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Body roundness index, frailty, and prevalent self-reported stroke: An exploratory cross-sectional decomposition analysis

Body roundness index showed a nonlinear association with prevalent self-reported stroke, while frailty demonstrated a stronger association with stroke status. (See full article p. 404)

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Body roundness index, frailty, and stroke

Laura Bee Gek Tay¹ MRCP

Stroke remains a leading global cause of death and disability. Primary prevention efforts to reduce the burden of stroke should focus on the management of modifiable risk factors, and 10 such factors were noted to account for approximately 90% of the population-attributable risk of stroke in the INTERSTROKE study.¹ These risk factors are often inter-related, with obesity contributing to major cardiovascular risk factors including hypertension, diabetes mellitus, and dyslipidaemia. A meta-analysis of prospective cohorts found that metabolically unhealthy phenotypes carry roughly double the stroke risk at any body weight, whereas metabolically healthy obesity confers only a modest excess (risk ratio of 1.17), suggesting that much of obesity-related stroke risk is transmitted through metabolic intermediaries, with a smaller direct contribution.² In INTERSTROKE, abdominal obesity defined by waist-to-hip ratio, rather than body mass index (BMI) carried an independent population-attributable risk of 18.6%,¹ and central adiposity has been linked to greater stroke severity and poorer early functional outcome in a single-centre prospective cohort,³ which may partly explain the obesity paradox previously described for BMI. This has been attributed to the detrimental effects of visceral fat accumulation in driving systemic inflammation, insulin resistance, and cardiovascular risk. The body roundness index (BRI) was introduced by Thomas et al. in 2013 to quantify abdominal adiposity and overall body fat by integrating the geometric relationship between waist circumference and height, with subsequent research validating its relationship with visceral adiposity and metabolic syndrome.^{4,5}

As populations age globally, growing attention has focused on frailty—characterised as a clinical syndrome of excess vulnerability to morbidity and mortality, owing to progressive decline in physiological reserves. Cross-sectional analyses of prevalent stroke in 2 nationally representative datasets—National Health and Nutrition Examination Survey (NHANES) in the United States and the Health and Retirement Longitudinal Study (CHARLS) in China—showed graded associations between a deficit-accumulation frailty index and stroke (odds ratio [OR] 2.90 and 1.78 per 0.1-unit increase, respectively).⁶ Beyond its

association with stroke risk, pre-stroke frailty influences treatment tolerance, complications, rehabilitation, and recovery.

Prior NHANES analyses had separately evaluated the relationship between BRI and prevalent stroke, and between BRI and prevalent frailty.^{7,8} In their current cross-sectional analysis of 36,324 adults from NHANES 1999–2023 (1236 with self-reported stroke; weighted prevalence 2.52%), Hu and colleagues extended prior work using the NHANES dataset, examining BRI estimates under progressively expanded covariate adjustment, and the effect of including frailty as measured using a 43-item deficit-accumulation frailty index (FI) on the BRI-stroke association.⁹ In this updated analysis, BRI was positively associated with self-reported stroke (OR 1.08, 95% confidence interval (CI) 1.05–1.12) in the primary model adjusted for age, sex, smoking, poverty-income ratio, education, physical activity, and energy intake. The restricted cubic spline curve supported the non-linear association between BRI and self-reported stroke, rising across lower-to-middle BRI values, before appearing to plateau at higher values.

Unadjusted threshold analysis further suggested a BRI breakpoint of 6.34 (bootstrap 95% CI 6.14–7.65), below which higher BRI values associated with increased odds of self-reported stroke, although the authors caution interpretation of the breakpoint as a clinical threshold owing to the sparsely populated upper range and lack of validation. The BRI association attenuated to the null (OR 1.01, 95% CI 0.98–1.04) once hypertension, diabetes and dyslipidaemia were added to the model, consistent with these comorbidities lying on the causal pathway from central adiposity to stroke rather than confounding it. The subsequent inversion of the BRI coefficient after FI was added (OR 0.91, 95% CI 0.88–0.95) should not be read as a protective effect: hypertension and diabetes were simultaneously covariates and components of the FI, creating collinearity and over-adjustment that the authors appropriately label exploratory. Meanwhile, each 0.1 unit increase in FI more than doubled the odds for self-reported stroke (OR 2.38, 95% CI 2.23–2.54). BRI negligibly improved the discriminative performance of an age-and-sex only model for self-reported stroke (AUC 0.769, 95% CI 0.758–0.781 versus [vs] 0.763, 95% CI 0.752–

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0.775; Δ AUC 0.006; Brier score 0.0318 vs 0.0319), a difference that reaches statistical significance only because of the sample size, while the addition of FI provided a much larger gain (AUC 0.868, 95% CI 0.860–0.877). This gain must be interpreted with care. A deficit-accumulation FI contains mobility, activities-of-daily-living and self-rated health items that rise mechanically after a stroke, so the FI partly detects the consequences of the very outcome it is being used to classify. Because BRI, FI, and stroke were measured concurrently, and the discrimination analysis was unweighted and internally validated only, the design cannot distinguish a BRI-frailty-stroke pathway from stroke-related disability raising the FI, a limitation the authors themselves acknowledge.⁹

The formula for BRI is well established and validated, but its clinical utility remains hampered by the lack of a universally accepted cutoff unlike the BMI. Threshold values of BRI for the prediction of metabolic syndrome vary across populations and across the outcomes against which they are derived^{5,10}; sex-specific cut-offs for metabolic syndrome in Brazilian adults, for example, fall at 3.8–4.0, far below the stroke breakpoint of 6.34. In stroke risk, the cutoff of 6.34 reported by Hu et al. was lower than the inflection point of 8.489 reported by Gan et al. using data from NHANES 1999–2018.⁷ However, the 2 estimates derive from different model specifications on overlapping samples, and Hu et al.'s own segmented model was unadjusted whereas their spline was covariate-adjusted, so part of the discrepancy reflects specification instability rather than population instability. For Asian readers, a BRI of 6.34 corresponds to a waist-to-height ratio of approximately 0.64, or a waist circumference of about 109 cm in a person 1.70 m tall,⁹ well beyond the ethnic-specific waist thresholds (90 cm for men, 80 cm for women) at which cardiometabolic risk is already elevated in Asian populations. No BRI threshold has been validated in an Asian general population, and any local derivation would need to be stratified by ethnicity given differences in visceral adiposity at a given BMI among Chinese, Malay and Indian Singaporeans.

NHANES also samples only the non institutionalised population, excluding the most disabled stroke survivors. Notwithstanding the limitations of both studies being observational data and relying only on self-reported stroke diagnosis, the premature adoption of BRI cutoffs runs the risk of misclassification and distraction from other established risk factors. Prospective population-specific validation, with adjudicated incident stroke, pre-stroke frailty assessment and pre-registered thresholds, will be necessary for clinical implementation of BRI as a target for stroke prevention and management. Until then, BRI, which is a monotonic transformation of waist-to-height ratio, adds no information beyond the waistbased measures already

embedded in vascular risk assessment, and there is no evidence that monitoring its trajectory improves stroke prevention. While frailty's apparent discriminative advantage is likely inflated by reverse causation, central adiposity, frailty, and cerebrovascular disease share pathophysiological processes such as chronic inflammation and oxidative stress. Thus, instead of establishing superiority of FI over BRI, or the temporal ordering of BRI-frailty-stroke relationship, the findings of Hu et al. change nothing for practice today: waist-based measures of central adiposity remain part of vascular risk assessment, and frailty assessment remains a prognostic rather than a preventive tool.

Ethics statement

Not applicable, as no study participants were recruited.

Declaration

The author declares there are no affiliations with or involvement in any organisation or entity with any financial interest in the subject matter or materials discussed in this manuscript. No funding was received for this work.

Keywords: *abdominal, adipose tissue, adiposity, body composition, body fat distribution, obesity*

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Body roundness index, frailty, and prevalent self-reported stroke: An exploratory cross-sectional decomposition analysis

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ABSTRACT

Introduction: Prior NHANES studies have reported nonlinear associations of the body roundness index (BRI) with prevalent stroke and frailty. The authors updated these observations using NHANES 1999–2023 and examined the additional contribution of frailty to the BRI-prevalent self-reported stroke association.

Methods: This cross-sectional study included 36,324 adults. Stroke was defined by self-reported physician diagnosis. Survey-weighted logistic regression and restricted cubic splines were used to assess BRI associations. Expanded models were fitted with and without the frailty index (FI). A post hoc 2-piecewise model estimated a potential BRI breakpoint using 1000 bootstrap resamples. Incremental discrimination was evaluated across nested age–sex, age–sex–BRI, and age–sex–BRI–FI models. Analyses were interpreted as cross-sectional associations.

Results: In the primary adjusted model, higher BRI was associated with prevalent self-reported stroke (odds ratio [OR]=1.08, 95% confidence interval [CI] 1.05–1.12). The spline showed increasing odds across lower-to-middle BRI values, followed by attenuation at higher values. The exploratory breakpoint was 6.34 (bootstrap 95% CI 6.14–7.65). In expanded sensitivity analyses, the BRI estimate was attenuated without FI (OR=1.01, 95% CI 0.98–1.04) and became inverse after FI was included (OR=0.91, 95% CI 0.88–0.95). FI remained strongly associated with prevalent self-reported stroke (OR=2.38 per 0.1-unit increase, 95% CI 2.23–2.54). Adding BRI to age and sex increased area under the curve (AUC) from 0.763 to 0.769, while adding FI increased AUC to 0.868.

Conclusion: BRI showed a nonlinear, model-dependent association with prevalent self-reported stroke, and frailty provided additional cross-sectional information. These findings support prospective evaluation of BRI and frailty as complementary markers in stroke-related assessment.

Keywords: adiposity, body roundness index, body mass index, frailty, nutrition surveys, obesity, stroke

CLINICAL IMPACT

What is New

- In a nationally representative US sample, BRI showed a nonlinear association with prevalent self-reported stroke, while frailty was strongly associated with stroke status.
- This study extends previous NHANES research by comparing BRI estimates across progressively adjusted models and examining the additional contribution of frailty.

Clinical Implications

- BRI and frailty may provide complementary cross-sectional information when characterising adults with prevalent stroke.
- Prospective, population-specific studies are needed before these measures are used for stroke prediction, screening, or clinical decision-making.

INTRODUCTION

Stroke remains one of the most pressing public health challenges worldwide, representing a leading cause of mortality and permanent disability. In the US alone, approximately 795,000 individuals experience a new or recurrent stroke each year, underscoring its substantial public health burden.^{1,2} Among the modifiable risk factors, obesity—particularly visceral adiposity—has been consistently associated with cerebrovascular disease. In the INTERSTROKE study, 10 potentially modifiable factors collectively accounted for approximately 90% of the population-attributable risk of stroke, whereas abdominal obesity—defined by an elevated waist-to-hip ratio—accounted for 18.6% (95% confidence interval [CI] 13.3%–25.3%).³ Traditional anthropometric indices

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such as body mass index (BMI) have long been used to classify obesity in both clinical and epidemiological settings. However, BMI fails to distinguish between fat and lean mass or to account for the distribution of adipose tissue, thereby limiting its utility in capturing the metabolic risks associated with central obesity.⁴

In recent years, the body roundness index (BRI) has emerged as an anthropometric measure that estimates abdominal body shape by incorporating waist circumference and height into an elliptical model of the human body.^{5,6} Unlike BMI, BRI more directly reflects central adiposity, which is associated with insulin resistance, dyslipidaemia, chronic inflammation, and endothelial dysfunction. BRI has been examined in relation to multiple cardiometabolic outcomes, including diabetes, hypertension, atherosclerosis, cardiovascular events, and mortality.^{7,8} The present work should therefore be viewed as an extension of the established BRI literature rather than as the first investigation of BRI and cerebrovascular disease.

Beyond adiposity, frailty commonly co-occurs with cerebrovascular disease. Frailty, a clinical syndrome characterised by diminished strength, endurance, and physiological function, has been associated with adverse outcomes in patients with stroke.^{9,10} Systematic reviews indicate that pre-stroke frailty is present in approximately one-quarter of patients with acute stroke and is strongly associated with mortality, disability, and prolonged hospitalisation.¹¹ Visceral obesity and frailty also share correlates, including chronic inflammation, oxidative stress, and hormonal dysregulation.¹² Previous National Health and Nutrition Examination Survey (NHANES) analyses have directly addressed the 2 component associations examined here. Gan et al. analysed 39,454 adults from NHANES 1999–2018 and reported a positive nonlinear

association between BRI and prevalent stroke using restricted cubic splines.¹³ Xu et al. analysed adults aged 60 years or older from NHANES 2007–2018 and reported a positive nonlinear association between BRI and prevalent frailty.¹⁴ These studies overlap substantially with the present analysis in both population and variables.

Accordingly, this study does not claim novelty for the BRI–stroke or BRI–frailty associations themselves. The authors update the BRI–prevalent self-reported stroke analysis through NHANES 1999–2023 and extend prior work by reporting model-specific BRI estimates under broader covariate adjustment, examining how the estimate changes after inclusion of FI, and quantifying incremental discrimination and calibration. Because BRI, frailty index (FI), and stroke were measured concurrently, the FI-related analysis is exploratory and descriptive and cannot establish mediation, temporal ordering, prospective risk, or a causal pathway.

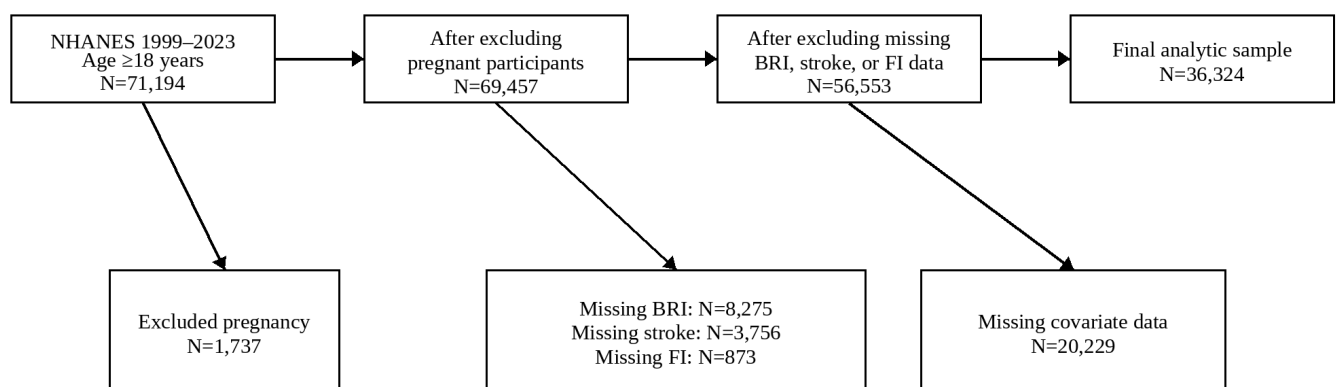
METHODS

Study design and sample

This cross-sectional study used NHANES data from 1999–2023. Participants were included if they were 18 years or older and had complete information on prevalent self-reported stroke status and BRI. The authors excluded individuals who were pregnant at the time of examination, those younger than 18 years, and participants with missing data on BRI, the stroke outcome, or covariates of interest.

After applying these criteria, 36,324 NHANES participants were included in the analytic sample. The participant selection process is summarised in Fig. 1.

Fig. 1. Flowchart of NHANES participant selection and exclusion.



BRI: body roundness index; FI: frailty index; NHANES: National Health and Nutrition Examination Survey

Flowchart of NHANES participant selection and exclusion. The flowchart illustrates the stepwise selection process for the NHANES cohort (1999–2023). After exclusions for pregnancy, missing BRI, stroke or FI data, and incomplete covariates, 36,324 participants were included in the analytic sample. Stroke denotes prevalent self-reported stroke ascertained using MCQ160F.

Assessment of stroke

Stroke status was determined using a standardised questionnaire administered during the household interview. Participants were asked whether they had ever been told by a health professional that they had experienced a stroke. Responses were coded using the variable MCQ160F, with “yes” indicating prevalent self-reported stroke and “no” indicating no self-reported history of stroke. This single item did not provide the date of onset, stroke subtype, or validation against medical records or neuroimaging.

Assessment of the BRI

BRI was calculated using the original geometric equation.⁵ In the equation below, WC denotes waist circumference in metres, H denotes height in metres, π denotes the mathematical constant pi, and 364.2 and 365.5 are constants from the original BRI model. For clinical orientation, BRI values of 5.24 and 6.34 correspond to waist-to-height ratios of approximately 0.592 and 0.639, respectively; for a person 1.70 m tall, these values correspond to waist circumferences of approximately 100.6 cm and 108.6 cm.

$$\text{BRI} = 364.2 - 365.5 \sqrt{1 - \left[\frac{\text{WC} / (2\pi)}{0.5 \times H} \right]^2}$$

Assessment of frailty

Frailty was assessed using a 43-item deficit-accumulation frailty index (FI) constructed according to the standard procedure described by Searle et al.¹⁸ Each deficit was coded from 0 to 1, and the FI was calculated as the mean of the 43 deficit scores among participants with complete FI data. Component definitions and scoring are provided in Supplementary Table S2. Descriptive FI values were retained on the original 0–1 scale, and regression estimates were reported per 0.1-unit increase. Hypertension and diabetes were included among the FI deficits; consequently, models that simultaneously included FI and these comorbidities were treated as exploratory sensitivity analyses susceptible to covariate overlap and overadjustment.

Covariates

Potential confounding factors were selected a priori based on established associations with both adiposity and stroke. Demographic variables included age, sex, race and Hispanic origin, marital status, and educational attainment. Socioeconomic status was assessed using the poverty-income ratio (PIR).¹⁶ Lifestyle factors comprised smoking history, alcohol consumption, a metabolic equivalent (MET)-based physical activity category, and daily energy intake

(kcal/day). Clinical comorbidities included hypertension, diabetes, and hyperlipidaemia. These covariates were incorporated into multivariable models to reduce confounding in the evaluation of the cross-sectional relationships among BRI, frailty, and prevalent self-reported stroke.

Statistical analyses

Analyses were conducted in R version 4.4.2 (R Foundation for Statistical Computing, Vienna, Austria). Survey-weighted estimation used the survey package (version 4.4-2); restricted cubic spline terms were generated using rms (version 8.0-0; Harrell, 2025); breakpoint grid searches used base R statistics (version 4.4.2), with nonparametric resampling implemented using boot (version 1.3-31; Canty & Ripley, 2024 and Davison & Hinkley, 1997); and receiver operating characteristic (ROC) curves and paired DeLong tests used pROC (version 1.18.5; Robin et al., 2011). Cycle-specific examination weights were rescaled for the pooled 1999–2023 analysis, and strata and primary sampling unit identifiers were nested within survey cycle. Continuous variables were summarised as survey-weighted mean $\pm$ standard error, and categorical variables as unweighted counts with survey-weighted percentages. Group comparisons used design-based t tests (design degrees of freedom=178) or design-based Wald χ^2 tests. Logistic regression models for BRI were specified hierarchically. Model 1 was unadjusted; Model 2 included age and sex; Model 3 additionally included smoking and PIR; and the primary Model 4 additionally included education, MET-based physical activity, and energy intake. FI was not included in Models 1–4. An expanded sensitivity model additionally included race and Hispanic origin, marital status, hypertension, diabetes, hyperlipidaemia, and alcohol consumption. FI was then added to the same expanded model to permit a matched model comparison. Because hypertension and diabetes were also FI components, the FI-adjusted model was considered exploratory and potentially affected by covariate overlap and overadjustment; its BRI coefficient was not interpreted as a causal direct effect. Nonlinear associations were assessed using restricted cubic splines adjusted for age, sex, race and Hispanic origin, and PIR. The segmented analysis was post hoc and unadjusted and was therefore not interpreted as direct quantitative confirmation of the adjusted spline. Candidate break-points between the 5th and 95th percentiles of BRI were evaluated in 0.01-unit increments, and the value maximising model likelihood was selected. A percentile-based 95% confidence interval for the breakpoint was obtained from 1000 participant-level nonparametric bootstrap resamples. For the secondary incremental-discrimination analysis, conventional unweighted logistic regression was used

to permit paired DeLong comparison of correlated ROC curves.¹⁷ Three nested models were evaluated: age and sex; age, sex, and BRI; and age, sex, BRI, and FI. Areas under the curve (AUCs) and 95% CIs were estimated using DeLong's method, and adjacent models were compared using paired DeLong tests. Calibration was evaluated using Brier scores, calibration intercepts, and calibration slopes derived from stratified 10-fold cross-validated predictions. These analyses described classification of contemporaneous prevalent self-reported stroke status and were not interpreted as prospective prediction or screening performance. Regression estimates for FI were expressed per 0.1-unit increase; descriptive FI values and the deficit-scoring table remained on the original 0–1 scale. A two-sided $P < 0.05$ indicated statistical significance.

Ethical considerations

All NHANES protocols were approved by the National Center for Health Statistics Ethics Review Board, and written informed consent was obtained from all participants. The present study used publicly available, de-identified data and required no additional institutional review.

RESULTS

Baseline characteristics

The analytic sample included 1236 unweighted participants with prevalent self-reported stroke and

35,088 participants without self-reported stroke; the survey-weighted prevalence of self-reported stroke was 2.52%. Compared with participants without self-reported stroke, those with prevalent self-reported stroke were older and had lower PIR, lower MET-based physical activity, and lower daily energy intake, whereas a higher proportion belonged to the overweight and obese BMI categories; their mean BRI and FI were also higher. Differences were also observed in sex, educational attainment, smoking status, race and Hispanic origin, marital status, hypertension, diabetes, hyperlipidaemia, and alcohol consumption. In the overall study population, BRI ranged from 1.05 to 23.48, with a mean of 5.24 (standard error=0.02) and a median of 4.84 (Q1=3.61, Q3=6.39). Detailed sociodemographic and clinical characteristics are presented in Table 1.

Model-specific logistic regression analyses

To distinguish the primary BRI association from estimates obtained under broader adjustment and after inclusion of FI, the relevant models are presented separately in Table 2. In the primary model without FI, BRI was positively associated with prevalent self-reported stroke (odds ratio [OR]=1.08, 95% CI 1.05–1.12, $P < 0.001$). In the expanded model without FI, the BRI association was null ($\beta = 0.009$; OR=1.01, 95% CI 0.98–1.04, $P = 0.601$). After FI was added to the same expanded model, the BRI coefficient was negative ($\beta = -0.090$; OR=0.91, 95% CI 0.88–0.95, $P < 0.001$), while FI was strongly associated

Table 1. Baseline sociodemographic and clinical characteristics of participants.

Variable	Total	No self-reported stroke	Prevalent self-reported stroke	Statistic	P
Age, mean (SE)	46.561 (0.214)	46.140 (0.213)	62.834 (0.560)	$t = 30.293$	< 0.001
Energy intake, kcal/day, mean (SE)	2152.698 (6.849)	2159.720 (6.815)	1880.866 (33.087)	$t = -8.484$	< 0.001
BRI, mean (SE)	5.236 (0.024)	5.212 (0.024)	6.162 (0.088)	$t = 10.363$	< 0.001
FI, mean (SE)	0.131 (0.001)	0.127 (0.001)	0.283 (0.005)	$t = 33.093$	< 0.001
Sex, n (%)				$\chi^2 = 5.503$	0.019
Male	18,522 (50.219)	17,881 (50.333)	641 (45.777)		
Female	17,802 (49.781)	17,207 (49.667)	595 (54.223)		
Education, n (%)				$\chi^2 = 69.769$	< 0.001
Less than high school	7416 (12.880)	7055 (12.664)	361 (21.226)		
High school or equivalent	8315 (23.138)	7961 (22.923)	354 (31.435)		
College or above	20,593 (63.983)	20,072 (64.413)	521 (47.339)		
Smoking, n (%)				$\chi^2 = 70.835$	< 0.001
No	19,806 (54.821)	19,342 (55.204)	464 (40.009)		
Yes	16,518 (45.179)	15,746 (44.796)	772 (59.991)		

Table 1. Baseline sociodemographic and clinical characteristics of participants. (Cont'd)

Variable	Total	No self-reported stroke	Prevalent self-reported stroke	Statistic	P
MET-based physical activity, n (%)				$\chi^2=96.294$	<0.001
Low physical activity	12,920 (31.839)	12,260 (31.351)	660 (50.727)		
High physical activity	23,404 (68.161)	22,828 (68.649)	576 (49.273)		
BMI, n (%)				$\chi^2=23.214$	<0.001
<18.5	521 (1.447)	504 (1.445)	17 (1.531)		
18.5 to <25	10,134 (29.429)	9860 (29.616)	274 (22.165)		
25 to <30	12,186 (33.285)	11,780 (33.291)	406 (33.068)		
≥30	13,483 (35.839)	12,944 (35.648)	539 (43.236)		
Race and Hispanic origin, n (%)				$\chi^2=90.787$	<0.001
Mexican American	5215 (7.210)	5105 (7.297)	110 (3.849)		
Non-Hispanic White	17,350 (71.066)	16,709 (71.025)	641 (72.639)		
Non-Hispanic Black	7403 (9.951)	7064 (9.838)	339 (14.335)		
Other	6356 (11.773)	6210 (11.840)	146 (9.178)		
Marital status, n (%)				$\chi^2=195.713$	<0.001
Married or living with a partner	21,863 (64.210)	21,206 (64.331)	657 (59.522)		
Widowed/divorced/separated	7688 (17.430)	7211 (17.013)	477 (33.558)		
Never married	6773 (18.360)	6671 (18.656)	102 (6.921)		
PIR, n (%)				$\chi^2=95.515$	<0.001
<1.3	10,076 (18.538)	9606 (18.279)	470 (28.567)		
1.3 to <3.5	13,539 (34.662)	13,027 (34.478)	512 (41.778)		
≥3.5	12,709 (46.799)	12,455 (47.242)	254 (29.655)		
Hypertension, n (%)				$\chi^2=637.923$	<0.001
No	21,295 (63.997)	21,049 (65.029)	246 (24.048)		
Yes	15,029 (36.003)	14,039 (34.971)	990 (75.952)		
Diabetes, n (%)				$\chi^2=176.197$	<0.001
No	30,168 (87.491)	29,411 (88.074)	757 (64.919)		
Yes	6156 (12.509)	5677 (11.926)	479 (35.081)		
Hyperlipidaemia, n (%)				$\chi^2=169.498$	<0.001
No	11,418 (32.073)	11,210 (32.508)	208 (15.246)		
Yes	24,906 (67.927)	23,878 (67.492)	1028 (84.754)		
Alcohol consumption, n (%)				$\chi^2=55.596$	<0.001
No	11,098 (26.244)	10,607 (25.932)	491 (38.313)		
Yes	25,226 (73.756)	24,481 (74.068)	745 (61.687)		

BMI: body mass index; BRI: body roundness index; FI: frailty index; MET: metabolic equivalent; PIR: poverty-income ratio; SE: standard error
 Categorical values are unweighted n (survey-weighted %). Stroke denotes prevalent self-reported stroke. Continuous-variable comparisons used design-based t tests with 178 design degrees of freedom; categorical comparisons used design-based Wald χ^2 tests.

Table 2. Comparison of primary, expanded, and FI-adjusted BRI models for prevalent self-reported stroke.

Model	Predictor	Adjustment set	β	OR (95% CI)	P
Primary association model (without FI)	BRI	Age, sex, smoking, PIR, education, physical activity, and energy intake	0.077	1.08 (1.05–1.12)	<0.001
Expanded model (without FI)	BRI	Primary model plus race and Hispanic origin, marital status, hypertension, diabetes, hyperlipidaemia, and alcohol consumption	0.009	1.01 (0.98–1.04)	0.601
Expanded FI-adjusted sensitivity model	BRI	Expanded model plus FI	-0.090	0.91 (0.88–0.95)	<0.001
Expanded FI-adjusted sensitivity model	FI (per 0.1-unit)	Expanded model plus FI	0.867	2.38 (2.23–2.54)	<0.001

BRI: body roundness index; CI: confidence interval; FI: frailty index; OR: odds ratio; PIR: poverty-income ratio

OR=exp(β). The expanded models used the same covariate set, differing only by inclusion of FI. Because hypertension and diabetes were also FI components, the FI-adjusted model is susceptible to covariate overlap and overadjustment and is not interpreted as a causal direct-effect model.

with prevalent self-reported stroke ($\beta=0.867$; OR=2.38 per 0.1-unit increase, 95% CI 2.23–2.54, $P<0.001$). Because hypertension and diabetes were included both as covariates and as components of the FI, the FI-adjusted estimates may reflect covariate overlap and overadjustment. This model was therefore treated as an exploratory sensitivity analysis and not as a causal direct-effect model.

Incremental discrimination and calibration analyses

In the secondary unweighted analysis, a prevalence-only model assigning the observed stroke prevalence (3.40%) to every participant had an AUC of 0.500 and a Brier score of 0.0329. The age-and-sex model yielded an AUC of 0.763 (95% CI 0.752–0.775) and a Brier score of 0.0319. Adding BRI increased the AUC to 0.769 (95% CI 0.758–0.781; Δ AUC=0.006; paired DeLong $P<0.001$) and changed the Brier score minimally to 0.0318. Adding FI increased the AUC to 0.868 (95% CI 0.860–0.877; Δ AUC=0.099; paired DeLong $P<0.001$) and reduced the Brier score to 0.0297. Thus, the BRI-related improvements in both discrimination and overall prediction error were small. Although the FI-containing model showed

a larger numerical improvement, FI was measured concurrently with prevalent stroke and included deficits that may reflect stroke-related disability; these results do not establish prospective predictive value or screening utility.

Primary BRI association models without FI

To evaluate the primary cross-sectional association between BRI and prevalent self-reported stroke, logistic regression models were constructed with progressive adjustment for potential confounders; FI was not included in any of these models (Supplementary Table S1). In the unadjusted model (Model 1), BRI was associated with higher odds of prevalent self-reported stroke (OR=1.16, 95% CI 1.13–1.19, $P<0.001$). After adjustment for age and sex (Model 2), the association remained significant (OR=1.11, 95% CI 1.07–1.14, $P<0.001$). The association persisted after additional adjustment for smoking and PIR (Model 3; OR=1.09, 95% CI 1.05–1.12, $P<0.001$). In the primary Model 4, which additionally included education, physical activity, and energy intake, BRI remained positively associated with prevalent self-reported stroke (OR=1.08, 95% CI 1.05–1.12, $P<0.001$).

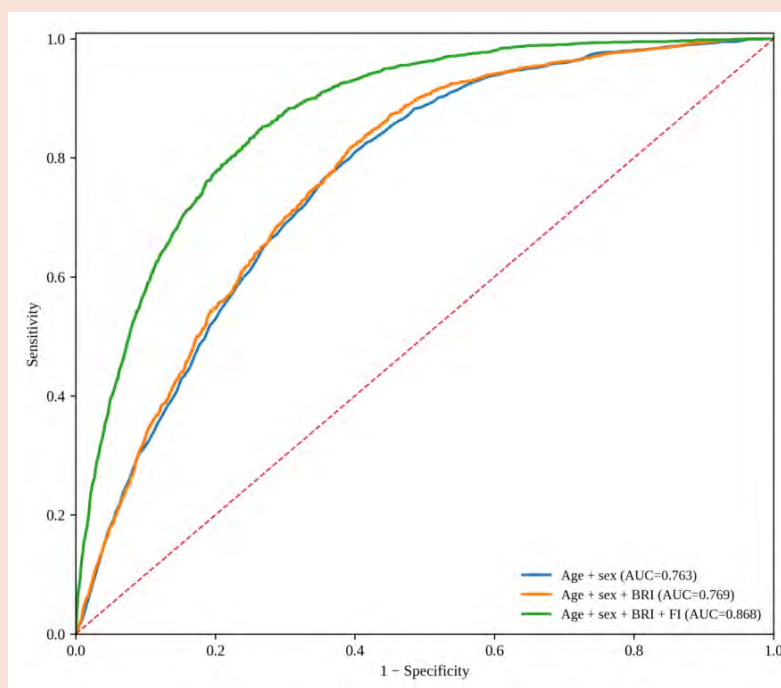
Table 3. Incremental discrimination and cross-validated calibration for nested models of prevalent self-reported stroke.

Model	AUC (95% CI)	Δ AUC vs previous	DeLong P	Brier score	Calibration intercept/slope
Prevalence-only reference	0.500 (by definition)	Reference	—	0.0329	Not applicable
Age + sex	0.763 (0.752–0.775)	Reference	—	0.0319	-0.007/0.998
Age + sex + BRI	0.769 (0.758–0.781)	0.006	<0.001	0.0318	-0.012/0.996
Age + sex + BRI + FI	0.868 (0.860–0.877)	0.099	<0.001	0.0297	-0.005/0.998

AUC: area under the curve; BRI: body roundness index; CI: confidence interval; FI: frailty index

The prevalence-only Brier score equals $p(1-p)$, where $P=0.0340$; lower Brier scores indicate lower mean squared prediction error. The age–sex model improved modestly over this reference, addition of BRI produced a minimal further reduction (0.0001), and addition of FI produced a larger numerical reduction that remains vulnerable to reverse causation.

Fig. 2. ROC curves for nested models classifying prevalent self-reported stroke status.



AUC: area under the curve; BRI: body roundness index; CI: confidence interval; FI: frailty index; ROC: receiver operating characteristic

ROC curves for nested models classifying prevalent self-reported stroke status. The age-and-sex base model had an AUC of 0.763 (95% CI 0.752–0.775). Adding BRI increased AUC to 0.769 (95% CI 0.758–0.781; Δ AUC=0.006; paired DeLong $P<0.001$), and adding FI increased AUC to 0.868 (95% CI 0.860–0.877; Δ AUC=0.099 versus the preceding model; paired DeLong $P<0.001$). These secondary, unweighted analyses classify contemporaneous prevalent self-reported stroke status and should not be interpreted as prospective prediction or screening performance.

Restricted cubic spline analysis

Restricted cubic spline models were used to examine the nonlinear association between BRI and prevalent self-reported stroke after adjustment for age, sex, race and Hispanic origin, and PIR (Fig. 2). At the low end of the observed BRI distribution, the fitted odds ratio was below 1.0 relative to the reference value. The curve then rose across lower-to-middle BRI values, reached a broad maximum around BRI 6–7, and attenuated gradually at higher values, with widening confidence intervals in the sparsely populated upper range (P for nonlinearity <0.001). This pattern does not indicate that individuals with low BRI have high odds of stroke, nor does it establish a prospective dose–response relationship. The spline is presented in Fig. 3.

Threshold analysis

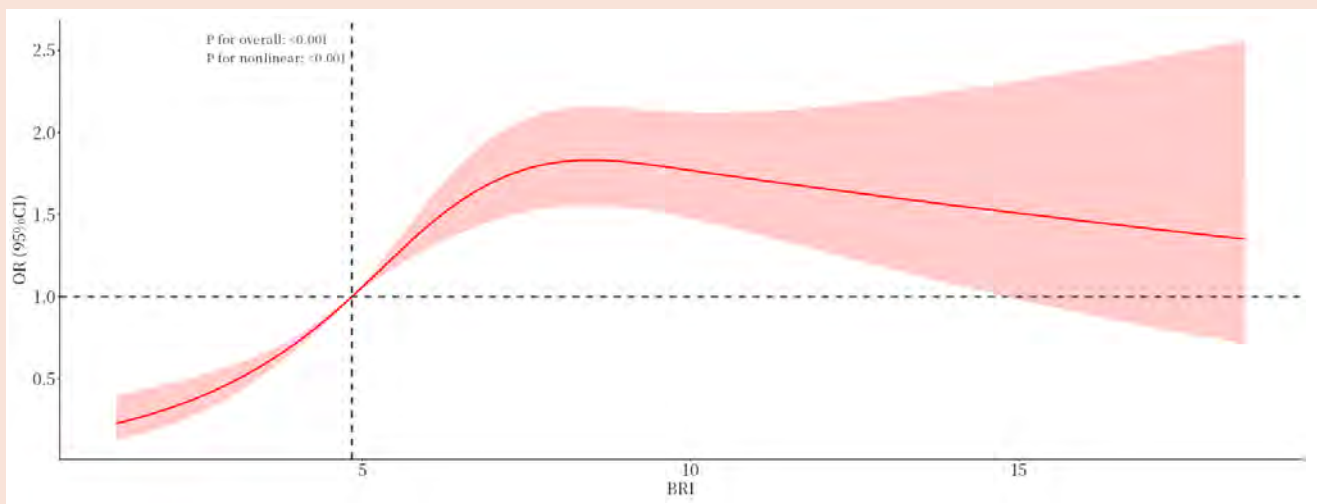
To further characterise the nonlinear association between BRI and prevalent self-reported stroke, a post hoc unadjusted 2-piecewise logistic regression was fitted. The likelihood-ratio test favoured the segmented model over a single linear term ($P<0.001$).

The estimated breakpoint was BRI=6.34, with a bootstrap 95% confidence interval of 6.14–7.65 based on 1000 nonparametric resamples. Below the breakpoint, higher BRI was associated with increased odds of prevalent self-reported stroke (OR=1.42, 95% CI 1.32–1.51, $P<0.001$). Above the breakpoint, the average slope was null (OR=0.99, 95% CI 0.95–1.04, $P=0.795$). Because this segmented model was unadjusted whereas the spline model was covariate-adjusted, the 2 analyses do not estimate the same curve and the breakpoint should not be interpreted as confirming the adjusted spline. The breakpoint and apparent plateau are exploratory statistical features rather than established biological or clinical thresholds. The broad uncertainty at high BRI values and lack of replication preclude use of 6.34 as a clinical cut-point. The results are shown in Table 4.

Exploratory cross-sectional decomposition analysis

The exploratory cross-sectional decomposition was interpreted together with the nested model comparison in Table 2. In the expanded model, the BRI

Fig. 3. Restricted cubic spline curve.



CI: confidence interval; OR: odds ratio

Restricted cubic spline curve. The curve illustrates the adjusted nonlinear cross-sectional association between BRI and prevalent self-reported stroke after adjustment for age, sex, race and Hispanic origin, and PIR. The fitted OR was below 1.0 at the low end of the BRI distribution, increased across lower-to-middle values, reached a broad maximum around BRI 6–7, and then attenuated gradually; confidence intervals widened at high BRI values. The solid line represents the estimated odds ratio, and the shaded area indicates the 95% CI (P for nonlinearity <0.001). The curve does not show a steeper rise above BRI 6.0 and should not be interpreted as an incident-stroke trajectory or a validated clinical threshold.

estimate was null before FI was included and changed direction after FI adjustment, whereas FI remained strongly associated with prevalent self-reported stroke. Because the FI-adjusted model simultaneously included hypertension and diabetes, which were also FI components, the coefficient change may reflect covariate overlap and overadjustment in addition to any association with frailty. This pattern is therefore better characterised as sensitivity of the adjusted coefficient to model specification than as evidence of a direct or indirect causal effect.

In the model with FI as the outcome, the reported BRI coefficient was $\beta=0.12$ on the FI $\times 10$ scale, equivalent to a 0.012-unit difference in FI on the original 0–1 scale per 1-unit higher BRI ($P<0.001$). However, because BRI, FI, and prevalent self-reported stroke were measured concurrently, neither this association nor the change in the BRI coefficient after FI adjustment establishes mediation or temporal ordering. The findings are also compatible with reverse causation, including stroke-related disability increasing the FI.

Table 4. Post hoc exploratory unadjusted segmented logistic regression of BRI and prevalent self-reported stroke.

Model/segment	OR (95% CI)	P
Single linear model	1.14 (1.12–1.16)	<0.001
2-piecewise model		
Breakpoint	6.34	
Bootstrap 95% CI for breakpoint	6.14–7.65	
<6.34	1.42 (1.32–1.51)	<0.001
≥ 6.34	0.99 (0.95–1.04)	0.795
P for likelihood-ratio test		<0.001

CI: confidence interval; OR: odds ratio

The segmented model was post hoc, unadjusted, and exploratory and was not directly comparable with the adjusted spline. The breakpoint confidence interval was obtained from 1000 participant-level nonparametric bootstrap resamples. The estimated breakpoint should not be used as a clinical cut-point without prospective and independent replication.

DISCUSSION

In this updated NHANES cross-sectional analysis, BRI was positively associated with prevalent self-reported stroke in the primary model adjusted for demographic, socioeconomic, and lifestyle factors. The adjusted spline rose across lower-to-middle BRI values and attenuated at higher values. A post hoc unadjusted segmented model yielded a model-dependent breakpoint at BRI=6.34 (bootstrap 95% CI 6.14–7.65); because this model did not use the same adjustment set as the spline, it was not interpreted as confirming the adjusted curve or as identifying a clinical threshold. The BRI estimate was also sensitive to broader covariate adjustment and inclusion of FI: it was null in the expanded model without FI and changed direction after FI adjustment. The latter model included hypertension and diabetes both as covariates and as FI components, so its coefficient change may partly reflect covariate overlap and overadjustment. In secondary discrimination analyses, BRI increased AUC beyond age and sex by only 0.006 and reduced the cross-validated Brier score from 0.0319 to 0.0318, compared with a prevalence-only Brier score of 0.0329. These small changes do not support a clinically meaningful screening claim. Addition of FI produced larger numerical changes (AUC 0.868; Brier score 0.0297), but the FI-related increment may reflect stroke-related disability embedded in the contemporaneously measured FI and cannot establish prospective utility. These model-dependent findings do not support causal mediation, a direct-effect interpretation, clinical prediction, screening, or policy adoption.

The positive association between BRI and prevalent self-reported stroke largely confirms prior NHANES findings rather than establishing a new association. Gan et al. reported a positive nonlinear association using NHANES 1999–2018,¹³ and longitudinal evidence also links BRI with incident stroke in other populations.¹⁹ Unlike BMI, BRI reflects abdominal body shape, and visceral adiposity is associated with atherosclerosis, endothelial dysfunction, and chronic inflammation^{20,21}; BRI has also been linked to broader cardiometabolic abnormalities.²² The present analysis extends the NHANES observation through 2023, but it is not an independent replication because of substantial overlap in survey cycles and participants. The estimated breakpoint was not stable across analyses: Gan et al. reported an inflection point of 8.489,¹³ whereas the present exploratory estimate was 6.34 (bootstrap 95% CI 6.14–7.65). This lack of concordance argues against treating either value as a reproducible clinical cut-point. The attenuation observed at high BRI values is unlikely to reflect metabolic adaptation. NHANES includes only living respondents who attended the examination, so

selective survival may attenuate or distort associations among individuals with the greatest adiposity. Collider or selection bias, reverse causation, post-stroke treatment or weight change, and sparse data at extreme BRI values are additional plausible explanations for the apparent plateau.^{23,24} Prospective replication with adjudicated incident stroke is required before any threshold interpretation is considered.

The association between BRI and frailty has likewise been established in prior NHANES work. Xu et al. reported a positive nonlinear association between BRI and prevalent frailty among older adults.¹⁴ The principal extension in the present study is the exploratory cross-sectional comparison of model-specific BRI estimates before and after FI inclusion, together with the incremental-discrimination analysis. Visceral obesity and frailty may share biological correlates, including chronic inflammation, hormonal dysregulation, and sarcopenia,^{25–27} while frailty is associated with endothelial dysfunction, hypercoagulability, and reduced physiological resilience.²⁸ In the present analysis, BRI was associated with higher FI, FI was strongly associated with prevalent self-reported stroke, and inclusion of FI materially changed the BRI coefficient. However, this extension is descriptive and methodologically limited: the coefficient change is model-dependent and cannot identify a temporal sequence or distinguish BRI → frailty → stroke from stroke-related disability → higher FI.

Furthermore, the concept of “brain frailty”—characterised by neuroimaging markers such as white matter hyperintensities, cerebral atrophy, and silent infarcts—may provide context for the co-occurrence of frailty and cerebrovascular disease. Frail individuals often exhibit evidence of cerebral small vessel disease and reduced cognitive reserve, which may be associated with stroke vulnerability and recovery. These observations may help explain why frailty and cerebrovascular disease are closely associated, but they do not establish that frailty lies on a causal pathway between BRI and stroke in this cross-sectional analysis.^{29,30}

These findings should be interpreted as descriptive rather than mechanistic. Although BRI and FI were associated with prevalent self-reported stroke status, the concurrent measurement of FI and stroke prevents inference that frailty transmits an effect of adiposity. In particular, a prior stroke may cause functional limitations that increase the FI.

This study has limitations. Stroke was ascertained from a single, undated self-report item and therefore represented prevalent self-reported stroke rather than an incident outcome; the absence of an onset date, stroke subtype, and validation against medical records or neuroimaging, together with the inability to capture silent or fatal strokes, creates potential recall

and classification error. Because only survivors who attended the examination were observed, selective survival may bias anthropometric associations and may contribute to attenuation at high BRI values.^{23,24} Because the analytic sample substantially overlaps with prior NHANES studies of BRI–stroke and BRI–frailty, the present results should not be considered independent replication of those component associations. The threshold analysis was post hoc and unadjusted, whereas the spline was covariate-adjusted; these analyses do not estimate the same curve. Although breakpoint uncertainty was quantified using 1000 bootstrap resamples, the estimate differed from the 8.489 inflection reported in a prior NHANES study and has not been independently replicated. Collider or selection bias, reverse causation, post-stroke treatment or weight change, and sparse data at extreme BRI values may also influence the observed nonlinear shape. The FI-adjusted sensitivity model included hypertension and diabetes both as covariates and as components of the FI, creating covariate overlap and potential overadjustment. The incremental-discrimination analysis was unweighted, internally evaluated, and based on prevalent stroke status. Statistical significance in the DeLong comparisons may partly reflect the large sample size, and the cross-validated calibration estimates do not demonstrate external transportability or prospective performance. BRI, FI, and prevalent self-reported stroke were ascertained at the same examination, and the timing of stroke occurrence relative to BRI and FI assessment was unavailable. Therefore, the FI-related analysis cannot establish mediation, temporality, or causality. A prior stroke may reduce physical activity and functional status and thereby increase the FI; because the 43-item FI includes functional and disability-related deficits that may reflect stroke sequelae, the observed model changes and FI-related classification gain are equally consistent with reverse causation. NHANES also lacks detailed information on treatment or control of hypertension, diabetes, and hyperlipidaemia, and residual confounding is possible. Results may not generalise beyond US adults. Anthropometric relationships and action points are population-dependent; Asian populations may have greater body fat at a given BMI and may experience cardiometabolic risk at lower BMI values than European populations.³¹ The exploratory BRI breakpoint of 6.34 was derived from a US sample, has not been validated in an Asian general population, and should not be extrapolated as an Asian screening threshold. This study did not assess implementation cost, feasibility, acceptability, equity, or workflow integration. Accordingly, the present evidence is insufficient for clinical, payer, or

policy adoption. Larger prospective, population-specific studies with temporally ordered measurements and adjudicated stroke events are required.

CONCLUSION

In summary, BRI showed a model-dependent nonlinear cross-sectional association with prevalent self-reported stroke. The post hoc unadjusted breakpoint estimate was not independently replicated and was not directly comparable with the adjusted spline; it should not be interpreted as a clinical cut-point. The BRI estimate was sensitive to expanded covariate adjustment and inclusion of FI, while frailty remained strongly associated with prevalent self-reported stroke. Because BRI, frailty, and stroke were measured concurrently, and because the FI-adjusted sensitivity model contained overlapping covariates, these findings do not establish mediation, a causal direct effect, or temporal ordering.

Any potential use of BRI or FI for clinical prediction or screening remains hypothetical. The present findings do not support routine screening, use of BRI 6.34 as a clinical threshold, or adoption by clinicians, payers, or policymakers. No general-population Asian validation is available, and population-specific prospective studies with adjudicated stroke events, together with evaluation of implementation cost, feasibility, equity, and workflow, are required before any clinical or policy application is considered.

Supplementary materials

Supplementary Table S1. Survey-weighted logistic regression models for prevalent self-reported stroke.

Supplementary Table S2. Frailty index variable scoring.

Ethics statement

The present study used publicly available, de-identified data and required no additional institutional review.

Declaration

This study was funded by the Shanghai Second Rehabilitation Hospital Research Project (Y2025-07) and the Medical Talents Training Program of Shanghai Pudong New Area Health Commission (PWRq2026-43). The authors declare that they have no other affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript. Generative artificial intelligence was used solely for English-language editing and stylistic refinement; the authors critically reviewed and revised all AI-assisted text and take full responsibility for the accuracy, integrity, and content of the manuscript.

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Evaluation of China's "1146" school-based myopia control programme in primary school children: A 12-month study

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ABSTRACT

Introduction: Structured school-based myopia prevention programmes are increasingly promoted, but real-world evidence supporting multicomponent models remains limited. This study evaluated the 12-month effectiveness of the "1146" programme in China in a routine primary school setting.

Methods: This prospective, non-randomised controlled study included 24 classes from a single primary school, assigned to intervention or control groups according to teaching schedule. After follow-up, 100 children from the intervention group and 98 children from the control group were analysed. Intervention classes received the multicomponent "1146" programme, which integrated education, visual behaviour, environmental measures, outdoor activity promotion, monitoring, and adjunctive professional components. Control classes followed standard teaching. Routine refractive correction was provided to myopic children in both groups when indicated. Continuous outcomes were analysed using linear mixed-effects models adjusted for baseline value, age, and sex, with class included as a random effect.

Results: At 12 months, axial length increased less in the intervention group than in controls (0.01 ± 0.11 mm versus [vs] 0.29 ± 0.37 mm; adjusted mean difference -0.288 mm; 95% confidence interval -0.363 to -0.213). Spherical equivalent changed by 0.20 ± 0.61 D vs -0.45 ± 0.77 D, and uncorrected visual acuity changed by 0.37 ± 0.30 vs -0.27 ± 0.25 (all adjusted $P < 0.001$). Improvement of ≥ 2 lines in uncorrected visual acuity (UCVA) occurred in 53.0% vs 1.0%, indicating meaningful functional gain. No subgroup interaction was significant.

Conclusion: The "1146" programme was associated with less axial elongation and more favourable refractive and UCVA changes over 12 months. The single-school, non-randomised design limited causal inference and generalisability. Larger randomised multicentre studies with longer follow-up are needed.

Keywords: axial length, eye, intervention study, ophthalmology, myopia, prevention & control, school health services

CLINICAL IMPACT

What is New

- This study evaluated a multicomponent school-based myopia prevention programme in China, called the "1146" model, in routine primary school settings.
- The programme was associated with reduced axial elongation, more favourable refractive changes, and improved unaided visual function over 12 months.

Clinical Implications

- Coordinated school-based implementation may support integrated myopia prevention in primary school children.
- Larger randomised multicentre studies with longer follow-up are needed to confirm effectiveness, generalisability, and component-specific contributions.

INTRODUCTION

Myopia is a major public health concern, with global prevalence projected to approach 50% by 2050.¹ In China, a large school-based study of 864,828 children aged 6–16 years reported a myopia prevalence of 54.71% in 2021.² During the COVID-19 pandemic, reduced outdoor activity and increased near-work demands contributed to a pronounced myopic shift among children and adolescents.^{3,4} School-based surveillance studies have indicated that the upper grades of primary school—usually corresponding to Grades 3–6 and approximately ages 8–12 years in the Chinese school system—represent a critical window for the onset and rapid progression of myopia, during which axial length (AL) and spherical equivalent (SE)

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may change within a single academic year.³ High myopia is associated with sight-threatening conditions such as glaucoma and myopic retinal detachment,⁵ and contributes to burdens on individuals, families, and society.⁶ Therefore, implementing myopia prevention and control interventions during sensitive periods of visual development is important in both clinical practice and public health.

In recent decades, national technical guidelines have emphasised a shift in myopia prevention from “single techniques” to “integrated strategies”.⁷ These strategies combine established approaches, including health education, visual behaviour interventions, improvements in the learning environment, promotion of outdoor activities, and optical correction, while traditional Chinese medicine (TCM)-based approaches are considered adjunctive components.⁸ Because comprehensive school-based programmes involve multiple components and implementation steps, they need to be understood not only in terms of ocular outcomes, but also in terms of how they are designed, delivered, adopted, and maintained in routine school settings. The Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) framework provides an implementation-science approach for assessing these aspects of health programmes, including their delivery, adoption, maintenance, and potential for scaling up in real-world settings.⁹ Current myopia control interventions include orthokeratology,¹⁰ defocus incorporated multiple segments (DIMS) spectacle lenses,¹¹ and low-concentration atropine eye drops.¹² Although these approaches have shown effectiveness, they may be limited by cost, suboptimal adherence, wearing discomfort, or rebound after discontinuation.^{13,14} Because myopia development is influenced by genetic, environmental, and behavioural factors,^{15–17} single interventions may be insufficient to address these influences simultaneously.

Previous studies have examined combined myopia control approaches, mainly integrating behavioural interventions, environmental modifications, and optical or pharmacological strategies.^{18,19} However, many studies differ in intervention structure, delivery setting, and outcome assessment, and few have evaluated structured and reproducible comprehensive programmes delivered in routine school settings. In addition, evidence remains limited and inconsistent regarding whether comprehensive intervention effects differ by baseline refractive characteristics, age, or sex. The authors therefore evaluated the “1146” comprehensive myopia prevention and control model over 12 months in a primary school in Hohhot, Inner Mongolia, China, where the programme was delivered as part of routine school settings. This model integrates health education, visual behaviour management,

environmental modification, outdoor activity promotion, optical correction, visual health monitoring, and professional adjunctive components, including TCM-based measures and visual training. The study aimed to evaluate its effects on AL, SE, and uncorrected visual acuity (UCVA), and to explore whether intervention effects differed across subgroups defined by baseline myopia status, age, and sex.

METHODS

Study design and participants

This was a prospective, non-randomised controlled study with class-level allocation. In September 2023, a total of 24 classes from Grades 1 to 6 (4 classes per grade) at a primary school in Hohhot, Inner Mongolia, China were enrolled using a class-based cluster sampling approach. Within each grade, 2 classes were assigned to the intervention group and 2 to the control group according to the school's teaching schedule, without individual-level or class-level randomisation. Only right-eye data were analysed to avoid inter-eye correlation.

The inclusion and exclusion criteria applied in this study were adapted from those commonly adopted in myopia-control trials involving low-concentration atropine eye drops²⁰ and DIMS spectacle lenses.¹¹ Children were eligible for inclusion if they met the following criteria: age 6–11 years; cycloplegic SE in both eyes ranging from -3.00 D to $+1.00$ D; astigmatism ≤ 2.50 D; and willingness to complete a 1-year follow-up. Children were excluded if they had received myopia interventions such as atropine, orthokeratology, or defocus-based lenses before or at baseline; had organic ocular disease affecting visual function, strabismus, or amblyopia; or had poor follow-up compliance or incomplete data. According to the 2019 diagnostic threshold issued by the International Myopia Institute, myopia in this study was defined as a cycloplegic SE of ≤ -0.50 D.²¹ This classification was used only for subsequent subgroup analyses.

Sample size

The sample size was estimated a priori using a 2-sample comparison of proportions, with myopia prevalence as the reference outcome. Based on the reported prevalence of myopia among urban children and adolescents in Inner Mongolia in 2021 (58.95%), the authors assumed the same prevalence in the control group and an expected reduction to 30.50% in the intervention group. With a 2-sided α of 0.05 and 80% power, the required sample size was 47 participants per group. Allowing for 10% attrition, the target sample size was 52 participants per group (total 104). Because allocation occurred at the class level, the calculation did not incorporate a design

effect and was therefore used only as a reference. All eligible children in the selected classes were screened.

Intervention

The intervention lasted 12 months. Intervention classes received the “1146” comprehensive myopia prevention and control programme, whereas control classes followed the usual teaching schedule. Myopic children in both groups received single-vision spectacle correction when clinically indicated.

The “1146” model, developed by Hohhot Myopia Prevention and Control Association, incorporated recommendations on near-work distance, interruption of prolonged near work, and outdoor activity, adapted to the school setting and lifestyle of primary school children in Inner Mongolia.²² The RE-AIM framework informed consideration of programme reach, effectiveness, adoption, implementation, and maintenance.²³ The conceptual framework is provided in Supplementary Fig. S1.

Components of the “1146” comprehensive myopia prevention and control model

“1” set of scientific myopia-prevention lectures

Centralised lectures for students, parents, and teachers covered healthy visual habits, near-work management, outdoor activity, and optimisation of the home visual environment.

“1” set of professional prevention and control records

An individual visual health record documented refractive status, intervention delivery, and adherence (Supplementary Annex S1).

“4” key prevention and control objectives

- (1) For children at the pre-myopic stage, to delay myopia onset;
- (2) For primary school children with low myopia ($-1.00\text{ D} < \text{SE} \leq -0.50\text{ D}$), to maintain good UCVA, prescribe spectacles as needed, and avoid premature correction;
- (3) For primary school children with myopia of $-6.00\text{ D} < \text{SE} \leq -1.00\text{ D}$, to limit refractive progression and axial elongation;
- (4) For primary school children with high myopia ($\text{SE} \leq -6.00\text{ D}$), to prevent related complications.

“6” intervention measures

- (1) Structured health education: Seventeen recorded myopia-prevention sessions were disseminated weekly online to students, parents, and teachers.

- (2) Behavioural habit correction: Behavioural targets included a reading distance of $\geq 33\text{ cm}$ and screen time $< 2\text{ hours/day}$, with adherence supervised by parents and teachers.
- (3) Environmental optimisation: Classroom desk illuminance was maintained at $\geq 300\text{ lx}$. The home visual environment and related behaviours were assessed using a study-specific checklist (Supplementary Annex S2).
- (4) Nutritional intervention: Parents received TCM constitution-based dietary guidance, covering regular breakfast, water intake of $\geq 1,000\text{ mL/day}$, and reduced sugar and fat intake.
- (5) Enhanced physical activity: Outdoor activity was targeted at $\geq 2\text{ hours per day}$.
- (6) Professional adjunctive interventions:
 - **Repeated low-level red-light therapy (RLRL):** Eligible myopic children received RLRL at $650 \pm 10\text{ nm}$ for 3 minutes twice daily, $\geq 4\text{ hours}$ apart, on $\geq 5\text{ days/week}$ under teacher supervision.
 - **Visual function training:** Monocular lens reading and binocular mirror training were performed for 20 minutes twice weekly.
 - **Auricular acupoint pressing:** The liver, kidney, heart, spleen, eye 1, and eye 2 points were pressed once weekly, with daily self-pressing.²⁴

The schedule, frequency, and participant coverage of each component of the “1146” programme are summarised in Table 1.

Compliance assessment

Adherence to RLRL, visual function training, and auricular acupoint pressing was calculated for each participant as completed sessions divided by scheduled sessions. Behavioural and environmental components were monitored at class level through teacher supervision and standardised classroom checks.

Outcome measures

The primary outcomes were changes in AL and SE from baseline to 12 months. AL was measured using an SW-9000 optical biometer (Tianjin Suowei Electronic Technology Co Ltd, Tianjin, China). The agreement of the SW-9000 with other optical biometers for paediatric ocular biometric measurements has been evaluated previously.²⁵ Each eye was measured 5 consecutive times, and the mean value was calculated. If the standard deviation (SD) of the 5 consecutive measurements exceeded 0.05 mm , the measurements were repeated. Flat and steep keratometry values (K1 and K2) were also recorded. Cycloplegia was induced with compound tropicamide (Shenyang Xingqi Pharmaceutical Co Ltd, Shenyang, China), and

Table 1. Components, schedule, and participant coverage of the “1146” programme.

Component	Schedule/frequency	Participant coverage
Structured health education	A total of 17 recorded sessions, disseminated weekly online	Students, parents, and teachers in intervention classes
Behavioural habit correction	Daily supervision during learning and daily activities	Students in the intervention group
Environmental optimisation	Classroom desk illuminance maintained at ≥ 300 lx	Intervention classrooms; students' home visual environment
Nutritional intervention	Throughout the intervention period, with parental cooperation	Students in the intervention group
Enhanced physical activity	Target of ≥ 2 h/day outdoor activity	Students in the intervention group
Visual health monitoring	Baseline and 12-month assessments; ongoing monitoring	Students in the intervention group
Routine refractive correction	According to refractive status and clinical need	Myopic children in both groups, when clinically indicated
Repeated low-level red-light therapy	3 min/session, twice daily, ≥ 4 h apart, ≥ 5 days/week	A total of 41 myopic students in the intervention group
Visual function training	20 min/session, twice weekly	21 students in the intervention group
Auricular acupoint pressing	Once weekly, with daily self-pressing	All students in the intervention group

adequacy was assessed using pupil diameter and the pupillary light reflex. Cycloplegic refraction was measured 3 times with an RM-1 autorefractor (Topcon, Tokyo, Japan), and the mean was used. Subjective refraction was performed when required. SE was calculated as sphere plus half the cylinder.

The secondary outcome was change in UCVA, measured at 5 m using an Early Treatment Diabetic Retinopathy Study chart (Precision Vision, Woodstock, IL, US) under standard illumination. The smallest correctly identified line was recorded in decimal units. Using the prespecified definition of a 0.1-logMAR change as 1 line, UCVA change was categorised as improvement (≥ 2 -line increase), stability (within ± 1 line), or deterioration (≥ 2 -line decrease). All ocular examinations were performed by the same experienced optometrist.

Quality control and blinding

All assessors received standardised training and followed a study-specific protocol. Devices of the same model were used throughout and calibrated before assessment. Quality-control staff reviewed records and attendance logs, and monitored protocol adherence during on-site assessments. Device-generated data were exported electronically, while manually collected data were independently entered by 2 researchers and cross-checked.

As the intervention was overt, participants and intervention providers could not be masked. However,

ocular outcome assessments and data analyses were conducted without knowledge of group allocation.

Adverse events

All participants who received any intervention were included in safety monitoring. A structured questionnaire completed by participants and their guardians recorded ocular and systemic symptoms, including ocular irritation, transient glare, photophobia, headache, and auricular tenderness. Events occurring between scheduled assessments were documented during unscheduled consultations. All reported events were documented in the case report forms and reviewed by the research team. Suspected serious intervention-related events prompted immediate suspension of the relevant intervention and clinical assessment according to predefined procedures. The full assessment form is provided in Supplementary Annex S3.

Statistical analysis

Analyses were performed using Stata version 18.0 (StataCorp, College Station, TX, US). Continuous variables are presented as mean $\pm$ SD or median (interquartile range), and categorical variables as n (%).

Baseline continuous variables were compared using independent-samples or Welch's t-tests, as appropriate, and categorical variables using Pearson's χ^2 test.

Changes in AL, SE, and UCVA were analysed using linear mixed-effects models with class as a random

effect and intervention group as a fixed effect. Models were adjusted for the corresponding baseline value, age, and sex.

Exploratory subgroup analyses were conducted by baseline myopia status, sex, and age group. Group-by-subgroup interaction terms were added to the models to assess effect modification. All tests were 2-sided, with $P < 0.05$ considered statistically significant.

RESULTS

Of 237 children screened, 216 were enrolled and allocated by class to the intervention and control groups (108 each). Eight intervention and 10 control participants were lost to follow-up, leaving 100 and 98 participants, respectively, for analysis (Fig. 1).

Baseline characteristics

At baseline, there were no statistically significant differences between the intervention and control groups with respect to sex, age, SE, UCVA, or corneal curvature parameters (K1 and K2) (all $P > 0.05$),

although a small but statistically significant difference in AL was observed ($P = 0.047$). Overall, the baseline characteristics of the 2 groups were broadly comparable (Table 2).

Compliance results

Individual-level adherence was $85.9\% \pm 12.1\%$ for RLRL, $85.5\% \pm 23.9\%$ for visual function training, and $89.3\% \pm 18.1\%$ for auricular acupoint pressing. Behavioural and environmental components were monitored at class level through teacher supervision and standardised classroom checks.

Changes in axial length (AL)

Over the 12-month period, the intervention group showed a smaller increase in AL, with a mean change of 0.01 ± 0.11 mm, whereas the control group showed a greater axial elongation, with a mean change of 0.29 ± 0.37 mm. After adjustment using the linear mixed-effects model, the between-group difference in AL change remained statistically significant, with

Fig. 1. Participant flowchart from eligibility assessment to study inclusion.

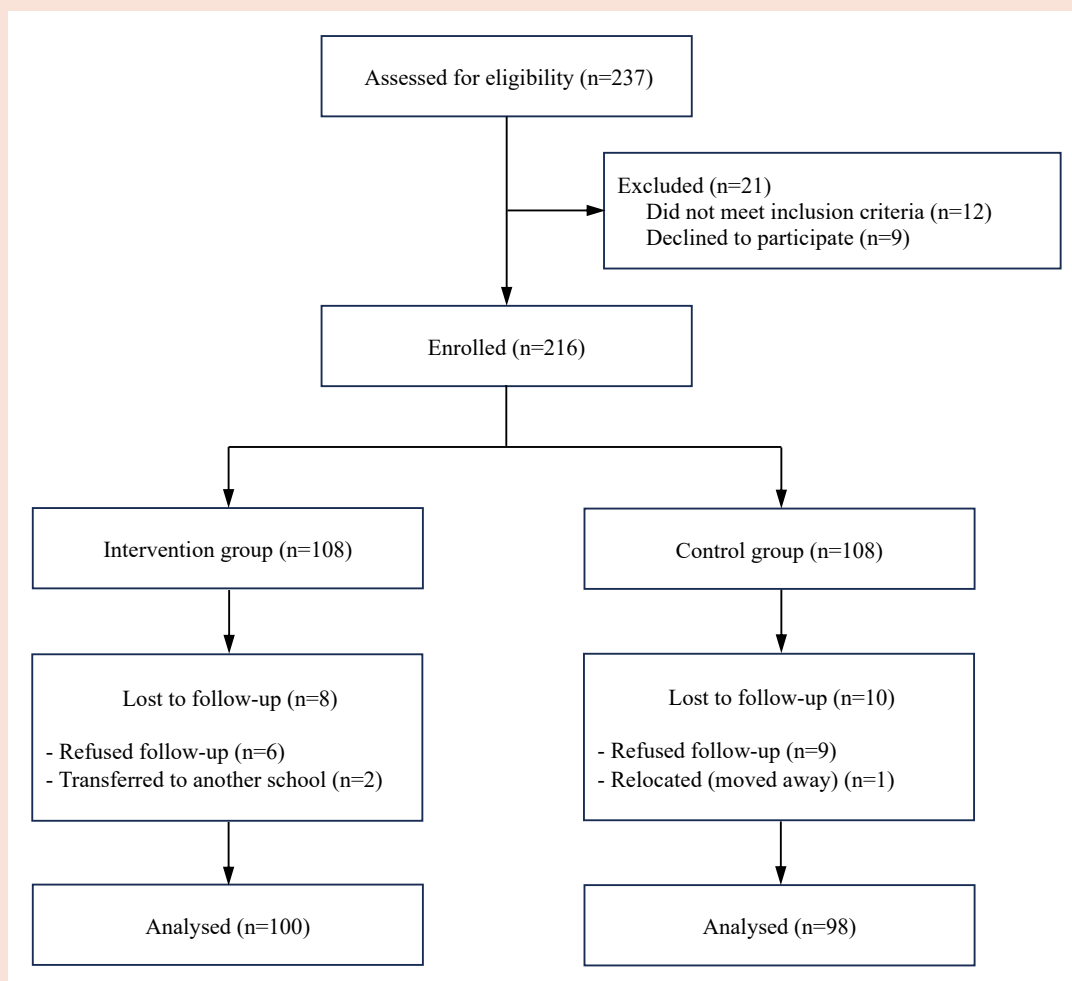


Table 2. Baseline characteristics of the study participants.

Variable	Intervention (n=100)	Control (n=98)	t/ χ^2 value	P value
Age, years	7.70 $\pm$ 0.67	7.61 $\pm$ 0.64	−0.942	0.348
Boys/girls, n (%)	52 (52.0)/48 (48.0)	56 (57.1)/42 (42.9)	0.528	0.467
AL, mm	23.24 $\pm$ 0.73	23.47 $\pm$ 0.93	2.001	0.047
SE, D	−0.56 $\pm$ 0.58	−0.78 $\pm$ 0.95	−1.95	0.053
UCVA	0.77 $\pm$ 0.18	0.84 $\pm$ 0.29	1.858	0.065
K1, D	42.69 $\pm$ 1.36	42.71 $\pm$ 1.49	0.075	0.940
K2, D	43.89 $\pm$ 1.40	44.12 $\pm$ 1.69	1.025	0.307

AL: axial length; K1: flat keratometry; K2: steep keratometry; SE: spherical equivalent; UCVA: uncorrected visual acuity

Data are presented as mean $\pm$ standard deviation or n (%).

P values were calculated using independent-samples t tests or Welch's t tests for continuous variables, according to variance homogeneity testing, and Pearson's χ^2 test for categorical variables.

an adjusted mean difference of −0.288 mm (95% confidence interval [CI] −0.363 to −0.213; $P < 0.001$). Detailed results are presented in Table 3 and Fig. 2.

Changes in spherical equivalent (SE)

The intervention group showed a slight positive shift in SE over 12 months compared with baseline (0.20 $\pm$ 0.61 D), whereas the control group showed a myopic shift (−0.45 $\pm$ 0.77 D). After adjustment using the linear mixed-effects model, the between-group difference in SE change remained statistically significant, with an adjusted mean difference of 0.684 D (95% CI 0.501 to 0.868; $P < 0.001$). Detailed results are presented in Table 3 and Fig. 2.

Changes in uncorrected visual acuity (UCVA)

With respect to UCVA, the intervention group showed a mean improvement (0.37 $\pm$ 0.30), whereas the control group showed a mean decline (−0.27 $\pm$ 0.25). After adjustment using the linear mixed-effects model, the between-group difference in UCVA change remained

statistically significant, with an adjusted mean difference of 0.628 (95% CI 0.553 to 0.702; $P < 0.001$; Table 3, Fig. 2).

Improvement of ≥ 2 lines occurred in 53.0% of intervention participants and 1.0% of controls, whereas deterioration of ≥ 2 lines occurred in 1.0% and 56.1%, respectively (Supplementary Table S1). Individual outcome distributions are shown in Supplementary Fig. S2.

Subgroup and interaction analyses

Subgroup analyses by baseline myopia status, sex, and age showed generally consistent intervention effects on AL, SE, and UCVA (Table 4). Across all subgroups, the intervention group had less axial elongation, more favourable SE changes, and greater UCVA improvement than controls, with statistically significant adjusted between-group differences. No significant interactions were observed for baseline myopia status, sex, or age for any outcome (all P for interaction > 0.05), indicating no clear evidence of effect modification.

Table 3. Changes in axial length, spherical equivalent, and uncorrected visual acuity at 12 months.

Outcome	Intervention (n=100)	Control (n=98)	Adjusted mean difference	95% CI	P value
AL change, mm	0.01 $\pm$ 0.11	0.29 $\pm$ 0.37	−0.288	−0.363 to −0.213	<0.001
SE change, D	0.20 $\pm$ 0.61	−0.45 $\pm$ 0.77	0.684	0.501 to 0.868	<0.001
UCVA change	0.37 $\pm$ 0.30	−0.27 $\pm$ 0.25	0.628	0.553 to 0.702	<0.001

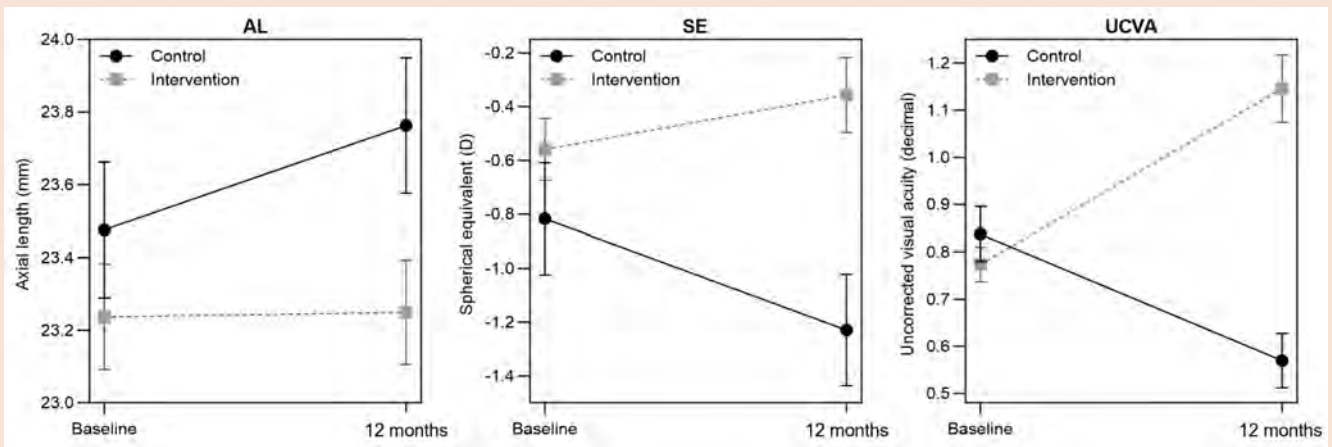
AL: axial length; SE: spherical equivalent; UCVA: uncorrected visual acuity

Data are presented as mean $\pm$ standard deviation.

Changes represent the difference between baseline and 12-month follow-up.

Adjusted mean differences and P values were estimated using linear mixed-effects models adjusted for the corresponding baseline outcome value, age, and sex, with class included as a random effect.

Fig. 2. Changes in AL, SE, and UCVA from baseline to 12 months.



AL: axial length; SE: spherical equivalent; UCVA: uncorrected visual acuity
Error bars (vertical lines) represent 95% confidence intervals.

Adverse events

No serious adverse events or adverse-event-related withdrawals occurred. Mild transient eye fatigue and auricular tenderness were reported and resolved without treatment.

DISCUSSION

Myopia is a multifactorial ocular condition influenced by genetic predisposition, environmental exposure, and behavioural patterns.²⁶ Although single-modality strategies such as low-concentration atropine and orthokeratology are effective, their practical use may be constrained by rebound after discontinuation, suboptimal adherence, and wearing discomfort.^{14,27} Comprehensive myopia prevention and control models have therefore received increasing attention.^{28,29} In the present study, the school-based “1146” programme was associated with less axial elongation, more favourable changes in SE, and improved UCVA over 12 months. Given the non-randomised class-level allocation, these findings should be interpreted as programme-level associations in a real-world school setting, where shared classroom environments and teacher supervision may also have contributed to intervention delivery and behaviour change.

After 12 months, children in the intervention group showed substantially less mean axial elongation than controls, suggesting that the programme may be associated with slower AL growth. Previous studies have reported reduced axial elongation or limited AL progression following RLRL.^{30,31} In the present study, RLRL was incorporated as 1 professional adjunctive component, while visual behaviour management, environmental optimisation, outdoor activity promotion, routine refractive correction, and visual health monitoring were implemented in parallel. The smaller

AL increase may therefore reflect the coordinated effect of the integrated programme rather than any single component.

Regarding SE, the intervention group showed a more favourable change than the control group after 12 months, consistent with previous school-based intervention studies. Cluster-randomised trials have shown that increasing outdoor activity at school can reduce myopic refractive shifts and may also slow axial elongation.^{19,32} In the present study, outdoor activity promotion was implemented together with behavioural, environmental, refractive, and professional adjunctive measures. Therefore, the more favourable SE change should be interpreted as part of the overall effect of the integrated programme and considered together with the AL findings.

Regarding UCVA, mean values improved in the intervention group but declined in controls, indicating different directions of change between groups. The categorical analysis based on the prespecified decimal-acuity thresholds showed a similar pattern: participants improved or remained stable, whereas deterioration was more frequent among controls. A threshold of at least 2 study-defined lines was used to distinguish larger changes from small fluctuations that may fall within test-retest variability.³³ However, UCVA may also be influenced by accommodation, participant familiarity, and testing variability. These findings should therefore be interpreted together with the refractive and structural outcomes. Overall, the results suggest that the comprehensive programme may help preserve unaided visual function in primary school children.

Subgroup analyses indicated that the direction of intervention effects was generally consistent across strata defined by baseline myopia status, age, and

Table 4. Subgroup and interaction analyses of changes in axial length, spherical equivalent, and uncorrected visual acuity at 12 months.

Characteristics	Intervention (n=100)	Control (n=98)	Adjusted mean difference (95% CI)	P value	P for interaction
Baseline myopia status					
(1) No myopia at baseline (n=101)					
AL change, mm	0.01 ± 0.05	0.25 ± 0.35	−0.246 (−0.351 to −0.141)	<0.001	0.356
SE change, D	0.08 ± 0.47	−0.64 ± 0.71	0.606 (0.345 to 0.867)	<0.001	0.427
UCVA change	0.41 ± 0.31	−0.28 ± 0.26	0.599 (0.489 to 0.709)	<0.001	0.732
(2) Myopia at baseline (n=97)					
AL change, mm	0.02 ± 0.16	0.32 ± 0.39	−0.316 (−0.424 to −0.209)	<0.001	-
SE change, D	0.38 ± 0.74	−0.31 ± 0.80	0.762 (0.490 to 1.034)	<0.001	-
UCVA change	0.32 ± 0.29	−0.26 ± 0.25	0.573 (0.467 to 0.678)	<0.001	-
Sex					
(1) Boys (n=108)					
AL change, mm	0.01 ± 0.07	0.23 ± 0.38	−0.229 (−0.330 to −0.129)	<0.001	0.090
SE change, D	0.28 ± 0.68	−0.47 ± 0.85	0.785 (0.539 to 1.031)	<0.001	0.229
UCVA change	0.38 ± 0.27	−0.30 ± 0.27	0.653 (0.550 to 0.757)	<0.001	0.482
(2) Girls (n=90)					
AL change, mm	0.01 ± 0.14	0.36 ± 0.35	−0.358 (−0.468 to −0.248)	<0.001	-
SE change, D	0.12 ± 0.52	−0.43 ± 0.68	0.562 (0.291 to 0.832)	<0.001	-
UCVA change	0.36 ± 0.34	−0.23 ± 0.22	0.598 (0.488 to 0.709)	<0.001	-
Age group					
(1) 6–7 years (n=85)					
AL change, mm	0.04 ± 0.12	0.29 ± 0.45	−0.270 (−0.385 to −0.156)	<0.001	0.678
SE change, D	0.13 ± 0.55	−0.55 ± 0.77	0.732 (0.452 to 1.012)	<0.001	0.695
UCVA change	0.41 ± 0.30	−0.24 ± 0.27	0.629 (0.514 to 0.744)	<0.001	0.957
(2) 8–10 years (n=113)					
AL change, mm	0.00 ± 0.10	0.29 ± 0.29	−0.302 (−0.401 to −0.203)	<0.001	-
SE change, D	0.25 ± 0.65	−0.37 ± 0.77	0.658 (0.417 to 0.898)	<0.001	-
UCVA change	0.35 ± 0.31	−0.29 ± 0.24	0.625 (0.525 to 0.724)	<0.001	-

AL: axial length; CI: confidence interval; SE: spherical equivalent; UCVA: uncorrected visual acuity

Data are presented as mean ± standard deviation unless otherwise indicated.

Changes in axial length, spherical equivalent, and uncorrected visual acuity represent the differences between baseline and 12-month follow-up.

Adjusted mean differences and P values were calculated using linear mixed-effects models adjusted for the corresponding baseline outcome value, age, and sex, as appropriate, with class included as a random effect.

Adjusted mean difference = Intervention – Control (95% CI).

P for interaction values were obtained from linear mixed-effects models with interaction terms between intervention group and each subgroup factor. Values are shown once for each outcome within each subgroup factor and are not repeated in the corresponding comparison subgroup.

sex, with no significant interactions. These findings provide no clear evidence that the programme effects differed across the examined subgroups and support the programme's potential applicability in routine primary school settings. Age and baseline refractive status remain biologically plausible effect modifiers because ocular growth varies across developmental stages;^{34,35} however, no significant effect modification was detected in the present study. As some subgroups included relatively few participants, the analyses were exploratory and may have had limited power to detect interactions. Further studies with larger samples and longer follow-up are needed to clarify whether baseline characteristics influence programme effectiveness.

The "1146" myopia prevention and control model developed and implemented in this study integrates strategies across multiple domains, including visual behaviour management, optimisation of learning and visual environments, outdoor activity promotion, visual health monitoring, routine refractive correction, and professional adjunctive components. Its practical value lies in the coordinated implementation of these measures within the school setting rather than in any single intervention component. In this class-based programme, shared classroom environments, teacher supervision, and routine school management may also have supported changes in students' visual behaviours and intervention adherence. The Guidelines for the Prevention and Control of Myopia (2024 edition) issued by the National Health Commission in May 2024³⁶ emphasise a prevention-first approach, early intervention, and multidimensional comprehensive strategies, which are broadly aligned with the design of the present programme.

Although comprehensive intervention strategies for myopia prevention and control in children and adolescents have gained increasing attention, many existing studies have focused on single interventions or short-term outcomes, and evidence regarding the effectiveness of long-term, systematic comprehensive intervention models remains limited.³⁷ Comprehensive interventions involve multiple components and are complex to implement and evaluate. Future studies should include longer follow-up and apply standardised implementation frameworks (such as RE-AIM) to assess reach, effectiveness, adoption, implementation, and maintenance in real-world school settings.^{9,23}

Limitations

Several limitations should be acknowledged. First, the 12-month follow-up may have been insufficient to capture long-term myopia control effects, and the exclusion of participants lost to follow-up may have introduced attrition bias. Second, although the analyses accounted for class-level clustering and

adjusted for the corresponding baseline outcomes, the non-randomised class-level allocation may still have introduced selection bias and residual confounding, limiting causal inference. Participants and intervention providers could not be masked, which may also have influenced behaviour and intervention delivery. Third, the absence of single-intervention comparator groups prevented assessment of the independent contribution of each programme component. The observed differences should therefore be interpreted as the overall effect of the integrated "1146" programme. Fourth, behavioural and environmental components were mainly monitored at class level rather than quantified for each participant, limiting the assessment of associations between individual adherence and outcomes. Fifth, the small sample size in some subgroups may have reduced the power to detect interactions. Finally, as a single-school study, the generalisability of the findings to other schools and regions remains uncertain. Larger multicentre studies with randomised allocation, longer follow-up, and more detailed adherence assessment are required.

CONCLUSION

After accounting for class-level clustering and baseline covariates, this study found that a comprehensive, school-based myopia prevention and control programme was significantly associated with reduced axial elongation and favourable changes in refractive status and UCVA over a 12-month period. The direction of these effects was generally consistent across subgroups stratified by baseline myopia status, age, and sex, with no significant interactions. Given that this was a non-randomised controlled study, causal inference should be made with caution. These findings provide preliminary evidence supporting the feasibility of integrated myopia control strategies in school settings and suggest their potential value for further evaluation in larger, multicentre studies.

Supplementary materials

Supplementary Annex S1. Myopia prevention and control record for children and adolescents.

Supplementary Annex S2. Self-assessment checklist for home visual environment, behaviours, and habits.

Supplementary Annex S3. Adverse event (AE) assessment form for the "1146" comprehensive myopia intervention.

Supplementary Annex S4. Informed consent form for research participants.

Supplementary Fig. S1. Conceptual framework of the "1146" comprehensive myopia prevention and control model.

Supplementary Fig. S2. Box plots of 12-month changes in AL, SE, and UCVA. Changes were calculated as 12-month follow-up minus baseline.

Supplementary Fig. S3. Forest plot of adjusted between-group differences in 12-month changes in AL, SE, and UCVA.

Supplementary Table S1. Comparison of changes in UCVA categories between the 2 groups at 12 months.

Ethics statement

This study was approved by the Medical Ethics Committee of the Inner Mongolia Autonomous Region Comprehensive Center for Disease Control and Prevention (Approval No. 202309271). The study was retrospectively registered with the Chinese Clinical Trial Registry (Registration No. ChiCTR2500114155). All study procedures complied with the Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent was obtained from the parents or legal guardians of all participants before enrolment (Supplementary Annex S4).

Declarations

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

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to ethical restrictions related to participant confidentiality. However, they are available from the corresponding author on reasonable request.

Use of generative AI and AI-assisted technologies

ChatGPT was used only to assist with English language editing. The authors have reviewed and edited the content and take full responsibility for the manuscript.

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Training for constraint in Southeast Asia: Rethinking adaptive expertise in a region of contrasts

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ABSTRACT

Modern clinical training is increasingly conducted in technology-rich environments supported by advanced diagnostics, automated systems, and structured workflows. These environments support efficient learning but may offer fewer opportunities for trainees to develop adaptive expertise, particularly when familiar resources, technologies, or processes are unavailable. Resource availability, however, exists on a spectrum, and even well-resourced systems can become stretched during pandemics, supply-chain disruptions, workforce shortages, or service overload. In such situations, clinicians need to prioritise, communicate clearly, reason with incomplete information, and adapt to changing conditions. For this reason, exposure to settings where resources are stretched, variable, or constrained can complement modern training by strengthening clinical judgement, observation, teamwork, and confidence in core clinical skills. Evidence on elective placements has described self-reported improvements in clinical examination skills, reduced reliance on extensive investigations and greater cultural awareness. However, such experiences must also be ethically and feasibly structured, with attention to host-institution needs, supervision, scope of practice, financing, and equity of access. Since external placements may not be available to all trainees, adaptive expertise should also be cultivated within existing training programmes through history-and-examination-first teaching, no-investigation case discussions, simulation under constraint, and structured reflection. The aim is not to privilege 1 training environment over another, but to prepare clinicians to practise safely and thoughtfully across the full spectrum of resource availability by intentionally building adaptive expertise.

Keywords: clinical competence, global health, health resources, internship and residency, medical education

INTRODUCTION

Modern clinical training frequently unfolds in hospitals filled with advanced tools, automated systems, digital platforms, and highly structured workflows. These settings are efficient and supportive, and they allow early-career clinicians (including students, medical

officers, residents, and junior consultants) to learn with clarity and precision.¹ Yet, this abundance can create an unspoken assumption that technology will always be available. This may limit opportunities to develop “adaptive expertise”—the capacity to balance efficient routine performance with flexible learning, problem reframing, and adjusted reasoning when familiar approaches, resources, or systems are insufficient.^{2,3} Many trainees in modern practice have never had to function without technology-enabled systems, familiar devices, complete equipment or full information. The belief that such tools are permanent becomes so ingrained that it goes unnoticed. What is often overlooked is that these systems are meant to support practice and not define it, and when clinicians train entirely in well-resourced settings, this distinction becomes less obvious. As a result, we may be inadvertently producing clinicians who are less prepared for uncertainty. Furthermore, formal curricula specifically teaching trainees and students about rationing, prioritisation, and adaptive decision-making remain limited.⁴⁻⁶

Adaptive expertise is essential whenever clinical practice moves away from ideal conditions. Even in routine practice, it enables clinicians to apply prior knowledge flexibly, understand why decisions work, and adjust their reasoning when faced with unfamiliar problems, limited resources, or disrupted systems.⁷ This is important because resource availability is not always uniform, even within the same country, region, or healthcare network. Well-resourced tertiary hospitals may coexist with smaller hospitals, rural facilities, crowded emergency departments, outreach services, or clinical situations where diagnostics, staffing, equipment, time, or supply chains are limited. This diversity is evident across Southeast Asia, where advanced tertiary centres, regional referral hospitals, rural facilities, and outreach services may operate within the same health system or regional ecosystem.⁸ Singapore, for example, has highly developed healthcare infrastructure but also functions as a regional referral and training hub within a diverse Southeast Asian healthcare landscape shaped by varying work-

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force, financing, geographic, and service-delivery constraints. The central issue here is whether clinical education prepares trainees to function across this spectrum. When trainees are educated and employed only within a single type of system, they may have limited opportunity to appreciate either the possibilities created by advanced infrastructure or the adaptations required when such support is unavailable. This is especially relevant for clinicians trained mainly in well-resourced environments, as adaptive expertise prepares them for sudden disruption when familiar systems, technologies or resources may become unavailable in unforeseen circumstances.

The value of constraint

Constraint is not limited to 1 type of healthcare setting. It may be seen in rural facilities, crowded emergency departments, outreach services, tertiary units during service overload, or during periods of supply-chain disruption. However, settings where resources are more visibly limited can make these constraints more explicit for trainees. In such environments, clinical work often depends more heavily on judgement, observation, hands-on skill, teamwork, and prioritisation. Trainees may learn to pause before ordering investigations, consider what information is truly necessary, and make decisions based on what is available and feasible. This does not mean that technology-rich settings lack uncertainty or that resource-constrained settings are educationally superior. Rather, each setting teaches a different part of clinical practice. Well-resourced environments show what advanced systems can provide, while constrained environments highlight how clinicians adapt when those supports are delayed, stretched, or unavailable. Exposure across this spectrum can therefore help trainees develop a more balanced understanding of clinical decision-making, where technology supports practice but does not replace clinical reasoning.

When systems are stretched

The COVID-19 pandemic reminded the world how quickly technology and supply chains can be disrupted.⁹ Many well-resourced centres had to function with reduced equipment availability, limited diagnostics, and unpredictable workflows. This did not just reflect poor planning, but also showed that even advanced healthcare systems remain vulnerable to global shocks. In such situations, clinicians may need to make decisions with incomplete information, prioritise resources, communicate clearly, and adapt when familiar systems are unavailable. This experience reinforces the need to prepare trainees for clinical practice beyond routine conditions. When systems are stretched, the ability to observe carefully, reason clinically, work within available resources and communicate

effectively becomes especially important. These skills translate directly into well-resourced settings, where the pace may be faster but the need for clinical judgement, teamwork and situational awareness remains the same. Clinicians who have learnt to function when resources and technology are limited may also understand their value more deeply because they have experienced their absence.

Building clinical adaptability

Clinical exposure across different resource settings can be valuable for early-career clinicians. It can expand their perspective and show that healthcare is not a uniform experience, with real-world practice varying across locations, systems and circumstances.^{10,11} Training in settings where resources are stretched or constrained may prepare trainees to adapt when technology fails, when situations are unfamiliar or when unexpected challenges arise, and it can strengthen cultural competence.¹² Students often pursue such experiences through electives in low- and middle-income countries, rural missions, community outreach programmes, and global health attachments.¹³ Such exposure does not replace modern education; rather, it can complement it by helping trainees develop resilience and confidence in core clinical skills. It can also help ground their adaptive expertise in lived experience rather than theoretical assumptions, allowing them to respond more practically when systems are stretched.

Multiple reports examining self-reported outcomes from elective participants showed improved clinical examination skills, reduced reliance on extensive investigations, enhanced cultural competence, greater ability to recognise diverse disease presentations and increased cost-consciousness in practice.¹⁴⁻¹⁶ These findings should be interpreted in light of the available evidence base, which relies largely on uncontrolled post-elective surveys with an attendant risk of selection and social desirability bias. Nevertheless, as healthcare grows more complex and uncertainty becomes the norm, these qualities remain important. However, the educational value of different settings should be understood as a spectrum rather than a simple contrast between well-resourced and resource-limited environments (Table 1). Such exposure across settings must also be ethically structured, as the educational value for visiting trainees should not come at the expense of host institutions, patients, or local learners.

Integrating adaptive expertise

Today, not every trainee has the opportunity to work across settings where resources are stretched, variable, or constrained. However, considering its importance, training for constraint should not be incidental, but a deliberate component of medical education. This requires moving beyond opportunistic

Table 1: Clinical learning across a spectrum of resource availability.

Theme	Well-resourced/ technology-rich settings	Well-resourced but stretched settings	Mixed-resource/district or regional settings	Resource-constrained settings
Learning environment	Advanced diagnostics, digital systems, and structured workflows are readily available	Resources are available but may be affected by crowding, workload, staffing or delays	Core services are available, but access to specialist care, diagnostics, or referral may vary	Access to diagnostics, equipment, staffing, or referral pathways may be limited
Decision-making	Supported by investigations, protocols, and specialist input	Requires prioritisation when services are busy or delayed	Requires balancing available investigations with clinical judgement and local capacity	Relies heavily on history, examination, observation, prioritisation, and practical judgement
Skill development	Efficient use of advanced tools and structured systems	Triage, situational awareness, and adaptation to service pressure	Flexible decision-making across variable resources	Adaptability, teamwork, improvisation, and reliance on clinical fundamentals
Response to uncertainty	Uncertainty may arise rarely during unusual cases or system disruption	Uncertainty increases during overload, delays or shortages	Uncertainty varies across location, time, and referral access	Uncertainty is often part of routine practice
Educational value	Builds technical competence and familiarity with modern systems	Builds prioritisation and resilience under pressure	Builds context-sensitive decision-making	Builds resource-conscious practice and confidence in clinical fundamentals
Overall contribution	Teaches what advanced systems can provide	Teaches how to work when systems are stretched	Teaches how to adapt across variable settings	Teaches how to care when ideal supports are unavailable

This table is an illustrative synthesis developed by the authors to show that resource availability exists on a spectrum, and adaptive expertise can be developed in all settings when training is intentionally structured. The categories shown are conceptual and may overlap.

exposure towards intentional curriculum design. Institutions, together with mentors and collaborators, can play an active role by establishing structured exchange programmes and partnerships, rather than leaving trainees to seek such experiences independently. In doing so, exposure to different resource settings can become a routine and supported part of training rather than an exception. However, such programmes require clear ethical guardrails.

Poorly structured placements may create unintended harm through inadequate supervision, work beyond the trainee's competence, disruption of host services, unequal benefit, or additional supervisory burden on host institutions.^{17,18} Therefore, formal partnerships should not merely streamline access for trainees, but should be based on host-identified needs, appropriate supervision, clear scope of practice, informed consent where relevant, ethics oversight, trainee preparation, and structured reflection. Partnerships should also be bidirectional, so that learning and benefit flow both ways between participating institutions. This may include reciprocal training opportunities, where learners from resource-constrained settings also gain exposure to advanced technologies, specialist services and structured systems in well-resourced environments. The guidelines developed by the Working Group on Ethics Guidelines for Global Health Training provide useful principles

for designing such programmes ethically, including mutual benefit, clear agreements between host and sending institutions, attention to host needs and costs, defined trainee roles, appropriate supervision, trainee preparation, safety, feedback, and periodic review.¹⁷ Subsequent work examining partner-organisation perspectives further reinforces the importance of matching trainee skills to host needs and ensuring that host institutions have a meaningful voice in programme design.¹⁸

Feasibility must also be considered before such programmes are implemented. Structured exposure across different resource settings requires clear planning for travel, accommodation, insurance, indemnity, visa and regulatory clearance, as well as clarity on scope of practice across jurisdictions. Host institutions may also require adequate supervisory capacity and appropriate support for the time spent orienting, supervising, and assessing visiting trainees.¹⁷ Programme design should also account for host-identified needs and ensure that trainee roles are matched to local priorities.¹⁸ To avoid making such experiences available only to trainees who can self-fund them, institutions should consider equitable funding models, bursaries or centrally supported placements. Therefore, implementation should involve not only educational planning, but also financing, governance, legal clarity, and equity of access.

In-house strategies to build adaptive expertise

While the above-mentioned strategies are being developed, adaptive expertise can also be deliberately introduced into routine training within any clinical setting. This may be the most immediately feasible approach for many institutions, including well-resourced training programmes, and is consistent with curriculum-design approaches that support the development of adaptive expertise.¹⁹ Practical strategies include history-and-examination-first teaching rounds, where trainees are asked to present an initial assessment and management plan before reviewing advanced investigations; “no-investigation” case discussions, where imaging, laboratory tests, or subspecialty input are temporarily withheld to encourage clinical reasoning; and simulation sessions in which familiar resources are deliberately made unavailable. For example, trainees can be asked to manage deterioration with limited monitoring, plan referral when transport is delayed, prioritise patients during service overload, or make decisions when diagnostic results are incomplete.

These exercises should be followed by structured debriefing that asks what assumptions were made, what resources were prioritised, what risks were accepted, and how decisions would change if additional support became available. Mentorship from clinicians with experience across different resource settings can further help trainees understand how clinical reasoning, communication, and teamwork change under constraint.²⁰ While these approaches may not fully replicate the perspective gained on the ground in settings where resource limitations shape daily practice, they can introduce the core principles of adaptive reasoning without the ethical, equity, and cost barriers of external placements. Without such intentional training, clinicians may become highly competent within familiar systems but less prepared for the realities of uncertainty.

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ChatGPT 5.3 Instant (OpenAI) was used solely as a general-purpose writing aid. The initial drafts were written by the authors, and AI was employed to polish grammar and improve coherence. All suggested edits were manually reviewed and selectively incorporated by the authors.

Ethics statement

Not applicable as no patient data was used in this article.

Declaration

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Novel insights on dementia care: Multidimensional benefits of doll therapy uncovered in cross-cultural meta-analysis

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Dear Editor,

Dementia affects 57 million people globally, with projections reaching 153 million by 2050.¹ Behavioural and psychological symptoms of dementia (BPSD) occur in 97% of patients, accelerating functional decline, intensifying caregiver burden, and raising risks of institutionalisation and healthcare costs.² Given the limited efficacy and adverse effects of pharmacological agents, non-pharmacological interventions are prioritised as first-line.³ Doll therapy (DT), rooted in attachment theory,⁴ regulates emotions by activating the limbic circuit through doll interaction, offering a low-cost approach to alleviating patient distress.⁵ However, existing evidence remains insufficient to draw firm conclusions, largely because previous studies have overlooked the cultural context of dementia care and have mixed random and non-random designs. Most research has been conducted in Western contexts. This overrepresentation is particularly problematic given that China accounts for approximately 25% of the world's dementia cases.⁶ This study reviews existing literature and conducts a meta-analysis to evaluate the effects of DT based exclusively on randomised controlled trial (RCT) evidence. It comprehensively assesses the multidimensional effects on behavioural symptoms (particularly agitation), cognitive function, and emotional states, and systematically analyses moderators of therapeutic efficacy.⁷ This review synthesises the evidence from different cultures, guides the development of cultural interventions, and lays the foundation for the implementation of evidence-based, person-centred care.

According to the Cochrane Handbook⁸ and Preferred Reporting Items for Systematic reviews and Meta-Analyses 2020 guidelines⁹ (PROSPERO

CRD42024506258), the authors searched 6 English-language databases (PubMed, Embase, Cochrane Library, Web of Science, Ovid, EBSCOhost) and 4 Chinese-language databases (China National Knowledge Infrastructure, Wanfang, VIP, Chinese Biomedical Database) from inception to 26 January 2024. Eligible participants were individuals aged ≥ 65 years with a dementia diagnosis. The review compared the effects of DT with standard care or other non-pharmacological interventions. Primary outcomes included behavioural symptoms (especially agitation), cognitive function, and emotional states; quality of life was a secondary outcome (Supplementary Table S1). Two reviewers independently screened studies, extracted data, and the Cochrane Risk of Bias tool was used to assess the risk of bias. Statistical analyses in Stata version 16.0 (StataCorp, College Station, TX, US) employed standardised mean differences (SMDs) under random effects models. Heterogeneity was quantified with I^2 ; sources were explored through subgroup, sensitivity, and meta-regression analyses. Evidence quality was rated with the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework.¹⁰

Twelve RCTs involving 1245 participants (mean age 78.7 years, 67.2% female) published between 2017 and 2022 in Australia ($n=2$), Italy ($n=3$), Switzerland ($n=1$), China ($n=5$), and Turkey ($n=1$) met inclusion criteria (Supplementary Fig. S1). Four studies were conducted in Chinese hospitals and the remainder in nursing homes, long-term care facilities, and other social institutions; most participants had mixed dementia (60.6%). Interventions used lifelike or empathy dolls; session lengths ranged from 15 minutes to 3 hours and total intervention duration from 2 to 72 weeks (Supplementary Table S1). Risk-of-bias

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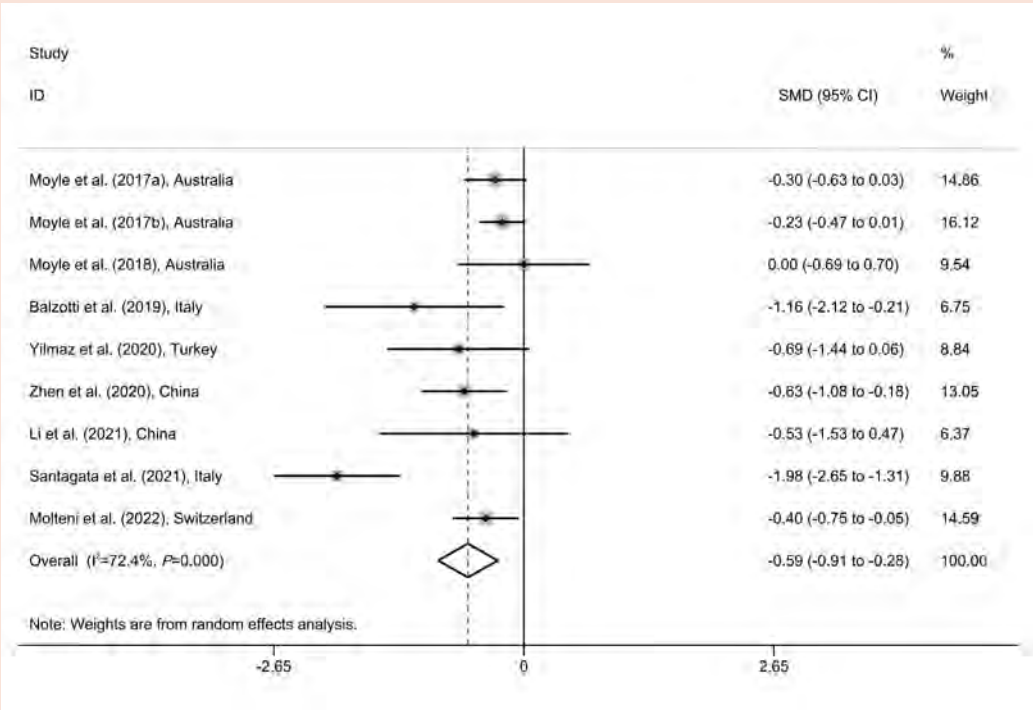
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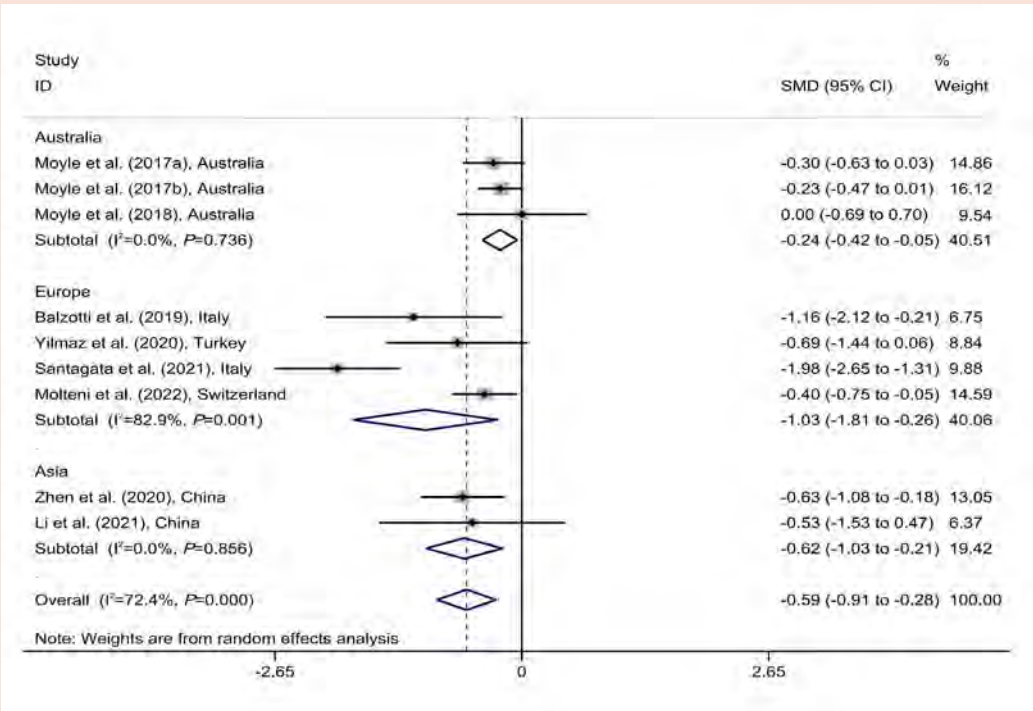
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Fig. 1. Forest plots of agitated behaviour and subgroup analysis. (A) Forest plots of agitated behaviour. (B) Subgroup analysis of regional differences. (C) Subgroup analysis of intervention design. (D) Subgroup analysis of control group.

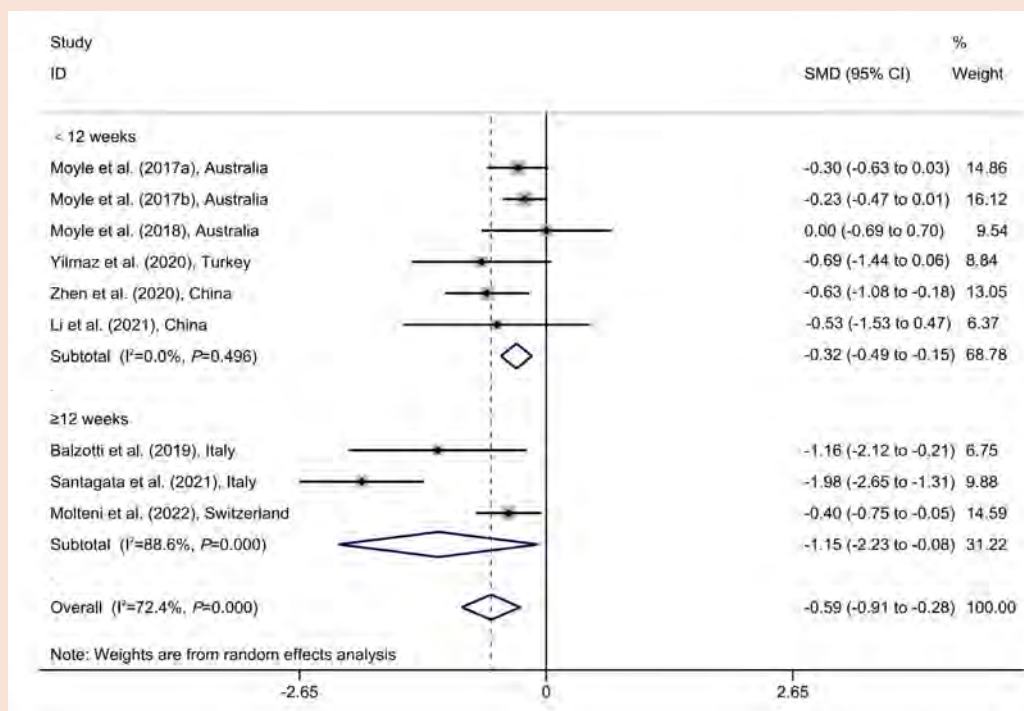
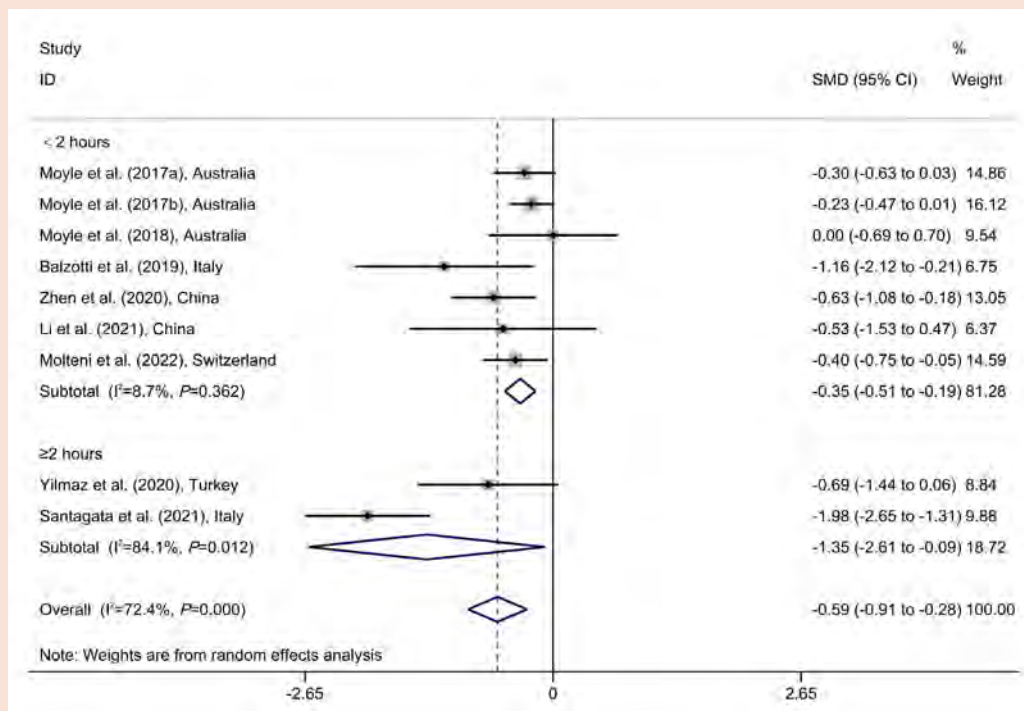
A. Forest plots of agitated behaviour.



B. Subgroup analysis of regional differences.



C. Subgroup analysis of intervention design.

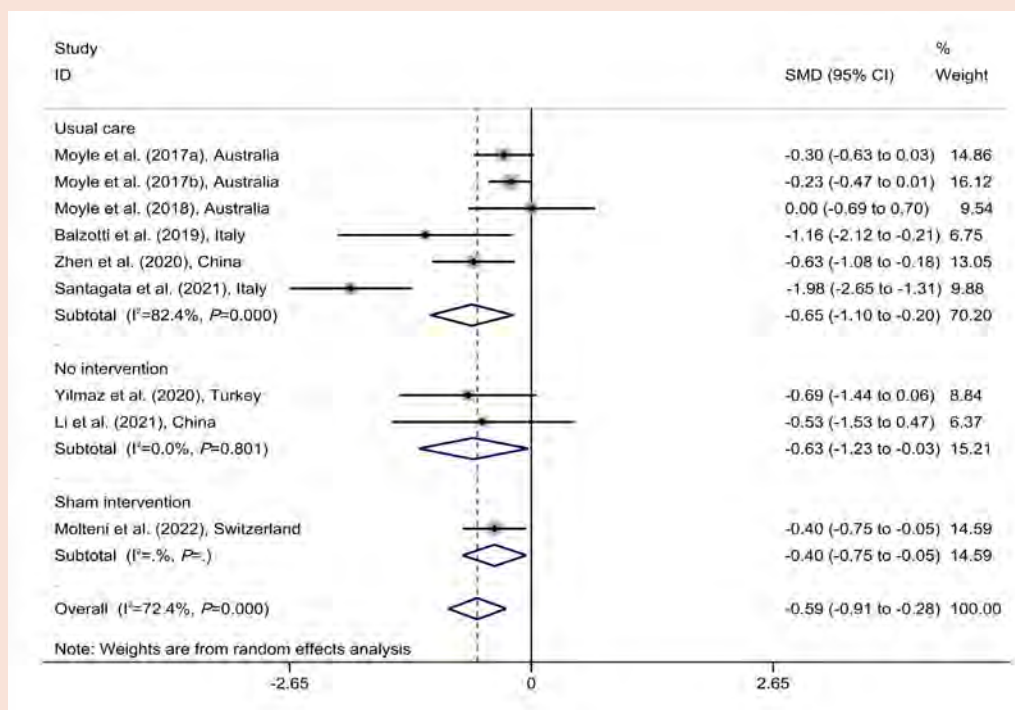


assessment showed good data integrity and appropriate randomisation in most trials, although allocation concealment and blinding required improvement (inter-rater kappa = 71.4–100.0%; Supplementary Table S2).

The meta-analysis demonstrated that DT significantly reduced agitation—the outcome supported

by the high-quality evidence (9 studies, $n=845$) and the only outcome awarded a high GRADE rating (Supplementary Table S3). The pooled effect was $SMD=-0.59$ (95% confidence interval [CI] -0.91 to -0.28, $P<0.001$; $I^2=72.4\%$) (Fig. 1). Egger's test showed no publication bias ($P=0.119$). Sensitivity analysis identified 1 outlier (Santagata et al.¹¹; $SMD=-$

D. Subgroup analysis of control group.



CI: confidence interval; SMD: standardised mean difference

1.98); its removal reduced heterogeneity to $I^2=5.1\%$ while preserving significance ($SMD=-0.36$, $P<0.001$), confirming robustness.

Subgroup and meta-regression analyses identified key moderators of efficacy. Regional differences revealed varying effect sizes: Europe¹² ($SMD=-1.03$, 95% CI -1.81 to -0.26), Asia¹³ ($SMD=-0.62$, 95% CI -1.03 to -0.21), and Australia¹⁴ ($SMD=-0.24$, 95% CI -0.42 to -0.05), underscoring the influence of cultural contexts on acceptance and implementation. Intervention intensity showed that longer session length (≥ 2 hours; $SMD=-1.35$, 95% CI -2.61 to -0.09) and greater total intervention duration (≥ 12 weeks; $SMD=-1.15$, 95% CI -2.23 to -0.08) produced markedly larger effects than shorter regimens. DT also showed the greatest advantage over standard care ($z=2.82$, $P=0.005$) (Fig. 1). Meta-regression confirmed region (coefficient = 0.39, $P=0.023$) and session length (coef = -1.04, $P<0.001$) as independent predictors; doll type and participant characteristics were non-significant ($P>0.05$).

For the remaining outcomes, DT improved overall behavioural symptoms (7 studies; $SMD=-0.95$, 95% CI -1.38 to -0.53, $P<0.001$, $I^2=66.2\%$), with parallel subgroup patterns favouring European studies and longer session length (Supplementary Fig. S2). Sensitivity analyses confirmed robustness despite

heterogeneity. Quality of life demonstrated a large, consistent gain (4 studies; $SMD=1.00$, 95% CI 0.81–1.18, $P<0.001$; $I^2=0.0\%$, moderate-quality evidence; Supplementary Fig. S3). Cognitive function showed a positive but non-significant trend (5 studies; $SMD=0.70$, 95% CI -0.05 to 1.45, $P=0.068$, $I^2=93.5\%$; Supplementary Fig. S4). Narrative synthesis revealed additional benefits for emotional states (reduced anxiety and depression, increased happiness) and other behavioural symptoms (apathy, irritability, and eating behaviour).

These findings indicate that DT significantly reduces overall behavioural symptoms and agitated behaviours while improving emotional states. Subgroup analyses showed that longer session lengths and European settings are associated with greater effectiveness, highlighting the critical role of sustained engagement and cultural factors. For agitation specifically, sensitivity analysis confirmed Santagata et al.¹¹ as the primary source of heterogeneity, attributable to its rigorous design and high-quality care delivery. Meta-regression and subgroup analyses verified that longer session length (≥ 2 hours), longer total intervention duration (≥ 12 weeks), and regional differences independently enhanced efficacy, aligning with attachment theory's emphasis on prolonged interaction for emotional bonding and regulation.

Notably, most of the studies with a session length of more than 2 hours and a total intervention duration of more than 12 weeks were conducted in Europe, which means that the effectiveness of DT is related to cultural factors and intervention design. In Asia, particularly in China, dementia care is inevitably influenced by ethical norms, demographic structure, and family caregiving practices. Moreover, most of the included studies were conducted in hospital settings and focused on specific patient subgroups. These settings are not conducive to fully realising DT's therapeutic potential for complex psychosocial needs. By contrast, European studies place greater emphasis on diversified activity-based interventions and emotional support, and the effectiveness of DT is relatively high. In Australian studies, the effectiveness of DT is relatively low, which is inevitably related to the intervention parameters and nursing environment.

In contrast, quality-of-life gains remained consistent across populations, affirming DT's universal provision of emotional support, psychological comfort, and social belonging. Cognitive effects displayed a complex cross-cultural pattern and overall non-significance, with stronger potential in culturally congruent Asian hospitalised populations due to early stimulation, while European studies focused on emotional support yielded mixed results, possibly reflecting differences in intervention objectives, patient subgroups, and assessment tools.

This is the first meta-analysis to analyse DT only from the perspective of RCTs, in order to eliminate the influence of design confounding, and to explore the differences between cultures through sensitivity analysis, GRADE and other methods, to enhance confidence. Nevertheless, there are some limitations, including the methodological heterogeneity, such as the unclear allocation concealment, the small sample size, the different protocols, and the geographical concentration, of which 5 studies were conducted in China, all in the hospital environment. The diagnostic scope was also limited, focusing on Alzheimer's disease and not analysing the aetiology. In addition, the intervention time is relatively short (4 weeks). The cultural adaptation framework (particularly regarding family-centred care in Asian contexts) remains underdeveloped, which restricts its applicability. Accordingly, future research should prioritise culturally tailored protocols (e.g. family-supervised community kits), large multicentre trials with extended follow-up across contexts, and investigations into neurobiological mechanisms connecting emotional security to behavioural and cognitive gains, thereby reinforcing the imperative for locally responsive evidence-based interventions.

In conclusion, DT is a valuable, cost-effective addition to dementia care that meaningfully improves behavioural symptoms, emotional states, and quality

of life, particularly when delivered with adequate session length, sufficient total intervention duration, and cultural sensitivity. By providing, to the authors' knowledge, the first quantitative evidence of cross-cultural variation and intervention intensity effects through rigorous subgroup, sensitivity, and meta-regression analyses, this study advances the field towards truly personcentred, culturally inclusive, and resource-optimised interventions worldwide.

Supplementary materials

Fig. S1. PRISMA diagram flow of the study selection process.

Fig. S2. Forest plots of overall behaviour and subgroup analysis.

Fig. S3. Forest plots of quality of life.

Fig. S4. Forest plots of cognitive function.

Table S1. General characteristics of the included articles.

Table S2. Summary of risk of bias judgements for each study.

Table S3. Summary of findings.

Ethics statement

Not applicable, as no study participants were involved.

Declaration

The authors declare that they have no affiliations with or involvement in any organisation or entity with any financial interest in the subject matter or materials discussed in this manuscript. There is no conflict of interest or funding to declare.

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Keywords: *behavioural symptoms, cultural adaptation, dementia, doll therapy, non-pharmacological intervention, nursing, quality of life*

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Percutaneous electrosurgical leaflet laceration to prevent coronary obstruction during TAVI for severe aortic regurgitation

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Dear Editor,

Percutaneous transcatheter aortic valve implantation (TAVI) has become an established therapy in elderly patients with severe aortic valve stenosis (AS) and an “off-label” option in selected patients with severe aortic regurgitation (AR) at high surgical risk.¹ There is also increasing use of TAVI to treat degenerated bioprosthetic surgical aortic valve replacement. Coronary artery occlusion (CAO) is an uncommon but life-threatening complication of TAVI, and occurs when the transcatheter heart valve (THV) pushes the native aortic or surgical valve leaflets outward and occludes the coronary ostia. Furthermore, as TAVI is increasingly performed in younger patients, preserving future coronary artery access has become an important consideration. Recently, catheter-based electrosurgical leaflet laceration with techniques, such as bioprosthetic or native aortic scallop intentional laceration to prevent iatrogenic coronary artery obstruction (BASILICA), has been developed to prevent CAO and to preserve coronary access by splaying open the native or surgical leaflet(s) (Figs. 1A and 1B).

Several studies have demonstrated that in patients undergoing TAVI at elevated risk of CAO, BASILICA is effective in preventing or reducing CAO.^{2,3} However, widespread use of this technique is limited by procedural complexity. The authors report a case of electrosurgical native leaflet laceration to prevent coronary occlusion during TAVI in a patient with severe AR and at significant risk of CAO.

A 63-year-old male with end-stage renal failure on haemodialysis, and a renal transplant that failed 4 years prior, presented with exertional dyspnoea (New York Heart Association [NYHA] class II). Echocardiography showed normal left ventricular ejection fraction (60%), dilated left ventricle (end-diastole 6.2 cm), and severe AR due to valve malcoaptation. There was no significant AS (aortic valve area by planimetry was 2.2 cm² by both echocardiography and computed tomography [CT]; mean pressure gradient was mildly elevated at 23 mmHg, consistent with increased forward flow due to the severe AR). Although the

patient's Society of Thoracic Surgeons score of 3.76% for 30-day mortality (22.9% for 30-day mortality/morbidity) indicated moderate surgical risk, he was deemed to be at high surgical risk by the cardiac surgeon owing to frailty, low body weight, previous major gastrointestinal bleeding, and splenic rupture—and was referred for TAVI. CT aortogram showed aortic annulus area 420 mm² (23 mm diameter), left ventricular outflow tract diameter 25 mm, sinus of Valsalva diameter 29 mm, and aortic leaflets were markedly thickened without calcification (Fig. 1C). The left coronary artery (LCA) take-off height was low at 7.9 mm, and the left coronary leaflet was bulky and long (length 14.1 mm) (Fig. 1D), indicating elevated risk of left CAO. TAVI with BASILICA was planned to reduce the risk of left CAO and to preserve future access to the LCA.

The procedure was performed under general anaesthesia with fluoroscopy and transoesophageal echocardiography (TEE) guidance. Details of the BASILICA procedure have been described elsewhere.⁴ In brief, through an 8-French size Amplatz Left 2 curve guide catheter, an Astato 20 (stiff 0.014-inch peripheral angioplasty) wire is positioned at the root of the left aortic cusp below the LCA (Fig. 1E). The wire is electrified using an electrosurgery pen, and advanced through the leaflet into the left ventricular outflow tract (LVOT) (Fig. 1F). A 25 mm Gooseneck snare pre-positioned in the LVOT then snares the Astato wire (Fig. 1G). The Astato wire is pulled back against the leaflet (Fig. 1H), a “flying V” is created and positioned at the leaflet base, and then the “flying V” is electrified and pulled upwards into the ascending aorta to lacerate the leaflet (Fig. 1I). Leaflet laceration was evident by a drop in diastolic pressure and visualisation of split leaflets on TEE (Figs. 1J and 1K). A balloon-expandable 26 mm Sapien 3 Ultra Resilia (Edwards Lifesciences, Irvine, CA, US) THV was successfully implanted (at nominal volume) with upfront cerebral embolic protection (Sentinel system, Boston Scientific, Marlborough, MA, US). Root aortography showed that the LCA was patent (Fig. 1L).

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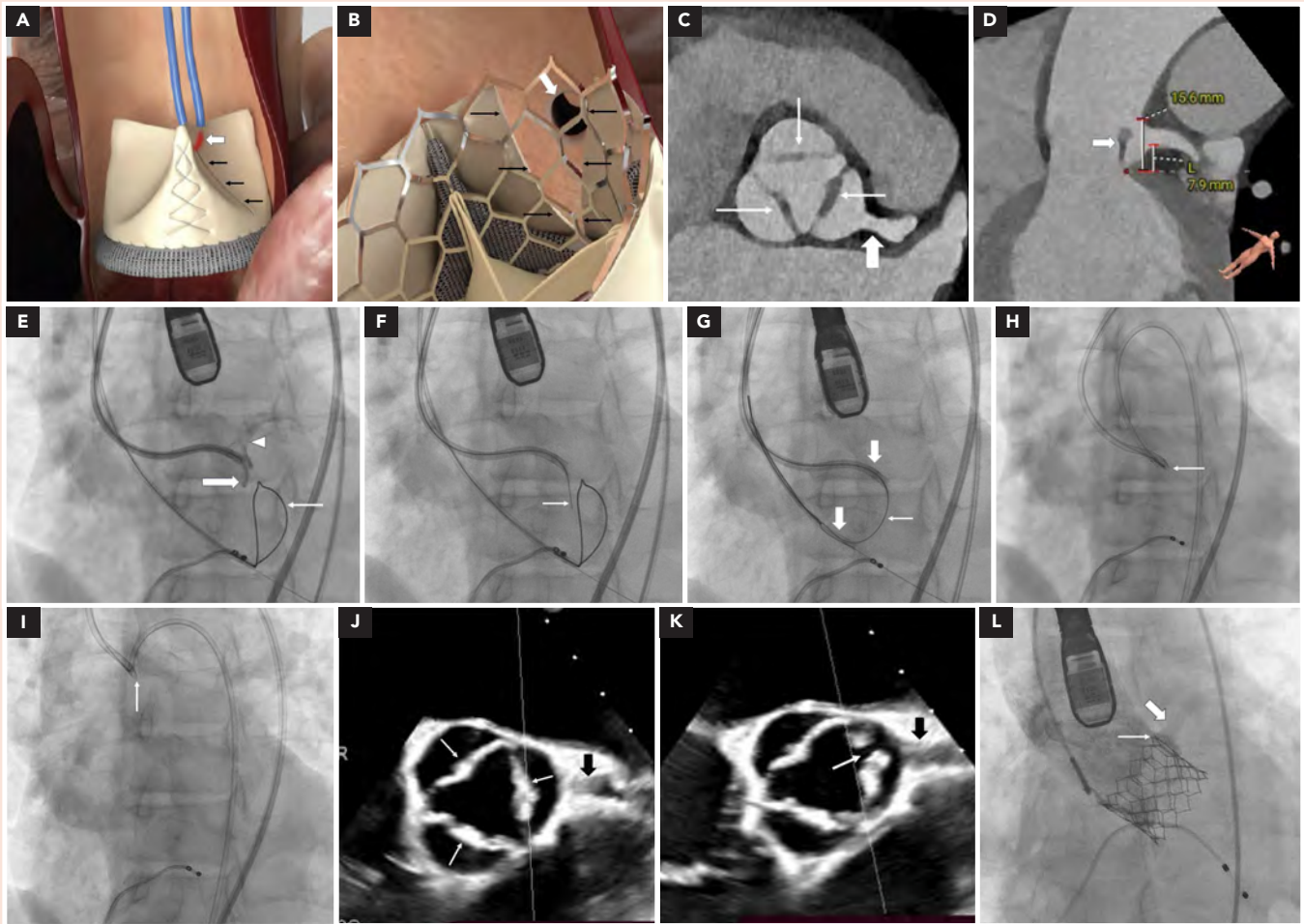
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Fig. 1. BASILICA illustration and images of electrosurgical leaflet laceration during TAVI.



(A) Picture illustrating the electrified guidewire (thick arrow) lacerating the aortic leaflet in a linear fashion (thin arrows). **(B)** Picture showing the leaflet splay (thin arrows) after BASILICA, allowing blood into the coronary artery (thick arrow). **(C)** CT image showing the thickened aortic leaflets (thin arrows) and the low-lying left coronary artery (thick arrow). **(D)** CT image showing the low-lying left coronary artery (7.9 mm) and the thickened bulky leaflet (thick arrow). **(E)** Fluoroscopic image showing the Astato wire within the microcatheter (thick arrow) at the root of the aortic cusp, contrast dye in the left main coronary artery (arrow head), and a snare positioned in the LVOT (thin arrow). **(F)** Fluoroscopic image showing the electrified guidewire traversal across the aortic cusp (thin arrow) into the LVOT. **(G)** Fluoroscopic image showing the snared Astato guide wire (thin arrow) internalised within the catheters (thick arrows). **(H)** Fluoroscopic image showing the pulling of the catheters with the “flying V” of the Astato wire (arrow) against the leaflet. **(I)** Fluoroscopic image showing the catheters being pulled upwards into the ascending aorta and lacerating the leaflet. **(J)** TEE image of the short axis view of the aortic valve in systole just prior to BASILICA, showing the thickened leaflets (thin arrows), unrestricted aortic valve opening, and the left main artery (thick arrow). **(K)** TEE image of the short axis view of the aortic valve in systole immediately after BASILICA, showing the split left coronary leaflet (thin arrow) and the left main artery (thick arrow). **(L)** Fluoroscopic image showing good contrast opacification in the left coronary artery (thick arrow) despite the valve abutting the sinotubular junction (thin arrow). If not lacerated, the bulky and long native leaflet would have been sandwiched between the valve frame and the left coronary artery, potentially causing coronary occlusion.

BASILICA: bioprosthesis or native aortic scallop intentional laceration to prevent iatrogenic coronary artery obstruction; CT: computed tomography; LVOT: left ventricular outflow tract; TAVI: transcatheter aortic valve implantation; TEE: transoesophageal echocardiography

The patient was discharged 2 days post-procedure. At 6 months, he was in NYHA functional class I. Echocardiography revealed satisfactory valve haemodynamics (mean pressure gradient 15 mmHg), no AR, and a reduction in end-diastolic left ventricle size to 5.6 cm.

CAO is a rare complication of TAVI, occurring in <1% of patients; it is however, associated with a high mortality rate of 40% at 30 days.⁵ Most of such cases

are due to direct CAO by the native aortic or surgical leaflets that are pushed outwards by the THV; in a minority of cases, CAO occurs due to sealing of the sinus of Valsalva when the native aortic or surgical leaflets are pushed against the sinotubular junction.

Certain CT measurements have been found to predict an elevated risk of CAO, such as a low coronary height as measured from the aortic annulus (≤ 10 mm), narrow sinus of Valsalva relative to size of the THV to

be implanted with a virtual valve-to-coronary distance of <4 mm, and bulky calcified leaflets (calcium volume >600 mm³).^{2,6}

Electrosurgery leaflet laceration (BASILICA) has been shown to be effective at preventing CAO in patients with native AS or bioprosthetic valve failure.² Using commercially available equipment, the target leaflet is lacerated, and after THV implantation, the lacerated leaflet is pushed outwards and is splayed open. This triangular space allows coronary blood flow through the THV stent struts. Another benefit of BASILICA is that it will likely facilitate cannulation of the coronary artery, which is relevant in younger patients who may require future percutaneous coronary intervention.⁷

Data from the BASILICA trials have been promising with rare CAO in patients with the highest risk anatomy. Previously to prevent CAO, a simpler technique—chimney/snorkel stenting, where a stent is implanted at the coronary ostium with protrusion into the aorta—was used. However, there is a lack of data on its longevity with the stent extending beyond the coronary ostium and sandwiched by a THV. There are concerns of inability to re-access the coronary artery, stent deformation, fatal in-stent restenosis or thrombosis, and need for indefinite dual antiplatelet therapy.^{8,9} In a non-randomised trial comparing BASILICA versus chimney stenting, both therapies were equally effective in preventing CAO; however, there was a numerically higher 1-year cardiovascular mortality with chimney stenting.³ Despite these advantages, there are several limitations of the BASILICA technique. There is a minute residual risk of CAO after BASILICA, particularly if the laceration was not performed from the base of the coronary cusp or directly below the coronary ostium. Hence, coronary protection with a guide catheter and coronary wire may still be necessary. Haemodynamic instability can occur after BASILICA leaflet laceration due to increased AR, although this fortunately, has been rare. As BASILICA is a technically complex procedure, a simpler alternative technique of leaflet modification has been developed—Undermining Iatrogenic Coronary Obstruction with Radiofrequency Needle (UNICORN)—where after leaflet traversal with the electrified Astato wire, the aortic leaflet is dilated with standard angioplasty balloons, and the THV is implanted directly within the aortic leaflet, pushing it away from the coronary ostium.

This case was unique for several reasons. First, this is 1 of the few reported cases of BASILICA in a patient with severe AR worldwide,¹⁰ and 1 of the early cases of BASILICA for native aortic valve in Southeast Asia. BASILICA for native aortic valve is a higher risk procedure than BASILICA for degenerated surgical aortic bioprosthesis. Without a radiologically visible sewing ring to help direct the electrified wire, there

is a higher risk of aortic root or myocardial injury in native aortic valve BASILICA. Second, the authors demonstrate that TAVI with a balloon-expandable valve is feasible in severe AR with markedly thickened leaflets, despite being an off-label indication. In this case, the thickened leaflets provided adequate surface friction for THV anchoring. This case is different from conventional pure non-calcific severe AR with thin leaflets where the risk of device embolisation or migration is significant using standard TAVI valves. JenaValve, the purpose-designed THV for AR is commercially available (JenaValve Technology, Irvine, CA, US); however, it is not readily available in Southeast Asia. Furthermore, the long-term durability of the JenaValve is unknown, unlike the Sapien 3 Ultra Resilia valve, where the Resilia tissue fixation has been demonstrated, in surgical bioprosthetic valves, to be more durable than previous tissue fixation technology.¹¹ This may be beneficial in a young patient on haemodialysis, although the crimping process that THVs undergo before implantation may affect valve durability, regardless of the tissue fixation technology.

In conclusion, this report demonstrates that electrosurgical leaflet laceration during TAVI is a feasible method of reducing the risk of CAO in patients with high-risk anatomy, and may also preserve coronary artery access which is an important consideration, particularly for younger patients who may have greater need for future percutaneous coronary intervention.

Ethics statement

Written informed consent was obtained for anonymised patient information to be published in this article.

Declaration

Dr Paul Chiam serves as a proctor for Edwards Lifesciences. The other authors declare they have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript.

Keywords: aortic regurgitation, aortic stenosis, coronary occlusion, electrosurgery, leaflet laceration, transcatheter aortic valve replacement

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Feasibility of targeted tonsillectomy histology in Southeast Asia: A review of 4115 paediatric tonsillectomies

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Dear Editor,

Tonsillectomy is commonly performed in paediatric patients to treat adenotonsillar hypertrophy and related symptoms, or chronic or recurrent tonsillitis.¹ In Singapore's KK Women's and Children's Hospital (KKH—the country's largest public hospital specialising in healthcare for women and children—all tonsillectomy specimens undergo histological examination, constituting 16% of the paediatric histopathology case-load. Opinions vary on whether all routine tonsillectomy specimens must undergo histological examination.

Recent studies show that tonsillar malignancies are rare and present with distinctive clinical features, such as tonsillar asymmetry and cervical lymphadenopathy.^{2,3} Some centres therefore limit histological examination to cases with high-risk clinical features (targeted tonsil histopathology). Proponents argue that this conserves healthcare resources while not missing critical diagnoses such as malignancies.³ This approach has been adopted in guidelines from the Royal College of Pathologists.⁴ Conversely, a study in a tuberculosis-endemic region described incidental detection of active tuberculosis through routine histopathological tonsil examination, arguing in support of examining all tonsils histologically.⁵ Most studies supporting targeted tonsil histopathology were performed in the US, with no large-cohort studies in Southeast Asia.⁶ The authors sought to assess the feasibility of targeted tonsil histopathology in a population through a retrospective review of tonsillectomy specimens at KKH.

All tonsillectomy pathology reports from 2015 to 2024 for patients under 21 years old who underwent tonsillectomy in KKH were retrospectively reviewed. Clinical indications were obtained from pathology request forms. Where necessary, electronic patient records were reviewed to ascertain clinical indications or clinical impact of pathologic findings. In accordance with SingHealth Centralised Institutional Review Board, department and institution representatives endorsed

this study as a service improvement project, not requiring review by institutional review board.

There were 4115 tonsillectomy cases, comprising 8176 individual tonsils. Patients' age ranged from 10 months to 20 years (median 7.00 years); 63.4% were male. The majority (3882, 94.3%) presented with tonsillar hypertrophy, sleep-disordered breathing, and/or recurrent tonsillitis, without the presence of tonsillar asymmetry, lymphadenopathy, or any other worrisome clinical features. Clinical tonsillar asymmetry and/or lymphadenopathy was present in 163 cases (3.96%), including 153 with only tonsillar asymmetry, 7 with only lymphadenopathy, and 3 with both. Other clinical presentations are outlined in Table 1. Histopathology revealed only reactive lymphoid hyperplasia in 4065 cases (98.8%). Malignant diagnoses comprised Burkitt lymphoma in 2 cases (0.05%). Other diagnoses included non-necrotising granulomatous inflammation (7, 0.17%), necrotising granulomatous inflammation (2, 0.05%), features reminiscent of Rosai-Dorfman disease (RDD) (3, 0.07%), and rare atypical squamous cells (1, 0.02%). Remaining diagnoses are outlined in Table 1. Specimens with granulomatous inflammation did not show fungal organisms or acid-fast bacilli on special stains.

Tonsillar malignancies invariably presented with lymphadenopathy or tonsillar asymmetry, both of which would have prompted histopathological examination under a targeted approach, consistent with previous reports.^{2,3} Of the 2 patients with Burkitt lymphoma, 1 patient presented with massive cervical lymphadenopathy, leading to overt clinical suspicion of malignancy. The other patient presented with upper respiratory tract symptoms, snoring, and mouth breathing. Clinical examination showed asymmetric tonsillar enlargement documented as grade 5+ right tonsil enlargement, crossing the midline, and grade 1 left tonsil enlargement. Tonsillectomy was performed to treat snoring and exclude lymphoma. Gross examination of the right tonsil showed soft to fleshy,

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Table 1. Characteristics of patients undergoing tonsillectomy.

Clinical presentation	no. (%)
Tonsillar hypertrophy (including snoring, obstructive sleep apnoea) and/or recurrent tonsillitis, with no other worrisome clinical features	3882 (94.34)
Asymmetry and/or lymphadenopathy	163 (3.96)
Otitis media with effusion	31 (0.75)
Peritonsillar cellulitis/abscess	13 (0.32)
Oropharyngeal mass lesion	11 (0.27)
Para/retropharyngeal abscess	5 (0.12)
Tonsillolith	3 (0.07)
Rosai-Dorfman disease	1 (0.02)
CHARGE syndrome	1 (0.02)
Excision of right branchial fistula	1 (0.02)
Chronic sinusitis	1 (0.02)
Raised Epstein-Barr virus antibody titres	1 (0.02)
Recurrent tonsillitis and infections on a background of previous leukaemia	1 (0.02)
Halitosis	1 (0.02)
Pathologic findings	
Reactive lymphoid hyperplasia only	4065 (98.78)
Abscess/microabscess	13 (0.32)
Acute +/- chronic inflammation	8 (0.19)
Granulomatous inflammation (non-necrotising)	7 (0.17)
Benign cyst	5 (0.12)
Histologic features similar to Rosai-Dorfman disease	3 (0.07)
Burkitt lymphoma	2 (0.05)
Granulomatous inflammation (necrotising)	2 (0.05)
Other reactive process	2 (0.05)
Organism	2 (0.05)
Rare atypical squamous cells	1 (0.02)
Choristoma	1 (0.02)
Squamous papilloma	1 (0.02)
Lymphangiomatous polyp	1 (0.02)
Fibroepithelial polyp	1 (0.02)
Lymphoid papillary hyperplasia	1 (0.02)
Total	4115 (100)

CHARGE: coloboma, heart defects, atresia of the choanae, retarded growth and development, genital abnormalities, and ear abnormalities
 In bold, the 2 most important diagnostic categories in this study's findings.

white nodular cut surfaces. Both patients were treated with chemotherapy, achieving remission. Given the worrisome clinical findings in the second case, there was no necessity to rely on an abnormal gross appearance of the specimen for the second case to raise suspicion of malignancy, suggesting that gross examination of all resected tonsils in the laboratory is unnecessary, as argued by others.³ No studies reported cases where detection of malignancy depended solely upon abnormal gross pathologic findings without suggestive clinical features.

Tonsillar granulomas were not associated with any particular clinical presentation or sinister pathology. Patients with non-necrotising granulomas were followed up routinely, and no additional clinical aetiologies were diagnosed. One of 2 patients with necrotising granulomatous inflammation defaulted follow-up and was clinically well 2 years later. The other patient's tonsils showed *Actinomyces* organisms and granulomas extending to connective tissue and skeletal muscle at the deep margin. Polymerase chain reaction was negative for tuberculosis. The patient was treated for *Actinomyces* infection with 3 months of antibiotics and remained well. Observation was offered as an alternative management strategy because *Actinomyces* infection is usually slowly progressive and clinically evident,⁷ giving ample opportunity for treatment. Omitting tonsil examination would not have had major implications if there had been adequate follow-up and return advice. Incidental histological detection of *Actinomyces* in tonsils is otherwise insignificant as the organism is part of the physiologic tonsil flora.⁸

The incidence of tonsillar granulomas in this study (9, 0.22%) is similar to that in other cohorts. Lack of tonsillar tuberculosis despite tuberculosis endemicity could be related to Singapore's comprehensive national tuberculosis programme. Absence of sarcoidosis is unsurprising given its low incidence in Singapore.⁹ Tonsillar granulomas in this study's population could be an exaggerated response to chronic tonsillitis, as postulated by other authors,¹⁰ or idiopathic.

Patients whose tonsils showed RDD-like features presented with tonsillar hypertrophy-related symptoms without the massive lymphadenopathy seen in typical RDD. Histopathology showed large, S100-immunoreactive histiocytes with ample cytoplasm and emperipolesis. The patients remained well with no clinical RDD. No other studies reported such histologic findings, which might not represent bona fide RDD. Incidental detection of such features is clinically insignificant in any case, as resected unifocal RDD can be observed.¹¹

The patient whose tonsil showed rare, atypical squamous cells presented only with snoring and

tonsillar hypertrophy. Histological examination showed a few keratinocytes with irregular nuclear membranes but normal chromatin, limited to 1 high-power field, far from the resection margin. This was interpreted as virus-induced or reactive to inflammation. The patient was well 11 months after surgery with no clinical abnormality, indicating that the histological finding was of no clinical significance.

In conclusion, tonsils removed from patients with only tonsillar hypertrophy, sleep-disordered breathing, or tonsillitis are invariably benign with no clinically significant pathologic findings, representing 94.3% of all tonsillectomy cases. Histological examination could be safely limited to cases with tonsillar asymmetry, lymphadenopathy, and/or other unusual or concerning clinical features, which would conserve use of finite healthcare resources in an age of increasing demand for molecular pathology and digital computational methods.

Ethics statement

In accordance with SingHealth Centralised Institutional Review Board, department and institution representatives endorsed this as a service improvement project, not requiring Institutional Review Board review.

Declaration

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

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Keywords: *histopathology, lymphoma, paediatrics, tonsil, tonsillectomy*

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Stroke publications in Southeast Asia: A bibliometric analysis

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Dear Editor,

Stroke is the second leading cause of death and a major cause of disability worldwide, disproportionately affecting low- and lower-middle-income countries.¹ The Association of Southeast Asian Nations (ASEAN) is a political and economic union of 11 member states (Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Singapore, Thailand, Timor-Leste, and Vietnam) with over 680 million people, representing more than 8% of the global population. It has a particularly high stroke incidence and mortality, with diverse healthcare systems, population sizes, geographies, and socioeconomic settings.²

This is a report on an updated bibliometric analysis of stroke publications from ASEAN countries, aiming to characterise research output, publication patterns, collaborations, and their associations with socioeconomic indicators, including stroke publications related to COVID-19. The authors conducted a bibliometric search in PubMed for publications indexed between June 2020 and May 2024 using the terms “Stroke”, “Cerebrovascular Accident”, or “Transient Ischaemic Attack” in combination with “Southeast Asia” and each Southeast Asian country, including alternative terminology where applicable. Publications were included if stroke was the primary focus and at least 1 author had an affiliation in an ASEAN country (Supplementary Annex S1). Publications addressing stroke as a secondary topic or outcome, commentaries, replies, conference abstracts, or articles in which “stroke” was used as a non-medical term were excluded.

A single reviewer extracted data on publication characteristics, study design, collaboration type, country of origin, journal, and whether the publication addressed both stroke and COVID-19 (Supplementary Tables S1, S3, and S4). Socioeconomic and healthcare indicators, including population, gross domestic product (GDP) per capita, neurologist density defined as the number of neurologists per million people, research and development expenditure, current health expenditure, and universal health coverage indices, were obtained from publicly available international

databases (Supplementary Table S2). Associations between publication volume and socioeconomic indicators (Supplementary Tables S5 and S6) were assessed using Spearman’s rankorder correlation in Microsoft Excel version 2410 (Microsoft Corporation, 2024), with statistical significance defined as $P < 0.05$.

Of 3363 records identified, 1210 publications from 472 journals met the inclusion criteria after duplicate removal and screening (Supplementary Fig. S1). As the publications with authors from multiple ASEAN countries were counted once in the country-level analysis, the total country-specific publication count was 1312.

Based on the country-level counts ($n=1312$; Supplementary Table S3), Singapore contributed the largest proportion of publications ($n=481$, 36.6%), followed by Thailand ($n=262$, 20.0%), Malaysia ($n=241$, 18.4%), Indonesia ($n=152$, 11.6%), and Vietnam ($n=103$, 7.9%), whereas Myanmar, Brunei, Cambodia, and Laos each contributed fewer than 10 publications. No publications were identified from Timor-Leste.

All subsequent analyses were performed at the publication level ($n=1210$; Supplementary Table S3). Cohort studies were the most common study design ($n=328$, 27.1%), followed by systematic reviews ($n=161$, 13.3%), case reports ($n=128$, 10.6%), and cross-sectional studies ($n=127$, 10.5%). Most publications appeared in international journals ($n=1057$, 87.4%). Of the 598 (49.4%) publications involving international collaboration, the vast majority were with non-ASEAN collaborators only ($n=532$, 89.0%), whereas only 45 (7.5%) involved both ASEAN and non-ASEAN collaborators, and just 21 (3.5%) involved collaboration exclusively within ASEAN. Among the included publications, 1154 (95.4%) were published in journals indexed in the Web of Science, with a median journal impact factor of 2.7 (interquartile range 2.0–4.1). Three-quarters ($n=870$, 75.4%) were published in journals with an impact factor ≥ 2.0 .

Publication volume correlated positively with GDP per capita ($\rho=0.715$, 95% confidence interval [CI] 0.202–0.920, $P=0.01$), neurologist density ($\rho=0.825$, 95% CI 0.0240–0.887, $P=0.001$), and the 2021 Universal Health

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Coverage (UHC) Service Coverage Index ($p=0.747$, 95% CI 0.267–0.930, $P=0.008$), but not with population, research and development expenditure, or health expenditure indicators (Supplementary Table S5).

Seventy-four publications (6.1%) addressed both stroke and COVID-19. The number of COVID-19-related stroke publications correlated with overall volume of stroke publication ($p=0.898$, 95% CI 0.681–0.977, $P=0.00018$), GDP per capita ($p=0.800$, 95% CI 0.385–0.946, $P=0.003$), and neurologist density ($p=0.744$, 95% CI 0.342–0.941, $P=0.006$) (Supplementary Table S6).

The authors observed that stroke research output in ASEAN was disproportionately concentrated in Singapore, Thailand and Malaysia, which collectively form over 80% of the region's publications, consistent with a previous bibliometric study.² Similar to past evidence, publication volume was positively associated with GDP per capita, neurologist density, and the UHC Service Coverage Index.^{2,3} However, these socioeconomic indicators do not fully explain the observed heterogeneity. For example, Singapore produced substantially more publications than Brunei despite both being high-income economies, while Thailand outperformed Indonesia and the Philippines among middle-income countries. These observations suggest that differences in research infrastructure, academic institutions, workforce capacity and international collaborations may also contribute to research productivity, with these advantages potentially reinforced by the Matthew effect, where early advantages compound over time, increasing disparities.^{4,5}

Regional collaboration within ASEAN remains limited, with most collaborative publications involving partners outside the region. Strengthening intra-ASEAN collaboration could facilitate multicentre studies and generate evidence addressing shared epidemiological and healthcare challenges.⁶ While higher-output countries may serve as regional hubs for mentorship and methodological support, sustainable improvement will require building research capacity in lower-output countries. Strategies include developing national stroke registries, investigator training, multicentre studies, shared research protocols, and regional funding initiatives.⁷ Existing networks, such as the ASEAN Neurological Association, may provide a platform for expanding regional partnerships.⁸

COVID-19-related stroke publications showed similar associations with GDP per capita and neurologist density to those seen for overall stroke publications. The absence of an association with short-term changes in healthcare expenditure suggests the possibility that established research capacity, rather than temporary

funding increment, underpins research productivity, though this study cannot establish causation.

This study has several limitations. Correlation analyses were based on country-level aggregate data from a small number of ASEAN countries and should be interpreted as exploratory ecological associations rather than causal relationships. Only PubMed-indexed publications were included, potentially excluding publications indexed elsewhere. Study selection was performed by a single reviewer, which may have introduced selection bias. Furthermore, bibliometric analyses treat all publications equally, regardless of study quality or impact; and socioeconomic and healthcare indicators were derived from publicly available sources with varying reporting years.

In conclusion, stroke research output across ASEAN remains uneven and is associated with socioeconomic and healthcare capacity. These disparities highlight the need to strengthen regional collaboration, support locally led research, and build stroke research capacity, particularly in lower-output countries.

Supplementary materials

Annex S1. Search strategy.

Fig. S1. PRISMA flow diagram.

Table S1. Details of information gathered for each eligible publication.

Table S2. Summary of socioeconomic markers of ASEAN countries.

Table S3. Summary of bibliometric indexes of stroke publications in ASEAN post-May 2020.

Table S4. Summary of characteristics of stroke publications in ASEAN post-May 2020.

Table S5. Correlations between socioeconomic markers and publication volume of total stroke publications and stroke-COVID-19 publications in ASEAN.

Table S6. Correlation between percentage change in publication volume of total stroke publications and markers in changes in healthcare funding over the course of the COVID-19 pandemic.

Table S7. Top 10 journals in publication volume of eligible publications.

Ethics statement

Not applicable, as no study participants were involved.

Declaration

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

Keywords: ASEAN, bibliometrics, COVID-19, neurology, stroke

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