.[89] Nevertheless, medications or vitamin and mineral supplementation prescribed by the physician should continue to be provided to the breastfed infant. Mothers should adhere to food safet y and hygiene recommendations, if breast milk is expressed and stored. Should human milk be unavailable, infants should be provided with formula milk. The main types of formula milk are cow' s milk-based formulas (most common), soy formulas and specialised formulas (usually for infants with specific medical conditions). These types of formula milk usually contain 60–70kcal of energy per

100mL and are fortified with iron.[90] For optimal bone development, vitamin D supplementation of 400IU per day is recommended for fully and partially breastfed infants due to its low bioavailability in breast milk.[89] With increasing energy and nutrient requirements, infants should be started on complementary foods from 6 months of life, depending on their developmental readiness. Start with small amounts of solid foods and progress to recommended portions (e.g. 1–2 servings of rice or bread per day) as specified in Singapore dietary guides.[91]

Iron-rich foods should be provided to infants consuming a non-iron fortified formula, due to the risk of developing iron deficiency anaemia. These include iron-fortified cereals, pureed meat and poultry, plain tofu or legumes, with textures suited to the infant's stage of development. Salt should not be added to foods for infants as their kidneys are immature and unable to excrete excess salt, thus presenting a safety concern. Food and drink containing added sugars should be avoided, thereby reducing the risk of dental caries and a learned preference for sugar. Overconsumption of sugar-laden food has been associated with an increased risk of becoming overweight or obese.[36,92] There is no evidence that delaying the introduction of potentially allergenic food prevents food allergies.[89] Therefore, potentially allergenic foods such as dairy products, egg, wheat, crustacean shellfish, fish, soy, tree nuts and peanuts should be introduced, one at a time, as part of complementary feeding from 6 months of age once the infant is able to tolerate solid food.[93]

Guidance on responsive feeding should be provided to caregivers, so as to promote appropriate weight gain among infants.[94] Caregivers should strive to recognise hunger and satiety cues that will support responsive consumption by timely initiation and termination of the feeding process.[94] Evidence reveals that non-responsive caregiver feeding practices, such as the use of extremely controlling, restrictive, rewarding or pressure feeding, is associated with a higher risk of childhood obesity.[95]

Toddlers are reliant on caregivers to establish their feeding habits.[89,96,97] Fresh, minimally processed foods should be prepared with little or no added sugar and salt, with continual exposure and/or provision of foods across all major food groups that are in unison with healthy family eating habits. There is no clear evidence that formula milk should be continued beyond 12 months of age,[89] and pasteurised full cream milk, or fortified unsweetened soy milk, can be incorporated in the toddler's diet from 12 months of age to meet protein, calcium and vitamin D requirements, particularly when accompanied by adequate solid foods.[89,97] Sugar-sweetened beverages (e.g. juice drinks, sports drinks and regular soft drinks) and caffeinated beverages (e.g. tea, coffee and cola drinks) should not be given before 2 years of age, and should be avoided as much as possible thereafter.[89] Plain water is recommended.

A structured routine for meal and snack times for toddlers is an important component of effective responsive feeding practices, where caregivers also recognise and react to hunger and fullness cues of the toddler.[96] Moderate evidence from randomised controlled trials suggests that providing responsive feeding guidance to teach mothers to recognise and respond appropriately to children's hunger and satiety cues can lead to "normal" weight gain and/or "normal" weight status in children aged 2 years or younger, compared with children whose mothers did not receive responsive feeding guidance.[94] Picky eating is also a natural occurrence in the feeding process, and toddlers should not be pressured to consume new foods.[89,97] Instead, they should be provided with regular and frequent exposure to non-preferred foods to increase familiarity and promote acceptance. Using food to soothe toddlers is associated with poor dietary quality and increased risk of obesity in early childhood,[97] and is therefore discouraged.

Dietary habits shaped at a young age persist later into life. Positive caregiver role-modelling, regular household eating routines, coordinated family meals and regulation of appetite influence the overall quality of diets among preschoolers.[89,98] Limiting the consumption of sugar-sweetened foods and beverages (including those naturally present in honey, syrups, fruit juices and fruit juice concentrates) to no more than 10% of total energy intake lowers the risk of overweight or obesity and dental caries.[36,89,92] Consuming a nutritious breakfast with a good combination of carbohydrates, fibre and protein is strongly encouraged, as it has been associated with better diet quality and healthy body weight.[99] Structure-based or limit-setting strategies, such as serving appropriate portions, disallowing screen time during meals (to avoid overeating and learning unhealthy food habits from advertisements and programmes), and a balance of caregiver guidance versus children's autonomy, helps children to self-regulate their eating behaviours. Excessive restraint of a preschooler's food intake may unintentionally teach him or her to use food to manage negative emotions.[98]

Integration

(A, B, C) Aim to achieve most or all recommendations on physical activity, sedentary behaviour, sleep and diet for the best results.

Supporting information

The recommendations for physical activity , sedentary behaviour, sleep and eating habits are closely related in terms of health benefits and making up the 24 hours of a child's day. The greatest health benefits can be achieved by meeting all the recommendations : more physical activity, less sedentary time, longer sleep duration, healthy eating habits and pos itive dietary choices.[10,38,100] However, in situations where all cannot be optimised, different combinations can be considered, such as more physical activity with longer sleep duration, or less sedentary time with longer sleep duration, which can improve cognitive development and reduce risks of adiposity.[6,10] Replacing sedentary time with physical activity is associated favourably with fitness and motor development.[6,10] Healthy and sensible dietary habits promote growth, development and maintenance of a healthy weight.[32,34]

CONCLUSION

Recent evidence has shifted the international trend towards integrating physical activity , sedentary behaviour and sleep within a 24-hour period for better health outcomes in young children (i.e. infants, toddlers and preschoolers). The inclusion of di et and eating habits complements these recommendations in supporting growth and development, as well as obesity prevention. Establishing these healthy behaviours in early childhood offers them the best protection against future NCDs. However, studies have demonstrated that a significant proportion of young children in Singapore do not adopt these recommendations and show poorer health outcomes. Therefore, it is timely to introduce and promote these guidelines to young children and their caregivers to give them the best start in their lives.

As these young children may be cared for by various caregivers (e.g. parents, grandparents and teachers) and transit through different environments as they grow (e.g. home, infant care, nursery and kinder garten), there is a role for these recommendations to be adopted as daily habits in family units and also as policies in childcare and preschool centres. In conclusion, infants, toddlers, preschoolers and their caregivers are recommended to adopt all domains of these guidelines to achieve the best health outcomes. As a first step, families and schools should start by identifying a domain in their child's daily life that they can feasibly embed or modify , thereby aiming to progressively integrate all the aforementioned recommendations to confer protection against NCDs from early childhood.

Annexes

1. *Consensus Statement on Singapore Integrated 24-Hour Activity Guide for Early Childhood: Consensus Statements*
2. *Practical Reference for Activities for Early Childhood*
3. *Consensus Statement on Singapore Integrated 2 4-Hour Activity Guide for Early Childhood: Summary Guide*

About the workgroup

This document was developed by the Singapore Integrated 24-Hour Activity Guide for Early Childhood Study Workgroup, which comprised key members from the Singapore community, including members from the College of Paediatrics and Child Health of the Academy of Medicine, Singapore; Singapore Integrated Platform for Research in Advancing Metabolic Health Outcomes in Women and Children (IPRAMHO), led by KK Women's and Children's Hospital (KKH), in partnership with SingHealth Polyclinics (SHP) and the National Healthcare Group Polyclinics (NHGP); National University Hospital and Yong Loo Lin School of Medicine, National University of Singapore. The initiative is supported by the research group of IPRAMHO, a National Medical Research Council-funded joint collaborative pot centre grant of KKH, SHP and NHGP. This multidisciplinary group is initiated by Prof Lee Yung Seng, Assoc Prof Ng Kee Chong and Prof Tan Kok Hian, and chaired by Dr Benny Loo Kai Guo.

Disclaimer

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for consideration by practitioners for incorporation into their practice. It is acknowledged that management may vary and must always be responsive to the need of individual patients, resources and limitations unique to the institution or type of practice.

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Minimal monitoring is a safe but underutilised strategy for hepatitis C virus management in Singapore

Dear Editor,

Chronic hepatitis C virus (HCV) infection is estimated to affect 57 million people globally .[1] Despite the availability of safe and ef fective pan-genotypic direct-acting antivirals,[2-5] many countries have yet to achieve the WHO goal of HCV elimination by 2030. [1] To facilitate HCV elimination, current guidelines recommend using a minimal monitoring (MM) strategy with pan-genotypic direct-acting antiviral (DAA) to streamline HCV treatment.[6] By minimising the need for extensive laboratory testing and clinic visits, the MM strategy may improve treatment adoption, improve treatment compliance and reduce healthcare costs. [7-9] However, the real-world safety, efficacy and uptake of the MM strategy remain limited.

Here, we examined the practical implementation and evaluated the safety and efficacy of the MM strategy compared to the current standard of care (SOC) in Singapore.

Using a prospectively maintained HCV treatment registry, we studied consecutively treated HCV patients with pan-genotypic DAA (either sofosbuvir/velpatasvir or glecaprevir/pibrentasvir), from J anuary 2019 to November 2021 in the Department of Gastroenterology and Hepatology, Changi General Hospital, Singapore. We assessed the eligibility for MM strategy based on the 2019 American Association for t he Study of Liver Diseases–Infectious Diseases Society of America (AASLD–IDSA) guideline, specifically treatment-naive HCV patients without prior liver decompensating events. We considered patients ineligible for MM when they had hepatitis B virus (HBV) or human immunodeficiency virus (HIV) co-infection, known or suspected hepatocellular carcinoma (HCC), prior liver transplantation, or end-stage renal disease.

Typically, all patients have baseli ne laboratory investigations and a recent ultrasound hepatobiliary system performed within 3 months of the first visit to exclude liver cancer and decompensated cirrhosis. Fibrosis staging was performed using a combination of FIB-4 score and vibration-controlled transient elastography. Amid the COVID-19 pandemic, some physicians adopted the MM st rategy due to resource constraints in our institution. For patients deemed suitable for MM, DAA will be initiated at the first visit and reviewed during a check for sustained virological response 12 weeks after treatment completion (SVR12). Patients in the MM group were instructed to self-monitor for potential drug-related adverse events. MM-monitored patients had only 2 visits from DAA initiation to SVR12 at our institution. Patients with additional outpatient visits between DAA initiation and SVR12 were classified as SOC-monitored. There is no protocol for teleconsultation or review by nurses between DAA initiation and SVR12.

The study aimed to investigate 2 outcomes: (1) serious adverse events (SAE), which were defined as adverse events resulting in early cessation of HCV treatment, hospital admissions, permanent disability or dea th, and (2) SVR12.

The study verified treatment compliance using both medical records and pharmacy databases. Statistical analysis was performed using SPSS version 23.0 (IBM Corp, Armonk, NY, US). The study adhered to the Declaration of Helsinki, and the institutional review board granted a waiver of consent.

The final analysis included a total of 608 HCV patients, with the majority being male (90.8%) and treatment-naive (97.7%). Among them, 60.2% had genotype 3 infections, 18.7% had cirrhosis at baseline, and 2% had co-infection with either HBV/HIV infection. Among the patients, 7.9% (n=48) were not eligible for MM due to being either treatment-experienced (2.3%), having decompensated cirrhosis (2.1%), HCC (1.3%), HBV/HIV co-infection (2.0%), or end-stage renal disease (0.3%).

While 92.1% (n=560) were eligible for MM, only 12.5% (n=70) were monitored with the MM strategy (Table 1). Among patients eligible for MM, the baseline demographics were similar between MM and SOC groups, except that the MM group was older (54 versus 50 years, P=0.0006). The overall SVR12 was 92.8%, which was similar between MM and SOC monitoring (92.9% vs 92.7%, P=0.952). Compared to those who underwent SOC monitoring, patients monitored with MM had similar treatment completion rates (100% vs 96%, P=0.093) and treatment compliance rates (95.7% vs 95.3%, P=0.882). Moreover, the MM group had significantly fewer clinic visits than the SOC group—the median number (interquartile range [IQR]) of clinic visits between MM and SOC was (MM: 2 [IQR: 2-2] vs 3 [IQR: 3-3], Mann-Whitney U test;

Table 1. Baseline characteristics of HCV patients eligible for MM (n=560).

	Minimal monitoring	Standard of care	
	(n=70)	(n=490)	*P* value
Baseline characteristics			
Age, mean (SD), years	53.5 (9.7)	50.0 (10.0)	0.0062
Male, no. (%)	65 (92.9)	441 (90.0)	0.442
Race, no. (%)			0.551
Chinese	4 (5.7)	84 (17.1)	
Malay	49 (70.0)	335 (68.4)	
Indian	12 (17.1)	58 (11.8)	
Others	5 (7.1)	13 (2.7)	
Smoker	19 (27.1)	115 (23.5)	0.510
Incarceration	62 (88.6)	419 (85.5)	0.486
HCV genotype, no. (%)			0.402
1	16 (22.9)	104 (21.2)	
2	0 (0.0)	4 (0.8)	
3	38 (54.3)	301 (61.4)	
4	1 (1.4)	0 (0.0)	
5	0 (0.0)	0 (0.0)	
6	0 (0.0)	1 (0.2)	
Not done	15 (21.4)	80 (16.3)	
Fibrosis stage, no. (%)			0.823
0	7 (10.0)	56 (11.4)	
1	13 (18.6)	97 (19.8)	
2	4 (5.7)	48 (9.8)	
3	5 (7.1)	33 (6.7)	
4	7 (10.0)	61 (12.4)	
Fibroscan not done	34 (48.6)	195 (39.8)	
Diabetes mellitus, no. (%)	5 (7.1)	37 (7.6)	0.882
Hypertension, no. (%)	17 (24.3)	107 (21.8)	0.638
Hyperlipidaemia, no. (%)	9 (12.9)	41 (8.4)	0.218
Cardiovascular disease, no. (%)	2 (2.9)	28 (5.7)	0.331
Laboratory results			
Creatinine, mean (SD), µmol/L	85.2 (19.5)	83.8 (18.1)	0.549
Albumin, mean (SD), g/L	43.7 (3.2)	44.6 (9.4)	0.428
Bilirubin, mean (SD), µmol/L	11.6 (6.3)	12.9 (10.6)	0.317
ALT, mean (SD), U/L	66.2 (44.3)	59.7 (57.6)	0.365
Haemoglobin, mean (SD), g/dL	14.7 (1.7)	15.1 (7.0)	0.634
Platelet count, mean (SD), x 103/µL	218.3 (60.1)	221.0 (68.2)	0.754
INR, mean (SD), sec	1.0 (0.1)	1.0 (0.1)	1
Baseline viral load, mean (SD), log IU/mL	6.0 (0.7)	6.0 (0.9)	1

ALT: alanine transaminase; HCV: hepatitis C virus; INR: international normalised ratio ; MM: minimal monitoring; SD: standard deviation; SOC: standard of care

P<0.001), averting a total of 556 clinic visits in this cohort. Only 1 SAE (angioedema) occurred in the SOC arm, which resolved after cessation of DAA.

Our study is the first in Singapore to demonstrate the safety and efficacy of MM among HCV patients, including those with cirrhosis and multiple comorbidities. A previous trial by Dore et al.[7] using simplified monitoring had excluded patients with cirrhosis and those for whom treatment compliance was a concern.[7] However, our study confirmed MM's efficacy and safety in real-world scenarios with comparable SVR12 results, and SAE was uncommon with pan-genotypic DAA.

Although 92.1% of this group met the criteria for the MM strategy, only 12% utilised it, highlighting the potential for improving HCV care. The low uptake of the MM strategy was related to the lack of awareness of this strategy and safety concerns over DAA among physicians with less experience in DAA. Adoption of the MM strategy may reduce healthcare resource utilisation without compromising treatment outcomes. MM can be advantageous in low and middle-income countries (where 80% of chronic HCV patients reside) because pre-treatment genotype testing and on-treatment monitoring may not be feasible in resource-limited settings.[7,8] Encouraging the use of MM can speed up HCV treatment expansion and facilitate treatment upscale for HCV elimination in Singapore. It is important to disseminate the real-world safety of the MM strategy and incorporate the MM strategy into

institutional HCV treatment protocol to provide confidence to physicians with less experience in DAA to adopt the MM strategy.

We acknowledge there were limitations in this study. Firstly, the introduction of the revised workflow to accommodate incarcerated patients for MM took place only in May 2020. Due to institutional safety requirements, incarcerated patients undergoing MM strategy were reviewed once by the prison medical team between DAA initiation and SVR12, which may affect the generalisability of our findings. Of note, none of the incarcerated patients undergoing MM was referred back to our institution during HCV treatment as a result of treatment-related adverse events. While there may be fewer opportunities to educate patients on treatment compliance and harm reduction, we found similar treatment compliance between MM and SOC groups.

In summary, MM with pan-genotypic DAA is an underutilised, efficacious and safe strategy in treatment-naive HCV patients without prior decompensation. Physicians should consider the adoption of MM in the management of HCV, particularly in a resource-limited setting, to save healthcare resources and improve HCV treatment and elimination in Singapore.

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Preferences for oral anticoagulant medications for managing atrial fibrillation

Dear Editor,

Stroke prevention in patients with atrial fibrillation (AF) using anticoagulants involves weighing the benefits of reduced ischemic stroke[1,2] against the elevated risks of serious bleeding events.[3] Warfarin and direct oral anticoagulants (DOACs) are the available oral anticoagulants for this indication. We developed a discrete choice experiment (DCE) survey[4] to assess the preferences of older Singaporeans for oral anticoagulants for secondary stroke prevention in a hypothetical scenario of prior stroke and history of AF.

Participants aged 50 and above who might or might not be diagnosed with AF were recruited from outpatient neurology clinics at Singapore General Hospital after the ethics approval was obtained (CIRB: 2021/2454). Once informed consent was obtained, interviewers administered the web-enabled survey from January to May 2022. Participants were presented with 9 choice tasks and were asked to choose 1 option from 2 treatments and a "No treatment" option in each choice task. Each treatment was defined by 6 attributes: risk of stroke, risk of bleeding, availability of antidote in case of bleeding, frequency of blood monitoring, negative interactions with food/other drugs and monthly out-of-pocket cost. The attribute levels were selected based on values indicated in clinical trials[1,2,5,6] and widely-used clinical guidelines.[7] Participants were asked to assume that: (1) they were diagnosed with AF, and (2) the risk assessment by their doctor(s) indicated that they had a 7% risk of stroke and a 1% risk of major bleeding if they did not use oral anticoagulants for AF. An example choice task is shown in Supplementary Fig. S1.

The DCE required a minimum sample size of 125 based on the formula by Johnson and Orme.[8] To analyse the data, we used a mixed logit model to allow for preference heterogeneity. Using the preference weights from the model, we calculated the relative attribute importance for each attribute out of 100%[9] and calculated the probability of choosing different medications. We predicted the choice between warfarin and DOACs based on the different levels of cost and frequency of blood monitoring. NLOGIT 6.0 (Econometric Software, Plainview, NY, US) and Stata version 15.1 (StataCorp, College Station, Texas, US) software were used for data analyses.

We recruited 131 participants. The mean (standard deviation) age was 64.0 (9.0) years old. Most of the sample were male (64%), married (73%) and Chinese (67%). Seventy-one percent of participants reported having pre-existing or chronic conditions, such as diabetes or cancer; 31% reported being diagnosed with stroke; and 33% reported a family history of stroke (Supplementary Table S1).

Participants preferred lower risk of stroke, lower risk of bleeding, availability of antidote for bleeding, few interactions with food and drugs and lower out-of-pocket cost. These findings are consistent with the findings from a systematic review on preferences for oral anticoagulation therapy.[3] While participants generally preferred less frequent blood monitoring, they strongly disliked not having any blood monitoring and preferred to have blood tests every 3 months the most. There may be several reasons for our results. First, participants may not have realised that new DOAC medications do not require blood monitoring (as opposed to warfarin) and therefore expected some monitoring. They may also have perceived the lack of follow-ups as poor quality of care. Participants strongly disliked the "No treatment" option and those who reported having family who had stroke were less likely to choose the "No treatment" option.

The risk of stroke was the most important attribute (33%), followed by the monthly out-of-pocket cost (22%). Participants valued the risk of bleeding, availability of antidote and frequency of blood monitoring equally (approx. 12%). The least important attribute was the number of interactions with food/other drugs (8%) (Supplementary Fig. S2). Other studies[10] also found that efficacy in stroke prevention was more important than bleeding risk.[3]

Table 1 shows the predicted choice of a new DOAC, warfarin and "No treatment" at different out-of-pocket costs and frequency of blood monitoring for the new DOAC. The cost of warfarin was assumed to be SGD10 per month in the predictions. When the cost of the new DOAC was SGD10 per month (same as warfarin), 33% would choose the new DOAC when blood monitoring was not required for the new DOAC and 58% would choose warfarin. When blood monitoring was required once every 3 months for the new DOAC, 51% would choose the new DOAC and 41% would choose warfarin. If the new DOAC costs SGD200, only 15% would choose the new DOAC when blood monitoring was not required, and 25% would choose it when blood monitoring was required once every 3 months. Overall,

Table 1. Predicted treatment choices (N=125).

Cost of new DOAC (SGD)	Frequency of blood test of new DOAC	New DOAC (%)	Warfarin (%)	No treatment (%)
200	None	15	76	9
100	None	21	70	9
50	None	27	64	9
10	None	33	58	9
200	Once/3 months	25	66	9
100	Once/3 months	36	55	9
50	Once/3 months	44	48	9
10	Once/3 months	51	41	8

DOAC: direct oral anticoagulants
New DOAC profile: risk of stroke: 3%, risk of bleeding: 2%, antidote for bleeding: no, interactions with food: few.
Warfarin profile: risk of stroke: 3%, risk of bleeding: 3%, antidote for bleeding: yes, interactions with food: many, frequency of blood monitoring: once every 3 months, out-of-pocket cost: SGD10.
No treatment profile: risk of stroke: 7%, risk of bleeding: 1%, out-of-pocket cost: SGD0.

fewer participants were predicted to prefer the new DOAC over warfarin if the cost of the new DOAC was higher than warfarin.

Predicted choice of "No treatment" remained stable at around 9% regardless of the out-of-pocket cost and blood monitoring frequency for the new DOAC. These findings emphasise the need for concerted efforts to explain the benefits associated with treatments, the treatment options, and provide clarification to alleviate concerns for patients to make decisions consistent with their preferences.

The main strength of our study was to systematically quantify how the predicted demand for different medications changed based on risks, blood monitoring frequency and out-of-pocket costs. To our knowledge, this is the only other study assessing patient preferences in Asia, following a previous study conducted in Japan. The main limitation of our study was that patients recruited were not necessarily diagnosed with AF. However, as these patients were recruited from the neurology departments, their concerns and therefore, preferences may be similar to those of newly-diagnosed AF patients who are at risk of stroke. Additionally, the preferences of the recruited patients were not subject to other influences, such as past consults, thus ensuring that the preferences and concerns may be akin to those of newly-diagnosed patients.

In summary, this study showed that the efficacy in stroke prevention and out-of-pocket cost were the top 2 attributes patients focused on when selecting medications for AF. A better explanation of each treatment's benefits and risks can help patients to understand their options and potential consequences. Additionally, policymakers should consider lowering the out-of-pocket cost of these medications to promote medication use in efforts to reduce AF-related stroke. Incorporating patient preferences into treatment decisions will help them make informed decisions consistent with their preferences.

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LETTER TO THE EDITOR

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Emergency department falls interventions improve osteoporosis management in frail older adults

Dear Editor,

Singapore's population is ageing rapidly and by 2030, around 1 in 4 citizens will be aged 65 and above.[1] Older adults represent 21–40% of emergency department (ED) users and proportionally are the highest users of ED services.[2]

One-third of community dwellers over 65 years of age fall each year, and 50% will fall again, with 10% of falls resulting in serious injuries such as hip fractures, head injuries, injury-related disability and death.[3] Frailty is common in older adults and can be prevented or at least delayed[4] with ED frailty interventions and hospital avoidance.[5] This letter describes Singapore's introduction of falls interventions and osteoporosis management in older adults attending an ED short stay unit (SSU) and describes integration of geriatric services in the ED.

The ED SSU is a protocol-led unit, staffed by emergency medicine physicians, with a 23-hour maximum length of stay. The falls protocol (FP) was introduced on 10 March 2019, and operates from Sunday 12pm to Friday 9am, following a service development collaboration between geriatricians and emergency medicine physicians. Inclusion criteria identify older adults with falls and aim to avoid acute hospital admission by undertaking comprehensive geriatric assessments (CGA) in the ED SSU administered by a consultant geriatrician, geriatric resident physician and an ED nurse who has received basic training in geriatric care, called a Geriatric Care Champion. A retrospective review was undertaken after 7 months to assess effectiveness of the FP, and a comparator group (CG) was identified in falls patients admitted to SSU under the Blunt Trauma and Head Injury Protocols at our institution between 1 January 2018 and 31 December 2018. Electronic patient records were reviewed, and data collection included demographics, functional assessments, hospital utilisation and mortality. Falls history and injurious fall defined by the presence of fracture, compliance to bone health recommendations, uptake of bone mineral density (BMD) scan and anti-resorptive treatment were reviewed and assumed compliant if anti-resorptive treatment was commenced following the SSU visit. Rockwood's Clinical Frailty Scale (CFS)[6] was calculated from the CGA and/or Occupational Therapy assessments and categorised into: CFS 1–3; CFS 4–5; and CFS 6–9. Ethics review exemption was granted by the SingHealth Centralised Institutional Review Board. Descriptive statistics of demographic and clinical variables were compared between FP group and CG. The categorical outcome measures were analysed using chi-squared or Fisher's Exact test and presented as proportions and percentages. T-test was used for continuous data and presented as means and standard deviations. Data were analysed using Stata version 14 (StataCorp, College Station, TX, US).

The FP group comprised 96 patients and CG 121 patients. Between FP group and CG, there were similarities in average age (79.8 years vs 77.9 years, respectively; $P=0.092$) and median age (80 vs 78; $P=0.072$). There were also more females in both groups (61.5% vs 51.2%; $P=0.169$) (Table 1).

Comparing FP group vs CG, FP patients were more frail with CFS 1–3 (23.9% vs 37.2%, respectively), CFS 4–5 (38.5% vs 22.3%, $P=0.0001$) and CFS ≥6 (37.5% vs 19.0%; $P=0.0001$), and more dependent for instrumental and basic activities of daily living (Table 1; $P<0.0001$). Recurrent falls were more common in the FP group vs CG (70.8% vs 41.3%; $P=0.0001$); they also experienced more falls with fracture (43.8% vs 24.8%; $P=0.04$), which increased their likelihood of hospital admission (60% vs 30.8%, $P=0.027$). First falls occurred more frequently in the CG for those with CFS 4–5 (27% vs 55.6%, $P<0.037$), whereas recurrent falls were more common in FP patients with CFS 4–5 (72.9% vs 44.4%, $P<0.037$) (data not shown).

Osteoporosis was newly identified in more patients in the FP group vs CG (30.2% vs 7.4%, respectively; $P<0.0001$). The FP group also had a higher proportion of patients with known osteoporosis (28.1% vs 11.6%), and osteopenia (19.8% vs 2.5%; $P=0.0001$). BMD was undertaken for more patients in the FP group (82.3% vs 24.8%) with both vitamin D (95.8% vs 24.8%; $P<0.0001$) and serum calcium (96.8% vs 28.9%; $P<0.0001$) checked more frequently (Table 1). Following the ED visit, total antiresportive use was much higher in the FP group, 58.3% vs 19%.

Home discharge was lower in the FP group vs CG (35.4% vs 63.9%, respectively; $P<0.0001$), but more patients transferred directly to St Andrew's Community Hospital, Singapore for subacute care (33.3% vs 3.4%; $P<0.0001$). Acute hospital admission was similar in both groups (31.3% vs 32.8%), as was hospital length of stay (15.3 SD 12.4 vs 11.6 days; SD 13.7 $P=0.164$). For both FP group and CG, there was low ED re-

Table 1. Demographics, bone health assessment, functional assessments, hospital utilisation and mortality (n=217).

	Falls protocol (FP) group	Comparator group (CG)	*P* value
	n=96 (44.2%)	n=121 (55.8%)	
Age, mean (SD), years	79.8 (7.3)	77.9 (8.2)	0.092
Ages, median (IQR), years	80 (74–85)	78 (71–84)	0.072
Age range, no. (%), years			
≤70	13 (13.5)	24 (19.8)	0.227
71–80	36 (37.5)	51 (42.2)	
>80	47 (48.9)	46 (38.0)	
Sex, no. (%)			
Female	59 (61.5)	62 (51.2)	0.169
Male	37 (38.5)	59 (48.8)	
BMI, no. (%)[a]			
Underweight (<18.5)	15 (18.1)	4 (19.1)	0.667
Normal weight (18.5–24.9)	45 (54.2)	12 (57.1)	
Pre-obesity (25–29.9)	16 (19.3)	2 (9.5)	
Obesity (≥30)	7 (8.4)	3 (14.3)	
Frailty and bone health			
Frailty groups, no. (%)			
Non-frail (CFS 1–3)	23 (23.9)	45 (37.2)	**<0.0001**
Very mildly and mildly frail (CFS 4–5)	37 (38.5)	27 (22.3)	
Frail (CFS 6–9)	36 (37.5)	23 (19.0)	
Not done	0 (0)	26 (21.5)	
Osteoporosis, no. (%)			
Normal BMD	4 (4.2)	4 (3.3)	**<0.0001**
New osteoporosis	29 (30.2)	9 (7.44)	
Prior osteoporosis	27 (28.1)	14 (11.6)	
Osteopenia	19 (19.8)	3 (2.5)	
No BMD	17 (17.7)	91 (75.2)	
Serum vitamin D (sufficient: ≥30μg/L), no. (%)			
≥30 replete	19 (19.8)	7 (5.8)	**<0.0001**
20 to <30 mild deficiency	39 (40.6)	11 (9.1)	
10 to <20 moderate deficiency	30 (31.3)	10 (8.3)	
<10 severe deficiency	4 (4.2)	2 (1.7)	
Not done	4 (4.2)	91 (75.2)	
Serum calcium (normal range 2.10–2.60mmol/L), no. (%)			
2.1 to <2.6	92 (95.8)	34 (28.1)	**<0.0001**
2 to <2.1	1 (1.0)	1 (0.8)	
Not done	3 (3.2)	86 (71.1)	
Bisphosphonate initiation			
New antiresorptive treatment, no. (%)			
No	67 (69.8)	112 (92.6)	**<0.0001**
Yes	29 (30.2)	9 (7.4)	
Prior antiresorptive treatment, no. (%)			
No	69 (71.9)	107 (88.4)	**0.003**
Yes	27 (28.1)	14 (11.6)	
Functional assessments			
Barthel index, no. (%)			
Independent (20)	41 (42.7)	41 (33.9)	**<0.0001**
Mild disability (16–19)	38 (39.5)	18 (14.9)	
Moderate disability (11–15)	12 (12.5)	9 (7.4)	
Severe disability (≤10)	4 (4.2)	6 (5.0)	
Not done	1 (0)	47 (38.8)	
IADL, no. (%)			
Independent (7)	33 (34.4)	34 (28.1)	**<0.0001**
Assisted (1–6)	48 (50.0)	24 (19.8)	
Dependent (0)	14 (14.6)	12 (9.9)	
Not done	1 (1)	51 (42.2)	
AMT (cognitive), no. (%)			
Normal (≥7)	59 (61.5)	46 (38.0)	**<0.0001**
Cognitive impaired (0–6)	31 (32.3)	13 (10.7)	
Not done	6 (6.3)	62 (51.2)	
Discharge			
Discharge destination, no. (%)			

Table 1. Demographics, bone health assessment, functional assessments, hospital utilisation and mortality (n=217). (Cont'd)

	Falls protocol (FP) group	Comparator group (CG)	*P* value
	n=96 (44.2%)	n=121 (55.8%)	
Changi General Hospital, Singapore	30 (31.3)	39 (32.8)	**<0.0001**
St Andrew's Community Hospital, Singapore	32 (33.3)	4 (3.4)	
Home	34 (35.4)	76 (63.9)	
Admission to hospital, no. (%)			
Falls, no fracture	12 (40.0)	27 (69.2)	**0.027**
Falls, with fracture	18 (60.0)	12 (30.8)	
Outcome measures			
Mortality, no. (%)	2 (2.1)	5 (4.1)	0.468
ED re-attendance, no. (%)			
7-day	1 (1.0)	5 (4.1)	0.231
30-day	10 (10.4)	14 (11.6)	0.831
Hospital re-admission, no. (%)			
30-day	6 (6)	11 (9)	0.612
6-month	29 (30.2)	32 (26.5)	0.547
Length of hospital stay			
Mean (SD), days	15.3 (12.4)	11.6 (13.7)	0.164
Median (IQR), days	12 (8–18)	8 (5–13)	**0.013**
History of fall, no. (%)			
Prior fall	68 (70.8)	50 (41.3)	**<0.0001**
First fall	28 (29.2)	71 (58.7)	
Fall with fracture, no. (%)			
Falls, no fracture	54 (56.2)	91 (75.2)	**0.004**
Falls, with fracture	42 (43.8)	30 (24.8)	

AMT: abbreviated mental test; BMD: bone mineral density; BMI: body mass index; CFS: Clinical Frailty Scale; ED: emergency department; IADL: instrumental activities of daily living; IQR: interquartile range; SD: standard deviation

P values in bold are statistically significant.

[a] BMI results available only for 83 cases in FP group, and 21 cases in CG group.

attendance at 7 days (1% vs 4.1%, P=0.231), 30 days (10.4% vs 1 1.6%, P=0.831), and 30-day unplanned hospital re-admission (6% vs 9%; P=0.612) that remained similar between both groups at 6 months (30.2 % vs 26.5%; P=0.547). Mortality was low in both groups (2.1% vs 4.1%; P=0.468) at 6 months.

Geriatric emergency medicine is gaining traction as an opportunity to identify frailty and improve patients' function by a voiding hospital admission.[5] A CGA undertaken at ED reduces both admission and re-admission rates.[7] Adverse outcomes occur in one-third of older patients after ED dischar ge,[8] but a CGA undertaken after discharge from the ED can lower 30-day hospital re-admissions (16.5% vs 22.2%; P=0.048), with improvements in both physical and mental functions compared to standard care.[9] In this review, FP patients were more frail and functionally impaired compared with CG, experienced more recurrent falls (70.8% vs 41.3%, respectively; P=0.0001) and more falls with fracture (43.8% vs 24.8%; P=0.004), which typically result in hospital admissions. However , FP patients achieved the same low 7 and 30-day ED re-attendance, unplanned hospital re-admissions and mortality rates as the CG, sugge sting geriatric assessment can help older patients destined for hospital admis sion to discharge safely from the SSU. The CG was discharged home more frequently than FP patients (35.4% vs 63.9%; P<0.0001), but over time home dischar ges from the SSU for FP patients increased from 35.4% to 75% (unpublished data from internal audit for the Geriatric Emergency Medicine Service, Changi General Hospital, January 2022). CG patients are not routinely screened for falls risk and osteoporosis, but many pre-frail patients frequently fall and would benefit from early interventions to prevent falls and osteoporotic fractures. Osteoporosis treatments have a strong evidence base[10] and the FP enables earlier falls interventions, as well as higher rat es of i dentification and treatment of osteoporosis.

The FP offers an opportunity to prevent hospital admission in older patients, provide treatment recommendations and onward referrals to mitigate falls risk and prevent future osteoporotic fractures.

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LETTER TO THE EDITOR

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A perfect match: The story of robotics in gynaecology

Dear Editor,

The first use of surgical robotics started in the domain of orthopaedic and urological surgery. However, it was the initial concept of using a robot in performing remote damage control surgeries on the battlefield that sparked the commercialisation of robotic surgical technology for use in operating rooms.[1] The use of robotic surgery in gynaecology has been rapidly adopted worldwide over recent years, resulting in a shift from open procedures to minimally invasive surgery (MIS).

The benefits of robotic surgery include three-dimensional stereoscopic vision, tremor-free handling, and increased agility with wristed instruments. The technology allows for greater surgical precision and a more intuitive way to operate, which translates into shorter hospitalisations compared to conventional laparoscopy.[2] Furthermore, an important factor for the successful adoption of robotic surgery is its ability to shorten learning curves in MIS. Research has suggested that about 50 robotic procedures are required before a surgeon achieves proficiency.[3] Significantly, proficiency must not be mistaken for mastery, which is a buildable, continuous process rather than an endpoint. Singapore's experience with robotic surgery in gynaecology has demonstrated this paradigm—that surgeons proficient in complex open surgery can efficiently transition from open surgery to MIS without compromising patient outcomes in the process.[4]

Robotic surgery has been especially beneficial for patients with gynaecological malignancies. In endometrial cancer, randomised control trials have demonstrated that laparoscopic surgery is non-inferior to open surgery when considering recurrence of the disease.[5] In a systematic review, robotic surgery for endometrial cancer was associated with lower complication rates, with reduced blood loss and conversion rates compared to conventional laparoscopy.[6] Robotic surgery as a potentially safe and effective modality for surgical management of obese patients with endometrial cancer has also been explored.[7] In ovarian cancer, MIS techniques have gained momentum over recent years. This is especially so in the setting of interval debulking surgery after neoadjuvant chemotherapy for advanced ovarian cancer.Optimal cytoreductive surgery may be achieved in a highly selected group of patients with low tumour burden following neoadjuvant chemotherapy.[8] Early-stage cervical cancer is treated primarily with radical hysterectomy with nodal assessment. The Laparoscopic Approach to Cervical Cancer (LACC) trial published in 2018 reported that MIS was associated with poorer disease-free survival and overall survival compared to open surgery.[9] However, since 90% of MIS procedures in the LACC trial were performed via conventional laparoscopy, one question is whether these results could be extrapolated to robotic surgery. Further trials that are ongoing may provide guidance in deciding the mode of surgery for early cervical cancer.

There is growing use of robotic surgery for benign gynaecological conditions such as hysterectomy, myomectomy, sacrocolpopexy, endometriosis surgery and tubal surgery. In a multicentre analysis comparing different routes of hysterectomy, robotic hysterectomy performed by high-volume surgeons saw lower periopera-tive complication and readmission rates.[10] Robotic assistance in benign gynaecology can facilitate more complex surgeries safely with comparable outcomes to laparoscopy. There needs to be more well-powered, randomised trials to compare both techniques.

Our journey in surgical robotics began in 2008, when the National University Hospital (NUH), Singapore was, to our knowledge, the first in Southeast Asia to perform robotic procedures for gynaecological cancer. The introduction of the Gynaecologic Robot-Assisted Cancer and Endoscopic Surgery (GRACES) programme at NUH filled the service gap of MIS for gynaecological cancer then. Leveraging the advantages of the da Vinci Surgical platform (Intuitive Surgical, Sunnyvale, CA, US) and the shorter learning curve, the transition rapidly proceeded from open surgery to MIS, with robotic surgery becoming the standard of care for our patients with early endometrial cancer.

The introduction of robotic surgery in NUH was not without its challenges. In Singapore's mixed-financing healthcare system where patient's out-of-pocket cost contribute to a sizeable proportion of their healthcare expenses, large bill sizes were the initial barrier to more patients accessing the benefits of robotic surgery. As the robotic surgical load grew, operating theatre utilisation became more efficient and patient outcomes improved. This resulted in savings, which lowered the overall cost of robotic surgery and improved patient access. In 2017, the hospital bill for robotic hysterectomy was lower than open hysterectomy for endometrial cancer.[11] Since 2016, patients who undergo robotic hysterectomy have been discharged on the same day. This has reduced the length of stay and cost of care

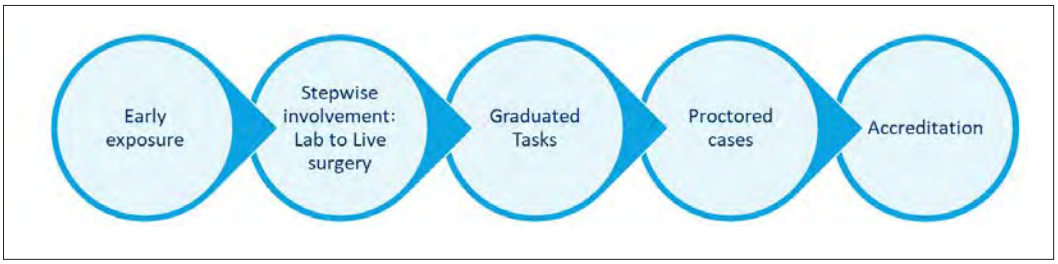

Fig. 1. Stepwise progression of trainees in robotic surgery during residency.

without compromising patient safety. Our experience demonstrates that surgical load and not per-case-amortisation is the foundation of a clinically relevant robotic surgical programme accessible to patients. The success of robotic surgery in gynaecological cancer has led to the increased adoption of robotic surgery in benign gynaecological surgery.

Training is one of the first tasks in introducing use of any new technology. Proficient open and conventional laparoscopy surgeons underwent "conversion" training modules using simulation, and proctoring by existing surgeons proficient in robotics both in Singapore and overseas. Training and assessment of competency should be incorporated into the residency programme to ensure safe and sustained growth in robotic surgery. In NUH, residents undergo a structured robotic surgical training and accreditation programme starting from their inception into residency (Fig. 1). Trainees begin with simulation-based training to gain competency under realistic conditions without compromising patient safety. Before moving on to live surgery, they need to undergo training in patient-side surgery, proper patient positioning, docking the robot correctly, and assisting in the robotic procedure. Only after attaining competence in both robotic surgical and non-technical skills can they progress to console time under supervision and with accreditation for independent practice. At the end of their residency training, the trainees are required to complete 5 proctored hysterectomies with good patient outcomes.

With the promotion of MIS techniques, the overall proportion of gynaecological procedures performed by laparotomy may reduce. There is growing evidence on the safety of robotic procedures to perform more complex gynaecologic procedures in patients with equivalent or reduced perioperative complications compared to laparoscopy. As robotic technology continues to rapidly advance, such as through the development of single-port robotic systems and artificial intelligence systems, the potential for surgical innovation is limitless. By training the next generation of gynaecologic surgeons in robotic surgery, more patients in the future can benefit from improved clinical outcomes.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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Streamlining multidisciplinary care in sarcoma management

Dear Editor,

Sarcomas are rare and heterogenous tumours that constitute fewer than 1% of a dult solid cancers.[1] Owing to their aggressive behaviour , relative rarity and occurrence at multiple anatomical sites, sarcomas can be challenging to treat.[2] Timely referral to specialist sarcoma centres is thus paramount and reduc es the incidence of "whoops" procedures, i.e. the inadvertent excision of an unsuspected soft tissue lump that is subsequently diagnosed as sarcoma. [3] Modelled after guidelines from the European Society for Medical Oncology and British Sarcoma Group, the National Cancer Centre Singapore and Singapore General Hospital's Department of Sa rcoma, Peritoneal and Rare Tumours (SPRinT) developed the Sarcoma Pre-Emptive Evaluation and Diagnosis (SPEED) protocol in 2019 to facilitate prompt referrals of s arcomas in Singapore.[4] Under this initiative, S PRinT welcomes all referrals of lumps suspected to be sarcoma without needing prior imaging. Criteria for referral include at least one of the following 5 FOES, namely, more than 5cm in size; deep to fascia; "ouch," i.e. painful; enlarging; and stuck to surrounding structures.

To assess the malignancy diagnostic rate and outcomes of the SPEED protocol, a retrospective review was performed for patients referred for a soft tissue lump and underwent sur gery at the National Cancer Centre Singapore and Singapore General Hospital under SPRinT over 6 years with comparison between 3-year periods from January 2016 t o December 2018 a nd July 2019 to March 2022.

A total of 177 patients were included. Following SPEED protocol implementation, majority of referrals were from general sur geons (27.4%) and general practitioners (22.6%). Table 1 shows the comparison between the number of referral criteria met in the benign and malignant groups. In both groups, a greater percentage of malignant lesions were >5cm in size compared with benign lumps, where it was statistically significant in the pre-SPEED protocol group (P=0.009). In the pre-SPEED protocol implementation group, 1 patient (1.3%) had a benign lump that was deep to the fascia compared with 3 patients (21.4%) with malignant lesions (P=0.007). Contrastingly, none of the benign lumps were deep to fas cia, whereas only 1 of the malignant lesions (5%) was deep to fascia enlar ging in the post-SPEED protocol group. A significant difference was found (P=0.038) between the number of painful lesions in the benign (n=5, 7.8%) and malignant cases (n=5, 25.0%), following SPEED protocol implementation. Our results show that there was a greater proportion of malignant lesions that met at least 1 of the 5 referral criteria. Although our study is not powered to show individual statistical dif ference in each criterion, it suggests that the criteria are useful collectively to allow timely diagnosis and management. These findings highlight the importance of recognising the 5 FOES to prompt early referral to a specialised centre.

Following SPEED protocol implementation, there was a relatively higher pick-up rate of 23.8% (n=20) of malignancy compared with 15.1% (n=14) prior , supporting the beneficial role of this service. Of the malignant cases, majority was sarcoma (80.0%). Although 76.2% of referrals in the current study turned out to be benign, we believe that the SPEED protocol is essential for t he provision of good he althcare for patients. Additionally, among the 14 patients who had malignant lesions pre-SPEED protocol implementation, 1 patient underwent a "whoops" procedure prior to referral to our department, whereas there was no occurrence of "whoops" procedures post-SPEED protocol implementation. Extrapolating this information, this referral pathway can prevent the occurrences of "whoops" procedures, which will be critical for the outcomes of sarcoma patients. This is particularly so when inadequate treatment during initial sarcoma surgery performed by a non-s arcoma specialist can result in involved sur gical margins, shorter mean time to recurrence and metastasis.[5, 6]

The rationale behind setting up t his initiative in Singapore is clearly supported in the literature. The management of sarcoma patients w ithin the netw ork of 26 re ference centres in France was found to be associated with better adherence to clinical practice guidelines and improved local relaps e-free and event-free survivals.[7] Another study conducted in British Columbia, Canada reported that patients who were referred prior to sur gery were more inclined to under go complete resection and adjuvant radiation in comparison to patients who were referred following sur gery.[8] Similar to these international referral pathways, the

Table 1. Comparison of referral criteria met between benign and malignant lesions pre- and post-SPEED protocol implementation.

Criteria	Number of benign lesions no. (%)		Number of malignant lesions, no. (%)		*P* value	
	Pre-SPEED protocol (n=79)	Post-SPEED protocol (n=64)	Pre-SPEED protocol (n=14)	Post-SPEED protocol (n=20)	Pre-SPEED protocol	Post-SPEED protocol
>5cm in size	23 (29.1)	19 (29.7)	5 (35.7)	9 (45.0)	**0.009**	0.565
Deep to fascia	1 (1.3)	0 (0)	3 (21.4)	1 (5.0)	**0.007**	0.372
Painful	30 (38.0)	5 (7.8)	2 (14.3)	5 (25.0)	0.157	**0.038**
Enlarging	41 (51.9)	27 (42.2)	10 (71.4)	9 (45.0)	0.093	0.824
Stuck to surrounding structures	1 (1.3)	3 (4.7)	3 (21.4)	3 (15.0)	**0.001**	0.118

SPEED: Sarcoma Pre-Emptive Evaluation and Diagnosis

Numbers in bold indicate statistical significance with *P* value <0.05.

SPEED protocol is a systematic programme that can augment the diagnosis and treatment outcomes of sarcoma and is highly relevant in Singapore. We believe that our experience can be adapted and applied in different healthcare systems within the region.

There are limitations to our study. Notably, centralising the management of all lumps to a tertiary centre requires some reallocation of healthcare resources and acceptance of a slight change in the doctrine of healthcare provision. To prevent the potential of negatively impacting care for other oncology patients, setting aside dedicated manpower to oversee such a programme is essential for tertiary units. This is similar to the National Health Service system in the UK where dedicated consultants manage "lumps and bumps" clinics, which are run within the sarcoma units of major hospitals.[9] Furthermore, reducing the possibilities of performing "whoops" surgeries and having a direct seamless integration with the sarcoma team in a tertiary centre can translate to more cost efficiency in the long run. We believe that adjusting resources to facilitate this referral pathway will enable high-risk cases to be channelled appropriately and promptly . This process will not only require time and concerted ef fort but more importantly, a slight revamp to the perception of the healthcare system in Singapore.

In conclusion, the SPEED protocol allowed for the timely diagnosis of patients with potential sarcoma and subsequent management in a multidisciplinary team, highlighting the usefulness of an efficient referral system to a dedicated unit specialising in sarcomas. Our experience can serve as reference for other cancer centres to augment the diagnosis and treatment outcomes of sarcoma.

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