RESEARCH ARTICLE

Development of a Prognostic Model for Poststroke Dementia Using Multiple International Cohorts

A STROKOG Collaboration Study

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Neurology® 2026;106:e214574. doi:10.1212/WNL.0000000000214574

Abstract

Background and Objectives

Dementia risk prediction models developed for the general population perform poorly in stroke cohorts. Existing stroke-specific models are few and limited by short prediction horizons or reliance on neuroimaging. The aim of this study was to develop a clinically practical model for predicting 5-year dementia risk after stroke using commonly available variables and individual participant data from the Stroke and Cognition Consortium (STROKOG).

Methods

Data were pooled from 12 studies across 10 countries. Dementia was diagnosed mainly by expert panel consensus and algorithmic classification. Fine-Gray subdistribution hazard models estimated dementia probability, accounting for death as a competing event. Candidate predictors included routinely collected baseline clinical and stroke-related variables, selected through backward stepwise elimination. Model performance was evaluated using discrimination (C-index) and calibration for prediction up to 5 years after stroke. Internal-external cross-validation (IECV) assessed generalizability across studies, regions, and study periods.

Results

A total of 2,663 participants (mean age 67.0 years [SD 11.1]; 40% female) were followed for a median of 2.0 years (IQR 1.0–5.0), during which 655 developed dementia (8.7 per 100 person-years). The final model included age, sex, education, history of previous stroke, diabetes, stroke severity, 2 interactions (age × sex; age × stroke severity), and study-level variables including national current health expenditure. An Excel-based risk calculator is available in the Supplement (eAppendix 1). The model demonstrated strong discrimination (C-index: 0.81; 95% CI 0.75–0.87) and excellent calibration in the full data set used for development. In IECV, discrimination was acceptable across individual studies (pooled C-index: 0.70 [0.67–0.73]) and higher in recent (post-2010; 0.79 [0.76–0.82]) and European (0.74 [0.71–0.78]) cohorts. Risks were slightly overestimated in Asian cohorts. Case numbers were too small for reliable assessment in other regions.

Discussion

We developed and internally-externally validated a 5-year dementia risk model for stroke survivors using routinely available clinical variables. The model showed strong performance in the full development data set and generalized well to recent and European cohorts, although external validation in diverse populations is needed. This tool can help identify high-risk individuals for targeted cognitive monitoring and follow-up. By informing clinical decision making and resource planning, it offers a practical means to improve long-term outcomes.

MORE ONLINE

Supplementary Material

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Stroke and Cognition (STROKOG) Consortium coinvestigators are listed online at Neurology.org/N.

Glossary

AF = atrial fibrillation; **CHE** = current health expenditure; **HDI** = human development index; **IECV** = internal-external cross-validation; **IQR** = interquartile range; **PSCI** = poststroke cognitive impairment; **PSD** = poststroke dementia; **sHR** = subdistribution hazard ratios.

Introduction

Stroke is a major risk factor of cognitive decline and dementia. Approximately 60% of stroke survivors develop cognitive impairment within the first year after stroke, and up to 30% are diagnosed with dementia within 5 years.[1,2] Recent studies have shown that stroke is associated not only with an acute decline in cognitive function but also with ongoing decline over time.[3]

Despite growing recognition of the link between stroke and cognitive impairment, poststroke rehabilitation remains largely focused on physical recovery, with limited attention to cognitive outcomes. Cognitive impairment and dementia often go undiagnosed in clinical settings. Unlike physical deficits, cognitive changes may be subtle or delayed, yet they are equally disabling and have a substantial impact on quality of life and independence.

More than 70 dementia risk prediction models have been developed for use in the general population, but our previous work showed that these models perform poorly in stroke cohorts.[4] Few models have been designed specifically for stroke survivors. Of these, most rely on magnetic resonance imaging, which is costly and not routinely available, or are limited to short-term prediction (e.g., 6 months), reducing their clinical utility.[5-9]

The aim of this study was to develop a practical prediction tool that could be used to estimate 5-year dementia risk after stroke. The purpose of the tool is to support clinicians in tailoring long-term care, including cognitive monitoring and timely intervention. Using international cohorts from the Stroke and Cognition Consortium (STROKOG)[10] and routinely collected clinical variables, we sought to develop a model to identify individuals at elevated risk across diverse ethno-racial groups. We also aimed to assess generalizability of the prediction model using internal-external cross-validation (IECV).[11]

Methods

Study Cohorts

Data were contributed by 12 STROKOG studies that accepted a 2024 data request and included at least one dementia assessment ≥1 year after stroke (Table 1). Seven of these studies were included in previous STROKOG publications on cognitive impairment and decline.[12,13] In all but one cohort, participants were recruited during hospital admission for stroke, which served as the baseline; one study recruited participants from a local stroke registry. Stroke diagnoses were confirmed by CT or MRI. All studies obtained informed consent from participants and received ethics approval from their respective institutions. A summary of each cohort is provided in eTable 1.

Patient Sample

Participants were excluded based on the following criteria: (1) a history of dementia, identified through medical records or informant questionnaires administered 1–2 weeks after admission; (2) absence of any poststroke dementia assessments; and (3) admission for transient ischemic attack rather than stroke. In addition, 19 participants aged 20–31 years were excluded as age outliers (more than 3 SDs below the mean age). Detailed exclusion criteria are provided in eTable 2.

Outcome

Dementia was diagnosed using one or more of the following methods: expert panel consensus (5 studies), single expert clinician assessment (4), algorithmic classification based on neuropsychological tests and normative data (4), medical record review (4), and cognitive screening tests (4). The most commonly applied diagnostic criteria were the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV; 5 studies) and Fifth Edition (DSM-5; 4 studies). Further details are provided in Table 1 and eTable 3.

Candidate Predictors

Predictors were selected based on previous evidence,[3,25] availability across cohorts, and routine use in clinical settings. Core variables included demographics (age, sex, education in years, ethno-racial group), medical history (diabetes, hypertension, previous stroke, atrial fibrillation, hypercholesterolemia, smoking), and stroke characteristics (subtype, severity). All 14 candidate predictors were collected within 1–2 weeks of hospital admission or at recruitment.

Variables with substantial missingness (>40% overall or missing in ≥5 studies), including myocardial infarction, angina, APOE4 status, and blood pressure, were excluded (eTable 4). Additional variables collected in different subsets of studies, such as depression, stroke location (laterality and infratentorial/supratentorial), and BMI, were tested in secondary analyses using the relevant study subsets.

Data harmonization followed procedures described in previous work,[3,13] with stroke variable definitions provided in eTable 5. Years of education were winsorized at ±3 SD to

Table 1 Contributing Studies

Study (abbreviation)	Location	Dementia cases/N	No. of assessments	Median follow-up (range; yr)[a]	Criteria used to diagnose dementia[b]	Study initiation year
Bulgarian Post-Stroke Study (Bulgarian)[14]	Bulgaria	37/78	3	1.0; (0.5, 2)[a]	DSM-IV	2012
Bundang Vascular Cognitive Impairment Cohort (Bundang)[15]	South Korea	134/597	Varies (up to 12)	2.9; (0.5, 15.7)	DSM-IV	2007
Cognitive Outcome After Stroke (COAST)[16]	Singapore	17/273	5	6.0; (0.36, 6.9)	DSM-IV	2009
Delirium and Risk of Vascular Dementia After a Stroke (DRIVERS)[17]	Nigeria	32/85	2	1.0; (0.25, 1.0)[a]	NINDS-AIREN	2017
Epidemiologic Study of the Risk of Dementia After Stroke (EpiUSA)[18]	United States	147/428	11	3.0; (0.20, 10.2)	Modified DSM-III-R	1988
The HKU TIA/Minor Stroke Cohort (HKU)[19]	Hong Kong	1/182	2	1.0; (0.55, 1.3)	DSM-V (MoCA)	2018
Cerebral Amyloid Imaging Using Florbetapir (IDEA3)[20]	France	11/91	3	3.0; (0.5, 7.1)	DSM-5	2014
Krakow Stroke Database (Krakow)[21]	Poland	54/197	2	1.0; (0.5, 1.0)[a]	DSM-IV	2000
PRospective Observational POLIsh Study (PROPOLIS)[22]	Poland	162/416	3	1.3; (0.25, 5.6)[a]	DSM-V	2014
Stroke Registry Study of Taipei Veterans General Hospital (SRS@TVGH)	Taiwan	6/39	1	1.0; (0.25, 2.2)	MMSE or MoCA	2009
Sydney Stroke Study (SSS)[23]	Australia	43/134	4	3.0; (0.25, 7.4)	DSM-IV	1997
Study of Factors Influencing Post-Stroke Dementia (STROKDEM)[24]	France	11/143	4	3.1; (0.5, 5.9)	DSM-5	2011

[a] Follow-up time was approximated because of unavailable assessment dates.
[b] Details on dementia diagnostic methods for each study are provided in eTable 3.

reduce the influence of outliers. Patient characteristics by study are presented in eTable 6.

Assessing Heterogeneity Across Studies

A structured questionnaire was developed to collect information on how dementia was diagnosed. Responses from study principal investigators are summarized in eTable 3. We compared study designs, inclusion/exclusion criteria (eTable 1), predictor distributions (eTable 6), and crude dementia incidence rates, accounting for censoring (eTable 7). Key sources of heterogeneity are summarized in eTable 8. To account for study-level variation, the following variables were considered: study initiation period (pre-2000, 2000s, 2010s), region (Africa, Asia, Australia, Europe, United States), and either human development index (HDI) or current health expenditure (CHE) per capita. HDI reflects broader socioeconomic conditions while CHE more directly captures health care access across countries (eTable 9).

Statistical Methods

Data Preparation

Missing data for core candidate predictors were imputed using single regression imputation. Given the low levels of missingness among these predictors (<6%; eTable 4), this method performs comparably to multiple imputation.[26] Details are provided in the eMethods.

Model Development

The Fine-Gray subdistribution hazards model was used to account for death as a competing risk.[27] Model development was based on one-stage individual participant data meta-analysis (IPD-MA). Forest plots from two-stage IPD-MA were used to assess between-study heterogeneity.

Random-effects models within a Cox modeling framework were initially explored to account for between-study variation but were not adopted because of poorer model performance (lower C-index), reduced interpretability of coefficients,[28] and incompatibility with the Fine-Gray model. Instead, clustering by study was addressed using robust standard errors that allow for intragroup correlation.

Variable Selection

Backward stepwise regression was used for variable selection because of its interpretability, capacity to test interaction terms and study-level covariates, and appropriateness, given the limited number of candidate predictors. The initial model included all core participant-level variables, clinically relevant interactions (with age and sex), and study-level variables as described above (eMethods). Covariates were mean-centered, and

the correlation matrix of model coefficients was checked to rule out multicollinearity. Variables were removed sequentially until all remaining predictors were significant at $p < 0.05$.

Linearity of continuous variables was assessed using fractional polynomials, and the proportional hazards assumption was evaluated using time interaction terms and Schoenfeld residuals. As a secondary approach, Lasso-Cox regression was used to confirm that no key predictors were omitted (eMethods). Additional candidate variables were explored using forward stepwise selection and retained if they improved model performance, as evaluated through discrimination and calibration, as described further.

Sample Size and Number of Predictors

A sample size calculation was performed to confirm adequacy and to determine the maximum number of parameters that could be included while minimizing overfitting and ensuring precise risk estimation.[29] Based on our sample size, event rate, and follow-up period, we calculated that up to 32 parameters could be included (eMethods). Because we planned to examine 14 potential predictors along with their interactions with demographic factors, the available sample size is sufficiently large to support the planned model development without substantial risk of overfitting.

Model Evaluation

A 5-year prediction time scale was selected based on available data (interquartile range of follow-up: 1.0–5.0 years in the pooled sample). Model discrimination was assessed using the concordance index (C-index), which quantifies the model's ability to distinguish individuals who develop dementia earlier than others.[30] To account for competing risks of death, an adjusted C-index was calculated using the inverse probability of censoring weights.[30,31] Calibration was assessed using a smoothed curve of observed vs predicted probabilities, along with slope and intercept estimates (eMethods).

Model performance and heterogeneity were evaluated using internal-external cross-validation (IECV),[11] a method recommended for multicohort studies.[32] Unlike split-sample or bootstrap approaches, IECV makes use of all available data, offering greater efficiency.[33-36] In this approach, each of the 12 studies was sequentially left out as a test set while the model was trained on the remaining 11 studies. This process was repeated across all studies using the same set of predictors. C-indices from the held-out studies were pooled using random-effects meta-analysis to evaluate overall model performance.

To further explore heterogeneity and ensure sufficient data for calibration plots (≥200 cases have been recommended[37]), IECV was repeated with studies grouped by region (Europe, Asia, United States/Australia) and study period (pre-2000, 2000s, 2010s).

Final Prognostic Tool

Individual probability of developing dementia within 5 years after stroke was calculated based on the patient's total score from the model (linear predictor) and the baseline cumulative incidence function. Further details are provided in eMethods.

All analyses were conducted using Stata v18.0.[38] Reporting followed the TRIPOD-Cluster guidelines for multivariable prediction models using clustered data.[32]

Standard Protocol Approvals, Registrations, and Patient Consents

Ethics approval was obtained from the UNSW Human Research Ethics Committee, which waived the requirement for individual consent for secondary data use (HC210709).

Data Availability

Deidentified individual participant data are available to qualified researchers on application to the STROKOG consortium.

Results

Twelve studies contributed data on 2,663 patients with stroke (40% female; mean age 67.0 years, SD 11.1; range 32–96). Most (96%) had experienced an ischemic stroke. The number of dementia assessments varied across studies (range: 1–11), with evaluations most commonly conducted at 3–6 months and 12 months after stroke (Table 1). Over a median follow-up of 2.0 years (interquartile range [IQR]: 1.0–5.0), 655 participants developed dementia and 193 died (eFigure 1 shows the Kaplan-Meier failure function for dementia). The overall crude dementia incidence rate was 8.7 per 100 person-years (95% CI 8.1–9.4), ranging from 0.5 to 58 across individual studies. Higher rates were observed in studies from Nigeria, Bulgaria, and Poland (24.2 per 100 person-years) and lower rates in cohorts from Asia, Australia, France, and the United States (5.8 per 100 person-years) (eTable 7).

Variable selection identified 8 patient-level predictors: age, sex, diabetes, education, previous stroke, stroke severity (mild vs moderate/severe), and 2 interaction terms: stroke severity × age and sex × age. Table 2 presents the model coefficients and subdistribution hazard ratios (sHRs), which indicate the relative change in dementia incidence among those still at risk.[39] Tests for fractional polynomial transformations of age and education did not demonstrate improved fit compared with linear terms. Assessment of the proportional hazards assumption indicated that it was reasonable for all included predictors (eTable 10).

The interaction between stroke severity and age yielded an sHR less than 1. This indicates that the increased probability of poststroke dementia (PSD) associated with older age was attenuated among individuals with more severe strokes, and conversely, the elevated risk linked to more severe strokes was reduced in older individuals. Similarly, the sHR for the sex and age interaction was also less than 1. Further examination showed that men had a higher probability of PSD at younger ages, with risk converging with that of women around age 80

(holding other predictors constant), after which women showed a higher incidence.

Two-stage IPD-MA results indicated low-to-moderate heterogeneity (I^2 = 0%–49%) for all predictors, except for the sex × age interaction, which showed higher heterogeneity (I^2 = 70%), although effect estimates remained consistent in direction (eFigure 2). Three study-level variables were selected to account for heterogeneity and improve model performance: study period, low national CHE, and its interaction with previous stroke (Table 2). Low CHE was defined as < USD $1,500 per capita, based on country grouping (eTable 11 presents details and alternative approaches tested). The interaction between low CHE and previous stroke had an sHR less than 1. Subgroup analysis showed that previous stroke was associated with higher PSD incidence in high-CHE studies only, but not in low-CHE cohorts.

In a secondary analysis of studies with additional data, bilateral stroke was significant when added to the model (eTable 12). However, it did not improve model performance, with the C-index remaining at 0.81 in the subset of studies. Therefore, an extended model was not pursued.

The final model achieved a C-index of 0.81 (95% CI 0.75–0.87), with the calibration plot showing close agreement between predicted and observed probabilities (Figure 1).

Internal-External Cross-Validation (IECV)

IECV by study yielded a pooled C-index of 0.70 (95% CI 0.67–0.73; I^2 = 33%), with individual results shown in the forest plot (eFigure 3). Table 3 summarizes IECV results by study period and region. When grouped by study period, the pooled C-index was 0.75 (95% CI 0.68–0.82), with more recent studies (post-2010) showing higher discrimination (C-index = 0.79; 95% CI 0.76–0.82). The pooled calibration slope and intercept were 1.02 (95% CI 0.73–1.30) and 0.016 (95% CI −0.27– 0.30), respectively. Calibration plots indicated some miscalibration in older (pre-2000) studies and good calibration in studies conducted after 2000 (eFigure 4).

By region, discrimination was highest in European studies (C-index = 0.74), with slightly lower values observed in cohorts from Asia, the United States/Australia, and Africa (range: 0.67–0.71). Calibration plots indicated good agreement in European studies. Underestimation was observed in the US/Australia group, which consisted of older, pre-2000 studies. In Asian cohorts, risk was overestimated at predicted probabilities above 0.3, with wide confidence intervals likely due to underrepresentation of moderate/severe stroke cases (8.5% across these studies). Calibration plots should be interpreted with caution because some groups included fewer than the recommended minimum of 200 cases for reliable calibration curve estimation.[37]

Clinical Application

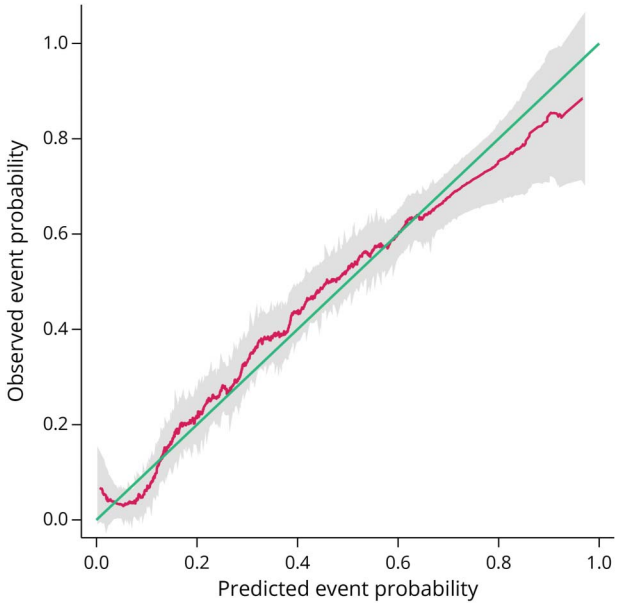
Five illustrative clinical scenarios with corresponding 5-year dementia risk estimates are presented in Table 4. An Excel-based calculator (available in the Supplement, eAppendix 1) allows users to input patient characteristics and generate individualized poststroke dementia risk predictions. Based on the study data used for model development, the tool includes input limits for age (32–96 years) and education (0–23 years). Values outside the age range may not yield valid predictions. For education, the tool assumes no further reduction in dementia risk beyond 23 years; values above this threshold are automatically capped. Study period is not included in the calculator interface, as the tool automatically

Table 2 Final Model Predicting 5-Year Probability of Poststroke Dementia, Presented as Model Coefficients β and Its Exponentiated Coefficients (sHR)

Predictors	sHR (95% CI)	β (95% CI)
Age, years per decade[a]	1.62 (1.44 to 1.83)	0.48 (0.37 to 0.60)
Sex (male/female)	1.32 (1.08 to 1.61)	0.28 (0.08 to 0.48)
Sex × age[a]	0.82 (0.76 to 0.90)	−0.19 (−0.28 to −0.11)
Education, per 5 y[a]	0.80 (0.67 to 0.95)	−0.23 (−0.40 to −0.05)
History of diabetes	1.48 (1.27 to 1.71)	0.39 (0.24 to 0.54)
Moderate/severe stroke	2.06 (1.55 to 2.74)	0.72 (0.44 to 1.00)
Age × moderate/severe stroke[a]	0.76 (0.66 to 0.87)	−0.28 (−0.41 to −0.14)
Previous stroke	1.35 (1.16 to 1.57)	0.30 (0.15 to 0.45)
Low-CHE countries	3.31 (1.67 to 7.00)	1.23 (0.51 to 1.95)
Previous stroke × low CHE	0.50 (0.37 to 0.68)	−0.69 (−0.99 to −0.39)
Study period (initiated before 2000)	1.85 (0.90 to 3.78)	0.61 (−0.10 to 1.33)

Abbreviations: CHE = current health expenditure per capita; sHR = subdistribution hazard ratio.
The baseline cumulative incidence of dementia up to 5 y after stroke is 0.190251.
[a] Predictors were centered at the sample mean to reduce collinearity, using the following values: age = 67; education = 10.

Figure 1 Calibration Plot Using the Full Sample for Development and Testing



Red line: smoothed fit of predicted vs observed probabilities. Green line: reference line for perfect calibration (slope = 1). Shaded area: 95% CI around the calibration curve.

assumes calculations for the current period, because estimates for earlier periods would not be relevant to current clinical practice.

Discussion

We developed and internally-externally validated a prognostic model to estimate the 5-year risk of PSD using pooled data from 12 cohorts across 10 countries. The final model included age, sex, education, diabetes, previous stroke, stroke severity, 2 interaction terms (age × sex and age × stroke severity), and 3 study-level variables (study period, low CHE, and its interaction with previous stroke). The model demonstrated strong discrimination and calibration in the development data set, and IECV showed good performance in recent studies and European cohorts. Performance was more variable in older and Asian cohorts, where predicted probabilities should be interpreted with caution. A user-friendly Excel-based tool is provided to support potential clinical use.

More than 70 dementia risk prediction models have been developed for use in the general population, with reported C-statistics ranging from 0.49 to 0.89.[40] Our previous work showed that 3 of the better performing models (C-statistic ≥0.70), which used routinely collected variables, performed poorly in several STROKOG cohorts (C-statistic/AUC [area under the curve]: 0.53–0.66).[4] By contrast, few models have been developed specifically for stroke survivors. A recent literature search (May 2025) identified 6 prediction models for poststroke cognitive impairment (PSCI), but none specifically for PSD.[5-9,41] These models had key limitations: 4 relied on MRI data; 4 predicted outcomes only up to 6 months; 3 used small samples for development (<300), increasing the risk of overfitting; and 4 relied solely on cognitive screening tools for outcome classification (summarized in eTable 13). In addition, all but one used split-sample or nonindependent cohorts for validation, which is now considered inefficient, less robust, and prone to optimistic performance estimates.[33] The only study predicting outcomes up to 5 years, a UK study (n = 2,468), reported an AUC of 0.75.[41] However, the model was validated on data from the same registry, which limits its generalizability, and relied on

Table 3 Results From Internal-External Cross-Validation (IECV) by Region and by Study Period

	Events/sample size (n studies)	C-index (95% CI)	Calibration slope (95% CI)	Calibration intercept (95% CI)
Region				
Europe	275/925 (5)	0.74 (0.71 to 0.78)	0.81 (0.56 to 1.06)	−0.19 (−0.44 to 0.06)
Asia	158/1,091 (4)	0.67 (0.63 to 0.72)	0.73 (0.47 to 0.99)	−0.27 (−0.53 to −0.01)
United States + Australia	183/547 (2)	0.68 (0.64 to 0.71)	1.16 (1.05 to 1.28)	0.16 (0.05 to 0.28)
Africa	32/85 (1)	0.71 (0.61 to 0.82)	NA	NA
Overall[a]	655/2,663(12)	0.70 (0.66 to 0.74)	0.92 (0.61 to 1.22)	−0.08 (−0.39 to 0.22)
Study period[b]				
Pre-2000	185/547 (2)	0.68 (0.64 to 0.71)	1.16 (1.05 to 1.28)	0.16 (0.05 to 0.28)
2000s	205/1,067 (3)	0.78 (0.74 to 0.82)	1.09 (0.56 to 1.61)	0.09 (−0.44 to 0.61)
2010s	260/1,034 (7)	0.79 (0.76 to 0.82)	0.78 (0.51 to 1.05)	−0.22 (−0.49 to 0.05)
Overall[a]	655/2,663 (12)	0.75 (0.68 to 0.82)	1.02 (0.73 to 1.30)	0.016 (−0.27 to 0.30)

NA = not calculated because of small sample size and low number of events.
[a] Overall C-index or calibration statistics were pooled using random-effects meta-analysis.
[b] For IECV by study period, the variable "study period" was not included in the model.

Table 4 Prediction of Dementia Probability for Illustrative Clinical Scenarios

Clinical scenario	Probability of poststroke dementia within 5 y
Male, 60 years old, 16 years of education, no diabetes, mild stroke, no history of previous stroke, from Australia	4%
Female, 65 years old, 12 years of education, diabetes, mild stroke, history of previous stroke, from the United States	11%
Female, 70 years old, 10 years of education, diabetes, moderate stroke, no history of previous stroke, from Singapore	19%
Male, 50 years old, 12 years of education, no diabetes, severe stroke, no history of previous stroke, from Bulgaria	34%
Male, 80 years old, 0 years of education, diabetes, severe stroke, history of previous stroke, from Poland	79%

variables not routinely collected (e.g., cognition at stroke onset and the Barthel Index). Furthermore, PSCI was defined using the Mini-Mental State Examination (MMSE), a tool known to have limited sensitivity in detecting early dementia. In summary, our model addresses these gaps and is unique within the PSD prognostic space.

Predictors retained in our final model, including age, education, diabetes, and previous stroke, are well-established risk factors of poststroke cognitive impairment.[3,42,43] Previous studies have also identified vascular risk factors such as atrial fibrillation (AF) and hypertension, but these were not retained in our final model. Preliminary univariable analysis showed that although these factors were associated with PSD, their effects were attenuated after adjusting for age and their inclusion did not improve the C-index, suggesting a limited contribution to model prediction. Notably, none of the existing PSCI prediction models includes hypertension or AF (eTable 13). While these factors are strong predictors of stroke, their predictive value for dementia may be diminished in stroke participants, possibly because their effects are confounded by age, previous stroke, or stroke severity. In addition, our study lacked detailed information on hypertension treatment and chronicity, factors that may influence PSD risk.

Sex differences in Alzheimer disease have been reported, with higher risk observed in women.[44] However, this association has not been found in most stroke studies.[25,43] In our analysis, a significant sex × age interaction was identified, with a crossover in risk around age 80: men had a higher probability of PSD at younger ages while women showed higher incidence beyond age 80. Although heterogeneity in this interaction was high across studies (I^2 = 70%), effect estimates were largely consistent in direction. These findings suggest age-dependent sex differences in PSD risk.

As expected, stroke severity and a history of previous stroke were both associated with an increased probability of PSD. However, this association with previous stroke was not observed in the Nigerian and Polish cohorts. These studies, along with the Bulgarian cohort (which excluded individuals with previous stroke), reported notably higher dementia incidence and a greater proportion of moderate-to-severe strokes. Limited access to acute stroke care and broader health care services may partly explain this pattern.[45] When studies were grouped by national CHE per capita, using a threshold of USD $1,500, the association between previous stroke and PSD was evident only in high-CHE cohorts. The lack of association in low-CHE settings may reflect increased mortality or loss to follow-up among individuals with multiple strokes. While health care systems in Nigeria differ substantially from those in Eastern Europe, grouping these countries under a single CHE variable yielded the best model performance. Other countries with low CHE are listed in the Excel tool. Additional data are needed to validate this approach, and predicted probabilities in low-CHE settings should be interpreted with caution.

The model demonstrated strong internal validity, with good discrimination (C-index = 0.81) and excellent calibration. IECV by study showed acceptable overall discrimination (pooled C-index = 0.70), with individual C-index ≥0.66, except for one (C-index = 0.51). The outlier likely performed poorly because of its small sample size (n = 39) and reliance on cognitive screening tests alone for dementia diagnosis, which may have introduced bias and outcome misclassification. The pooled C-index from IECV was lower than in the development sample, reflecting performance in cohorts not used for development as well as heterogeneity in case-mix and study characteristics. Several cohorts were small, had few events, or included predominantly mild strokes, limiting variability. As discussed further, discrimination generally improved when evaluated across larger clusters.

IECV analyses showed that discrimination was highest in recent studies and European cohorts (C-index = 0.79 and 0.74, respectively), both with acceptable calibration. By contrast, performance was poorer in Asian cohorts, likely due to several factors: (1) limited variability in stroke severity, with 91% of patients having mild stroke, which may lead to overestimation of risk—consistent with this, Asian studies reported a low PSD incidence rate (3.8 per 100 persons); (2) small sample sizes or few dementia cases in 2 studies, reducing statistical power and making performance metrics less stable; (3) reliance on algorithmic approaches, including screening tools in 2 studies, which may increase the risk of misclassification; and (4) potential ethno-racial differences in risk factor associations. Although two-stage IPD-MA did not show

consistent differences between Asian and Western studies, subtle variations may exist within subpopulations (e.g., Korean vs Chinese from Singapore). Further investigation using multiple studies per country is needed to explore this. Consequently, predicted probabilities in Asian settings may be overestimated and should be interpreted as broad estimates.

The US and Australian cohorts in our analyses were initiated before 2000, which may explain poorer calibration and discrimination in these regions. These studies predate advances in stroke care and rehabilitation, which have improved patient outcomes and likely reduced dementia risk in contemporary cohorts.[42] Consequently, we adjusted for study period, which improved model performance.

A key strength of this study is the inclusion of diverse stroke cohorts from multiple regions, resulting in a large, pooled sample and broad representation of stroke populations. Individual cohorts lacked sufficient power for model development because more than 20 events per predictor variable are generally recommended,[46] requiring at least 220 cases for the 11-predictor model. We accounted for time-to-event data with death as a competing risk, reducing the potential for upward bias in effect estimates.[39] An IECV framework was used to robustly assess model performance across studies, regions, and periods. Dementia diagnoses were largely based on comprehensive neuropsychological assessments, with 5 studies using consensus diagnosis, considered the gold standard. The final model uses routinely collected clinical data and is implemented as a simple Excel-based tool to estimate 5-year dementia risk at the point of care.

However, the diversity of cohorts also introduced methodological challenges. Variations in study design, follow-up duration, participant characteristics, and diagnostic methods contributed to heterogeneity. We addressed this using IECV, two-stage IPD-MA, and inclusion of study-level variables and interaction terms, although some unmeasured heterogeneity likely remains. The effects of differing diagnostic methods were difficult to disentangle, particularly because several studies used more than one approach. Harmonization of predictors required dichotomization of some variables, resulting in information loss. In particular, stroke severity was simplified to a binary variable across different scales, reducing variability especially in cohorts consisting of primarily mild stroke cases. The unavailability of data on certain relevant factors, such as APOE4 status and antihypertensive use, may introduce residual confounding and limit the inclusion of potentially important predictors. Finally, the exclusion of individuals without any dementia assessment likely biased the sample toward participants with better cognitive outcomes and less severe strokes.

Our prognostic tool may assist clinicians in identifying stroke survivors at elevated risk of developing dementia, enabling more targeted follow-up and earlier intervention. It offers a practical approach to informing poststroke cognitive care and resource planning. External validation in large, independent data sets from diverse regions is needed to assess generalizability. Future research should explore model updating or recalibration for specific populations, as well as incorporate additional predictors, such as APOE4 status, detailed stroke severity measures, and hypertension data, to further enhance model performance and generalizability. In summary, we present a practical tool for estimating 5-year dementia risk after stroke, based on routinely collected clinical data. While further validation is warranted, this tool represents a step toward more personalized poststroke care. By identifying individuals who may benefit from cognitive monitoring and follow-up, it has the potential to support clinical decision making, inform service planning and resource allocation, and improve long-term outcomes.

Acknowledgment

The authors thank Professor Raj Kalaria from Newcastle University, United Kingdom, for sharing data from the CogFAST UK study, which he led. Unfortunately, this data set could not be included in our analysis because of the absence of key predictor variables.

Author Contributions

J.W. Lo: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data. J.D. Crawford: drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data. D.W. Desmond: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data. O. Godefroy: major role in the acquisition of data. M. Roussel: major role in the acquisition of data. R. Bordet: major role in the acquisition of data. T. Dondaine: major role in the acquisition of data. A.-M. Mendyk: major role in the acquisition of data. H.-J. Bae: major role in the acquisition of data. J.-S. Lim: major role in the acquisition of data. A. Ojagbemi: major role in the acquisition of data. T. Bello: major role in the acquisition of data. C.P.L.H. Chen: major role in the acquisition of data. E. Chong: major role in the acquisition of data. N. Venketasubramanian: major role in the acquisition of data. A. Klimkowicz-Mrowiec: major role in the acquisition of data. L.D. Traykov: major role in the acquisition of data. S. Mehrabian: major role in the acquisition of data. C.-P. Chung: major role in the acquisition of data. N.-F. Chi: major role in the acquisition of data. G.K.K. Lau: major role in the acquisition of data. D.X. Liu: major role in the acquisition of data. H. Welberry: drafting/revision of the manuscript for content, including medical writing for content. H. Brodaty: major role in the acquisition of data. P.S. Sachdev: major role in the acquisition of data; study concept or design.

Study Funding

Research reported in this article was supported by the National Health and Medical Research Council (NHMRC) Centres of Research Excellence (ID2006765). Funding information for studies reporting financial support is as follows: Bulgarian Post-

Stroke Study: European Union-NextGenerationEU (National Recovery and Resilience Plan of the Republic of Bulgaria, grant number BG-RRP-2.004-0004-C01), and the Bulgarian National Science Fund (BNSF, KP-06-N53/3 and DN 03/12); Bundang Vascular Cognitive Impairment Cohort: Seoul National University Bundang Hospital Research Fund; Cognitive Outcome After Stroke: National Medical Research Council (NMRC/CG/NUHS/2010) and National University Health System National Clinician Scientist Program (NUHS NCSP); Delirium and Risk of Vascular Dementia After a Stroke: Medical Education Partnership Initiative Junior Faculty Research Training Program under Fogarty international grant (D43TW010140); Epidemiologic Study of the Risk of Dementia After Stroke: NIH (grants R01-NS26179 and P01-AG07232); Cerebral Amyloid Imaging Using Florbetapir: Amiens University Hospital and by a grant from the French Department of Health "Direction générale de l'offre des soins" (DGOS R1/2013/144); PRospective Observational POLIsh Study: Leading National Research Center; Stroke Registry Study of Taipei Veterans General Hospital: Taipei Veterans General Hospital (V114C-063) and the National Science and Technology Council, Taiwan (NSTC 114-2314-B-075-002); Sydney Stroke Study: National Health and Medical Research Council; Study of Factors Influencing Post-Stroke Dementia: French Health Ministry (PHRC) and Fondation Coeur et Artères.

Disclosure

J.W. Lo reports receiving grants from the Australian Government Research Training Program Scholarship during the conduct of the study. J.D. Crawford reports receiving grants from the NIH to fund his position at UNSW. H. Brodaty is or has been an advisory board member or consultant to Biogen, Eisai, Eli Lilly, Medicines Australia, Roche, and Skin2Neuron; and reports receiving funding from the National Health and Medical Research Council (NHMRC). P.S. Sachdev reports occasional advisory engagements with Biogen (2020-21), Roche (2022), Eli Lilly (2025), and Novo Nordisk (2025), unrelated to the topic of this article. D.W. Desmond, O. Godefroy, M. Roussel, R. Bordet, T. Dondaine, A.-M. Mendyk, H.-J. Bae, J.-S. Lim, A. Ojagbemi, T. Bello, C. Chen, E.J. Chong, N. Venketasubramanian, A. Klimkowicz-Mrowiec, L. Traykov, S. Mehrabian, C.-P. Chung, N.-F. Chi, G.K.-K. Lau, D.X. Liu, and H.J. Welberry report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

Publication History

Received by *Neurology*® August 6, 2025. Accepted in final form November 4, 2025. Submitted and externally peer reviewed. The handling editor was Editor-in-Chief José Merino, MD, MPhil, FAAN.

Appendix Coinvestigators

Coinvestigators are listed at Neurology.org/N.

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