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Discrimination of ischemic versus hemorrhagic stroke type by presenting symptoms or signs: A systematic review and meta-analysis

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ABSTRACT

Background: Valid discrimination of ischemic and hemorrhagic stroke relies exclusively on neuroimaging. Novel biomarkers in acute stroke present an opportunity to reconsider combination diagnostic approaches with standardized clinical assessment. Our systematic review evaluates diagnostic properties of acute clinical features in determining primary stroke etiology.

Methods: We conducted a systematic review and meta-analysis according to PRISMA guidelines. PubMed and EMBASE were searched from inception to 6th March 2025. Eligibility criteria included cohort, cross-sectional, case-control, or randomised controlled trial; consecutive adults with an acute stroke confirmed by neuroimaging; and one or more acute stroke symptom(s) or sign(s) recorded by stroke subtype. A random-effects model was used to pool odds ratios.

Results: A total of 60 studies, (n = 12,879,006; ischemic stroke = 10,814,474; hemorrhagic stroke = 2,064,532), were eligible. Mean age was 70.45 ± 14.36 years and 51.9 % were women. Clinical presenting symptoms/signs associated with significantly higher odds of hemorrhagic stroke (compared to ischemic stroke) included coma (odds ratio 8.81 [95 % confidence interval, 5.02–15.45]), neck stiffness (5.21 [2.22–12.21]), Glasgow Coma Scale ≤8 (4.37 [2.35–8.16]), vomiting (3.86 [2.71–5.49]), altered consciousness (3.55 [2.55–4.95]), headache (3.49 [2.63–4.64]), syncope (2.74 [1.96–3.83]), seizure (2.67 [1.72–4.15]), abnormal plantar response (1.94 [1.24–3.04]) and vertigo/dizziness (1.32 [1.04–1.68]). Clinical symptoms/signs associated with significantly lower odds of hemorrhagic stroke included morning onset (0.41 [0.32–0.54]), facial weakness (0.66 [0.46–0.94]), hemiplegia (0.68 [0.50–0.91]), and ataxia (0.73 [0.61–0.86]).

Conclusion: Our review reports substantive differences in prevalence of stroke symptoms and signs between ischemic and hemorrhagic stroke subtypes.

Introduction

Stroke is the second leading cause of death and leaves most survivors with permanent disability.[1,2] Stroke etiology may be primarily divided into acute ischemic stroke (AIS) and intracranial hemorrhage (ICH), and rapid determination of primary etiology is required for reperfusion

Abbreviations: AIS, Acute Ischemic Stroke; ICH, Intracranial Hemorrhage.

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therapy.[3,4] In current clinical practice, valid and reliable distinction between AIS and ICH mandates neuroimaging with CT or MRI.[1] Both modalities have a sensitivity of almost 100 % in excluding ICH, which allows their use as stand-alone tests.[5] Delays, or lack of availability of neuroimaging, poses significant challenges to effective reduction in disability due to AIS, particularly in resource-limited settings.[6]

While acute stroke relies on a single test modality, the diagnosis, and discrimination, of other acute vascular presentations employ the combination of pre-test clinical probability with biomarkers (e.g. D-Dimer combined with the Wells' score for pulmonary embolism (PE) diagnosis,[7] and troponin combined with electrocardiogram (ECG) for acute myocardial infarction (MI) diagnosis).[8] Although acute stroke presents distinct diagnostic challenges compared to other acute vascular conditions, due to its subtypes of ischaemic and haemorrhagic stroke, as well as potential mimics, the recent emergence of promising biomarkers[9] suggests that multimodal diagnostic strategies which integrate clinical assessment with biomarker data, may be feasible in the future. This supports the rationale for re-evaluating current approaches to early stroke subtype differentiation.[10,11]

However, a multimodal diagnostic technique that incorporates pre-test clinical probability, necessitates a standardized approach to clinical assessment. Accordingly, we sought to determine whether specific clinical features can meaningfully discriminate haemorrhagic from ischaemic stroke in the acute setting. While there have been previous systematic reviews,[12] there has been an expansion in the literature since the most recent meta-analysis. We completed an updated systematic review and meta-analysis of studies reporting the prevalence of clinical symptoms and signs in patients with acute stroke, by ischemic stroke and intracranial hemorrhage subtype.

Materials and methods

This systematic review and meta-analysis was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement[13] and Meta-analyses Of Observational Studies in Epidemiology (MOOSE) guidelines.[14] It was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42024547248). The data that support the findings of this study are available from the corresponding author upon reasonable request.

Data sources and search strategy

Comprehensive search strategies were developed by the authors for individual databases (PubMed and EMBASE). Databases were searched from inception to March 6th, 2025 (last search date). Search results were imported into Rayyan citation management software.[15] Additional articles were identified from use of the search tool "all related articles" in PubMed and examination of bibliographies of systematic reviews identified through the search, and included articles. The complete search strategy is provided in the Supplemental Material.

Screening and study selection were undertaken using Rayyan.[15] Two authors (C.McD. and A.S.) independently screened articles for inclusion. Studies considered potentially eligible for inclusion were read in full by C.McD. and A.S., who independently determined their suitability. Any disagreements were resolved via consensus ($n = 5$), or by arbitration by a third investigator (M.O.) if no consensus could be reached ($n = 2$).

Eligibility criteria

Eligible studies were: (1) cohort, cross-sectional, case-control, and randomised controlled trial, which enrolled patients presenting to a hospital or emergency department with a diagnosis, or suspicion, of stroke, who were representative of the general population, (2) Recruited consecutive admissions of individuals with an acute ischemic or hemorrhagic stroke, (3) Clinical assessment was undertaken by a trained physician, nurse, paramedic, or other trained specialist, (4) The study used either neuroimaging (CT or MRI) or autopsy to distinguish hemorrhagic from ischemic subtype, (5) Comparisons were possible between stroke subtypes in ≥1 acute stroke symptom(s) or sign(s), (6) Included patients were ≥18 years of age, (7) Each study, or the relevant subgroup within the study, were required to include a sample size of ≥100 adult participants.[16] Stroke was defined as per the World Health Organization definition, as focal (or at times global) neurologic impairment of sudden onset and of presumed vascular origin.[17] Non–English-language publications were included. Abstracts and non–full–text publications were included provided sufficient information could be obtained from the body of work. If multiple publications originated from the same cohort, the study reporting on the largest number of participants with the symptom(s) or sign(s), was included.

Data extraction

Characteristics of the included studies were collected, independently by two authors C.McD., and A.M. or A.S., using a data abstraction form. Descriptive data abstracted included author(s), year of publication, country, study design, study period, total participant number, mean or median age of the population, sex distribution, number of ischemic and hemorrhagic strokes, and individual symptom or sign distribution in the population. Where non–English language studies were included, abstraction was aided by translation using Google Translate (May 2024).[18] If not explicitly stated, measures were calculated from available data.

Risk of bias assessment

The risk of bias was assessed with a customized version of the Newcastle-Ottawa Quality Assessment Scale.[19] This customized version was adapted from that previously developed by Ali et al.[20] Two authors (C.McD. and S.C.) independently assessed the risk of bias for each included study. Disagreements were resolved through consensus, with discrepancies occurring in only 18 out of 244 assessed domains. Studies were scored low risk, high risk or possible/unclear in the domains (1) validation of diagnosis; (2) assessment of symptoms; (3) adjustment for confounding; (4) generalizability (Supplemental Material). All studies, regardless of format, underwent the same risk-of-bias assessment.

Statistical analysis

To estimate individual odds ratios (ORs) within each study, the specific number of symptom/sign occurrences per stroke subtype provided in the study, along with the total number of AIS or ICH cases studied, were used. This information was used to calculate the corresponding 95 % confidence intervals (CIs), as well as the sensitivity, specificity, positive likelihood ratio (LRs) and negative LRs for hemorrhage prediction, using a bivariate random effects model[21,22] via the mada package.[23] For all analyses, ICH were considered cases, while controls were AIS. Therefore, an OR >1 reflects the symptom, or sign, is associated with a higher odds of ICH versus AIS. True positives were defined as cases where the symptom/sign was present in individuals with ICH, false negatives when symptom/sign was absent in ICH, true negatives when symptom/sign was absent in AIS, and false positives when symptoms/sign was present in AIS. Positive LRs (+LRs) were calculated using the formula Sensitivity/(1–Specificity), and negative LRs (-LRs) were calculated using (1−Sensitivity)/Specificity.

We completed individual meta-analyses for each symptom and sign reported by at least 2 independent studies. Where a patient presented with multiple symptoms/signs, this participant was included in multiple analyses relating to each individual symptom/sign reported. A random-effects model, using the REML estimator, was used to pool results for these analyses as heterogeneity is expected to be present due to known differences in symptom definitions and stroke patient characteristics.

The overall effect estimate and 95 % CIs of the forest plots per symptom/sign were used to create summary forest plots.

In a subgroup analysis, we meta-analyzed the symptoms/signs per stroke subtype within geographical regions (Africa, East Asia, South Asia, South East Asia, Eastern/Central Europe/ Middle East, and Western Europe/North America/Australasia) to investigate whether the symptom/sign at presentation varied by region for AIS and ICH. Publication bias was assessed using a combination of funnel plots based on univariate effect measures, the Egger regression test for asymmetry, and trim-and-fill using the log diagnostic odds ratio.[24] Sensitivity analyses involved excluding all studies determined at a high risk of bias, excluding studies only available in abstract or non-full-text form, and AIS vs intracerebral hemorrhage (excluding studies where subarachnoid hemorrhage was not distinguished from intracerebral hemorrhage). Heterogeneity was assessed using the I^2 statistic. A p-value of $\leq$0.05 was considered statistically significant. All statistical analysis was undertaken using R statistical software version 4.3.1.

Results

In total, 2,537 articles were screened, with 350 reviewed in full (Fig. 1). Of the 60 included studies, there were 61 distinct populations from 35 different countries (sTable 3). Retrospective (n = 26) and prospective studies (n = 34), comprising observational, cohort, cross-sectional, case-control, single-centre and multi-centre studies, and registries were included. Study characteristics, in addition to reported symptoms and signs in each included study, are summarized in sTable 1. Year of publication ranged from 1984 to 2025. One eligible study was a non-English language publication.[25] Two studies were available only in abstract form.[26,27]

Overall, the population comprised a total of 12,879,006 patients (AIS = 10,814,474; ICH = 2,064,532). The mean age of participants was 70.45 years (±14.36 years), with 51.9 % women. The prevalence of ICH among included studies was 16.03 % (range: 6.96 %–65.64 %) and 25.91 % (95 % CI 22.0 %–30.3 %) among the entire population (random-effects) (sFigure2). A total of twenty-six symptoms were reported in two or more of the included studies.

Diagnostic odds ratio for symptoms and signs associated with intracranial hemorrhage (versus Ischemic Stroke)

The ORs, and 95 % CI, of each symptom/sign by stroke subtype are reported in Fig. 2. Clinical presenting symptoms and signs associated with a significantly higher odds of ICH (compared to AIS) include coma (OR, 8.81 [95 % CI, 5.02–15.45]; AIS/ICH = 10,418,718/2,001,780, 9 studies), neck stiffness (5.21 [2.22–12.21]; AIS/ICH = 511/168; 3

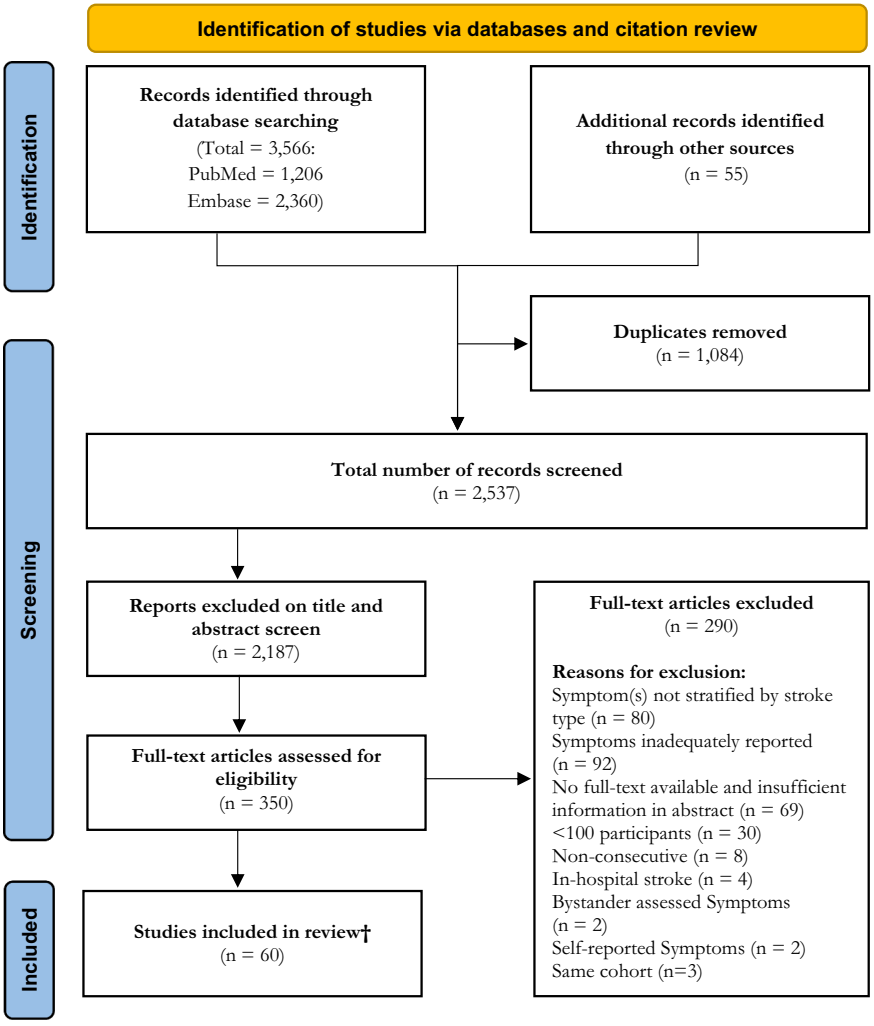

Fig. 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses flowchart of included studies. Preferred Reporting Items for Systematic reviews and Meta-Analyses flowchart of included studies. The sources of each study identified, number of studies screened, number of studies with full-text review for eligibility, reasons for excluding full-text articles, and number of studies included, are outlined. †Complete list of included studies, with references, are included in the supplementary material.

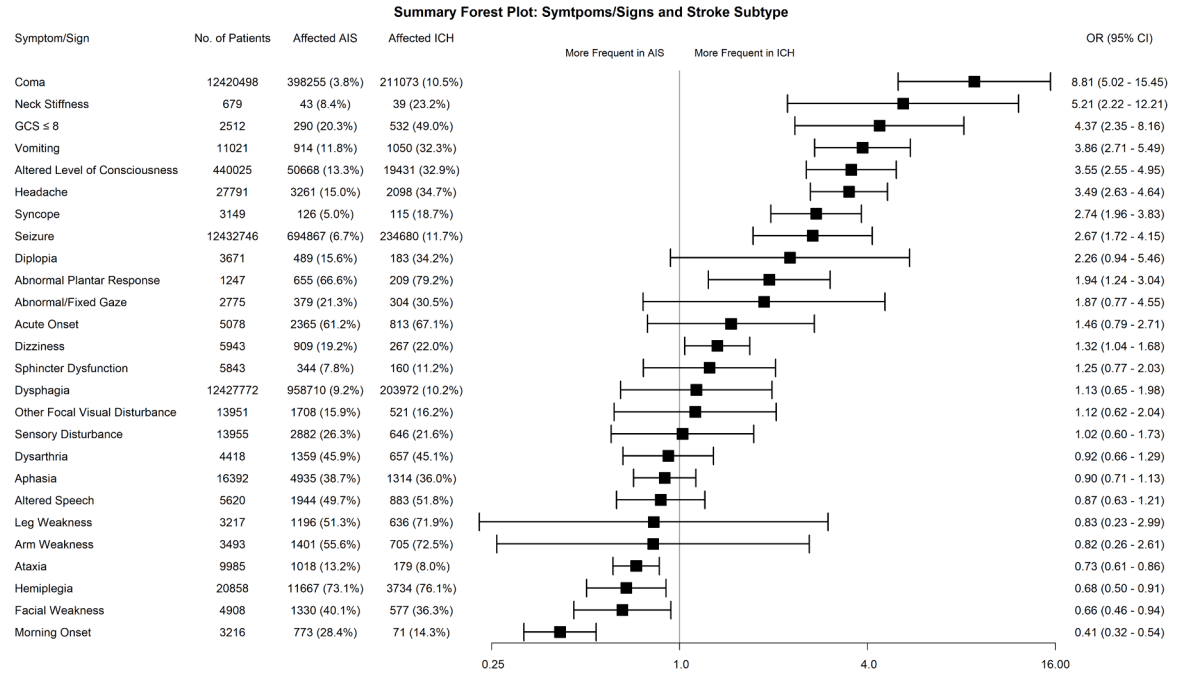

Fig. 2. Summary Forest plot for symptoms or signs in patients with ischemic and hemorrhagic stroke. Summary forest plot demonstrating the association of individual symptoms or signs and stroke subtypes of ischemia or hemorrhage. Cases were hemorrhagic strokes and ischemic strokes were controls. The squares reflect the combined association as calculation from individual forest plots per symptom (sFigure 3 –30). The bars represent 95 % confidence intervals of the association. The vertical line represents the line of no difference. GCS – Glasgow Coma Scale, ICH – intracranial hemorrhage, AIS – ischemic stroke, OR – Odds Ratio, CI – Confidence Interval.

studies), Glasgow Coma Scale (GCS) ≤8 (4.37 [2.35–8.16]; AIS/ICH = 1,427/1085, 7 studies), vomiting (3.86 [2.71–5.49]; AIS/ICH = 7,772/3,249; 26 studies), altered level of consciousness (3.55 [2.54–4.95]; AIS/ICH = 380,950/59,075, 37 studies), headache (3.49 [2.63–4.64]; AIS/ICH = 21,748/6,043; 44 studies), syncope (2.74 [1.96–3.83]; AIS/ICH = 2,533/616; 7 studies), seizure (2.67 [1.72–4.15]; AIS/ICH = 10,427,811/2,004,935; 22 studies), abnormal extensor plantar response (1.94 [1.24–3.04; AIS/ICH = 983/264; 5 studies]) and vertigo/dizziness (1.32 [1.04–1.68]; AIS/ICH = 4,730/1,213; 11 studies). Clinical symptoms/signs association with significantly lower risk of ICH (i.e. higher risk AIS) include symptom onset in morning time (0.41 [0.32–0.54]; AIS/ICH = 2,721/495; 4 studies), facial weakness (0.66 [0.46–0.94]; AIS/ICH = 3,318/1,590; 15 studies), hemiplegia (0.68 [0.50–0.91]; AIS/ICH = 15,953/4,905; 31 studies), and ataxia (0.73 [0.61–0.86]; AIS/ICH = 7,741/2,244; 8 studies).

Sensitivity, specificity and LRs for accuracy of ICH diagnosis by symptom/sign are presented in Table 1. Specificities range from 20.7 %–96.9 % and +LR range from 0.51 to 7.20. Symptoms considered most clinically relevant for identifying ICH, based on a combination of high specificity (≥85 %) and high +LR include coma, GCS ≤8, vomiting, seizure, headache and syncope. The feature most indicative of AIS, with a combined specificity <50 % and low +LR, is hemiplegia. The +LRs for hemorrhage diagnosis are similar to diagnostic ORs calculated from the meta-analysis.

A comparison between AIS and ICH symptoms/signs by geographical region is outlined in sTable 4. A widening of CIs is noted due to the reduced sample size but overall, the direction of association remains consistent.

Sensitivity analyses showed the direction of associations between symptoms/signs and stroke subtype remained consistent. However, in studies that distinguished intracerebral hemorrhage from subarachnoid hemorrhage (n = 22; sFigure 38), some associations were no longer statistically significant. Specifically, hemiplegia, ataxia, facial weakness, and dizziness were not significantly associated with a stroke subtype.

Risk of bias assessment

Of the included studies, high risk of bias was identified in 48 studies, and 7 studies had low risk of bias across all 4 domains.[28–34] A sensitivity analysis was performed restricted to studies which did not score high risk of bias in 1 or more of the domains (sTable 2), which was directionally consistent with the overall analysis (sFigure 39).

Funnel plots, using univariate effect measures, were generated for each symptom or sign to visually assess publication bias, and Egger's regression test was applied to formally test for funnel plot asymmetry. Most funnel plots appeared symmetrical, however, Egger's test suggested potential publication bias for altered level of consciousness (p = 0.015), arm weakness (p = 0.047), leg weakness (p < 0.001), and acute symptom onset (p = 0.002) (Supplementary Figures 41, 48, 49, and 67, respectively). In several cases, adjustment using the trim-and-fill method resulted in attenuation of pooled odds ratios toward the null for facial weakness (0.76, [0.53–1.08]) and neck stiffness (2.82, [1.11–7.26]), and away from the null for sphincter dysfunction (1.60, [1.07–2.40]), indicating potential publication bias in these domains.

Discussion

In this systematic review of 60 studies, including 12,879,006 patients, we report 10 symptoms/signs significantly associated with an increased diagnostic odds of ICH versus AIS, including abnormal extensor plantar response, altered level of consciousness, coma, GCS ≤ 8, headache, neck stiffness, syncope, seizure, vertigo/dizziness, and vomiting, while four symptoms were associated with a lower odds of ICH, namely ataxia, facial weakness, hemiplegia and symptom onset in morning time. Our findings support further investigation of the utility of a standardized pre-test clinical probability.

Our study provides an updated meta-analysis, that includes a larger number of studies compared to the most recent meta-analysis (19 studies).[12] Our larger sample size relates to inclusion of interval publications and extending eligibility to studies of single symptoms/signs,

Table 1
Accuracy of Symptoms or Signs for diagnosing hemorrhagic stroke.

Symptom or Sign	Number of Studies	Sensitivity (%) (95 % CI)	Specificity (%) (95 % CI)	+LR (95 % CI)	-LR (95 % CI)	Diagnostic ORs (95 % CI)
Coma*	9	22.05 (14.85–31.45)	96.84 (94.52–98.2)	7.20 (4.18–11.60)	0.80 (0.71–0.88)	8.81 (5.02–15.45)
GCS ≤ 8*	7	41.72 (26.93–58.16)	87.05 (69.01–95.30)	3.42 (1.76–6.32)	0.68 (0.56–0.78)	4.37 (2.35–8.16)
Vomiting*	26	31.50 (23.43–40.88)	88.75 (84.76–91.80)	2.82 (2.15–3.62)	0.77 (0.68–0.85)	3.86 (2.71–5.49)
Seizure*	22	8.12 (6.08–10.77)	96.87 (95.26–97.94)	2.65 (1.73–3.88)	0.95 (0.92–0.97)	2.67 (1.72–4.15)
Headache*	44	37.37 (30.97–44.25)	85.01 (80.92–88.35)	2.51 (2.01–3.10)	0.74 (0.67–0.80)	3.49 (2.63–4.64)
Syncope*	7	17.38 (5.40–43.66)	92.87 (78.14–97.94)	2.43 (1.74–3.34)	0.88 (0.71–1.08)	2.74 (1.96–3.83)
Altered GCS	37	50.88 (42.36–59.35)	76.72 (69.66–82.55)	2.20 (1.76–2.74)	0.64 (0.55–0.73)	3.55 (2.55–4.95)
Diplopia	4	19.71 (3.77–60.64)	89.23 (73.74–96.07)	1.80 (0.90–2.62)	0.86 (0.53–1.00)	2.26 (0.94–5.46)
Abnormal/ Fixed Gaze	6	37.62 (21.75–56.68)	75.56 (58.64–87.08)	1.61 (0.84–2.86)	0.83 (0.59–1.08)	1.87 (0.77–4.55)
Dizziness	11	18.34 (10.84–29.34)	86.16 (76.13–92.40)	1.33 (1.09–1.63)	0.95 (0.90–0.98)	1.32 (1.04–1.68)
Abnormal Plantar	5	81.43 (63.18–91.8)	31.55 (19.01–47.51)	1.19 (1.09–1.31)	0.60 (0.39–0.84)	1.94 (1.24–3.04)
Acute Onset	9	62.31 (53.95–70.00)	46.01 (28.55–64.50)	1.18 (0.93–1.61)	0.84 (0.64–1.17)	1.46 (0.79–2.71)
Other Focal Visual Disturbance	13	12.13 (4.88–27.07)	88.31 (79.07–93.80)	1.07 (0.60–1.70)	0.99 (0.89–1.05)	1.12 (0.62–2.04)
Arm Weakness	5	64.52 (43.13–81.35)	31.34 (12.44–59.46)	0.98 (0.65–1.49)	1.25 (0.56–2.62)	0.82 (0.26–2.61)
Leg Weakness	4	63.51 (38.91–82.62)	32.40 (13.02–60.55)	0.98 (0.59–1.55)	1.25 (0.50–2.74)	0.83 (0.23–2.99)
Dysarthria	9	42.63 (30.53–55.68)	55.46 (43.16–67.13)	0.96 (0.79–1.15)	1.04 (0.89–1.19)	0.92 (0.66–1.29)
Aphasia	22	26.21 (19.35–34.46)	72.50 (63.30–80.12)	0.96 (0.81–1.12)	1.02 (0.96–1.09)	0.90 (0.71–1.13)
Sensory Disturbance	13	20.07 (6.93–45.84)	78.55 (59.59–90.10)	0.95 (0.58–1.36)	1.01 (0.85–1.11)	1.02 (0.60–1.73)
Dysphagia	5	10.76 (1.68–46.02)	88.05 (69.64–95.95)	0.94 (0.38–1.67)	0.99 (0.76–1.06)	1.13 (0.65–1.98)
Altered Speech	13	45.82 (34.9–57.15)	50.95 (42.20–59.63)	0.94 (0.78–1.10)	1.06 (0.91–1.22)	0.87 (0.63–1.21)
Hemiplegia†	31	72.00 (65.55–77.66)	20.67 (15.64–26.81)	0.91 (0.84–0.97)	1.36 (1.09–1.69)	0.68 (0.50–0.91)
Facial Weakness	15	27.33 (16.85–41.10)	66.11 (48.41–80.22)	0.82 (0.64–1.04)	1.11 (0.99–1.30)	0.66 (0.46–0.94)
Ataxia	8	7.92 (4.38–13.88)	89.23 (82.36–93.63)	0.74 (0.62–0.86)	1.03 (1.01–1.06)	0.73 (0.61–0.86)
Morning Onset	4	14.59 (10.93–19.22)	70.95 (65.22–76.07)	0.51 (0.40–0.63)	1.20 (1.14–1.28)	0.41 (0.32–0.54)

Neck Stiffness and Sphincter Dysfunction have been excluded as only 2 studies reported these symptoms and the MADA package in R requires 3 or more studies for a bivariate random effects model. GCS – Glasgow Coma Scale, CI – Confidence Interval, +LR – Positive Likelihood Ratio, -LR – Negative Likelihood Ratio, OR – Odds Ratio.

broader eligibility criteria related to study design, resulting in a substantially larger population size (12,879,006 versus 6,438).[12] Our study specifically addressed the question of discrimination of AIS from ICH, rather than the preceding clinical question of discriminating acute stroke from other syndromes. Several tools have been developed to identify stroke from clinical features alone and are used in clinical practice.[35–37] For example, the ROSIER (Recognition of Stroke in the Emergency Room) score was specifically developed to aid physicians identify true stroke versus stroke mimic cases, in those presenting with acute neurological symptoms.[36] The ORs for individual symptoms predictive of true stroke ranged from 27.6 to OR of 0.1, which is consistent with estimates in our analyses.

To date, the rationale for not pursuing a standardized clinical pre-test probability score is the absence of biomarker diagnostic tests, and the excellent diagnostic properties of CT/MRI in excluding ICH, which have become so central to the practice of stroke diagnosis that a thorough clinical assessment of a stroke patients has been neglected. Prior to CT imaging, there was an advanced understanding of the pathophysiology of AIS and ICH and its manifestations at the bedside. Clinicians depended primarily on basic clinical skills to diagnose ICH. In regions where neuroimaging is scarce,[6] diagnosis on clinical features alone is still used. As promising biomarkers for stroke differentiation emerge,[9] particularly point-of-care biomarkers,[11] consideration for a combination of pre-test clinical probability and biomarkers for stroke differentiation may now be possible.[10]

Combining pre-test clinical probability with biomarkers, as is used in other acute vascular presentations, relies on the diagnostic properties of a standardized clinical assessment and biomarkers, both alone and in combination. A systematic review which investigated the accuracy of symptoms for diagnosing MI, revealed symptom ORs ranged from 0.17 with chest wall tenderness, to 4.54 with sweating.[38] In one study, typical chest pain alone was associated with an OR of 2.8 for MI, which increased substantially when combined with troponin (OR 15.9) and ECG findings (OR 44.5).[8] Similarly, in PE, individual symptoms had

limited discriminatory value (e.g., chest pain OR 0.6; signs of DVT OR 5.1), but when combined with a negative D-dimer, the probability of PE was reduced by up to 59 % when pre-test probability was high.[7] These examples highlight that while no symptom or sign is stand-alone in diagnosis, combining clinical features with other diagnostic modalities has shown enhances diagnostic accuracy in acute vascular presentations.

Applying a similar approach in acute stroke, integrating standardized clinical assessments with emerging point-of-care tools, may hold promise in early subtype differentiation. This is particularly relevant in low- and middle-income countries (LMIC) or remote settings, where access to timely neuroimaging is limited or unavailable, and early clinical decision-making relies more heavily on bedside assessment.

Sensitivity, specificity and LRs were calculated for each symptom or sign for accuracy of diagnosing ICH. Specificity results range from 20.7 % with hemiplegia to 96.8 % with coma. Seizure has the highest specificity indicating that when a patient presents without seizure, it would seem rational for the clinician to assume this is not a hemorrhagic stroke. However, the significantly higher prevalence of AIS (between 55 % and 83 % depending on region (sFigure 1)), must be given due consideration. Even with symptoms or signs that have high specificity for ICH, such as coma (96.8 %) or seizure (96.9 %), the overall probability of the individual having an AIS when presenting without the symptom, is high in part due to relatively high prevalence of AIS compared to ICH.

The variation in ICH prevalence by region, reported in our study and others,[1,12] may reflect both a true difference in the epidemiology of stroke subtypes, but also differences in access and management. According to the Global Burden of Disease study, there is almost double the proportion of ICH in LMIC compared with high-income countries (HIC) (29.5 % vs 15.8 %), and age-standardized stroke-related mortality rates and DALY rates are over 3.5 times higher in the LMIC compared to the HIC.[1] Access to acute diagnostic neuroimaging, and reperfusion therapies, is more limited in many LMIC, compared to HIC.[6] One meta-analysis found that up to 60.5 % of patients presenting with stroke symptoms in LMIC, were being diagnosed >24 hours after symptom onset.[39] This contrasts with a pooled analysis from HIC, where time from symptom onset to treatment was 233 minutes,[40] suggesting patients in HIC can receive diagnosis and treatment, long before patients in LMIC receive a stroke diagnosis. Without dedicated efforts to improve stroke care and outcomes, stroke morbidity and mortality will worsen in these regions over time. Despite difference in prevalence, our findings report consistency in direction of association for symptoms/signs among regions.

Limitations

Our systematic review has several limitations. Firstly, we report substantial heterogeneity among studies (up to I^2 98.8 %). While much of the heterogeneity relates to variations in population, measurement, and study design, there are inherent limitations to the I^2 statistic in meta-analyses of large sample sizes.[41] We adopt the observed consistency in the direction of association among studies to support the strength of our conclusions. Therefore, the level heterogeneity does not necessarily limit the reliability of our findings.

Second, publication bias cannot be entirely excluded. While Egger's test did not indicate significant asymmetry for most symptoms/signs, changes in effect estimates following application of the trim-and-fill method suggest the presence of possible small-study effects. In particular, findings related to facial weakness, neck stiffness, and sphincter dysfunction should be interpreted with caution, as their effect sizes were meaningfully altered after adjustment. The possibility remains that non-English language studies were missed. Additionally, inclusion of abstracts and non–full–text studies may introduce incomplete reporting bias. However, sensitivity analyses excluding these records demonstrated that our principal results remained materially unchanged.

Third, most of the included studies had 1 or 2 sources of bias. Most studies did not explicitly differentiate between subarachnoid hemorrhage and intracerebral hemorrhage, instead reporting features of intracranial hemorrhage as a whole. However, sensitivity analyses restricted to studies without high risk of bias, or those specifying intracerebral hemorrhage, were materially consistent with overall findings (sFigure 38/39).

Fourthly, a key limitation is the unavailability of individual patient data in the included studies. This prevented assessment of symptom combinations, or patterns, and their association with stroke subtype. Consequently, only ORs for individual symptoms/signs were analyzed. Despite this limitation, our results indicate that even when assessed in isolation, individual symptoms remain predictive of stroke subtype. However, we acknowledge that, given the overall modest diagnostic performance of individual symptoms, the application of pre-test probability remains somewhat speculative.

Fifthly, while previous meta-analyses have examined the association between presenting characteristics in acute stroke compared to other syndromes, our study focuses solely on their association with stroke subtypes. Therefore, these findings are only applicable in populations where stroke is suspected.

Sixthly, classifying ICH as "cases" and AIS as "controls" represents a simplification that does not fully capture the clinical complexity, particularly given the overlapping presentation of many symptoms and signs, as well as overlap in scenarios such as haemorrhagic transformation in AIS. Importantly, the primary function of pre-test clinical probability, and ultimately any resulting clinical tool, is to help exclude ICH. Neuroimaging, particularly non-contrast CT, is currently the first-line modality for stroke evaluation. Decisions regarding the initiation of reperfusion therapies are based primarily on these scans during the acute phase. Notably, CT has only a modest sensitivity for AIS detection in the acute phase, but a sensitivity of close to 100 % for ICH detection.[5] Thus, CT's principal role is to rule out ICH. For a clinical tool to be effective in this context it must be both usable and reliable in real-world conditions, including when diagnostic uncertainty is high, in order to identify ICH. From this standpoint, classifying ICH as "cases" is appropriate. We acknowledge that this approach may limit interpretability in some clinical contexts, but it serves as a pragmatic starting point for developing novel, structured diagnostic tools in the acute stroke setting. It supports the development of a pre-clinical probability score for ICH detection based on presenting symptoms and signs, which we envision as one component of a future multimodal clinical prediction model incorporating additional diagnostic modalities, such as biomarkers.

Finally, three of the included studies did not use neuroimaging to diagnose stroke subtype in all included cases,[42–44] while extent of neuroimaging use was unclear in twelve studies (sTable 2). The lowest percentage of CT use was a cohort in Northwest Ethiopia, where 49.8 % elected not to have a CT scan due to cost,42 which may introduce verification bias.

Conclusion

Our review reports consistent differences in the prevalence of certain clinical features between ischemic and hemorrhagic stroke subtypes. While these findings may inform future diagnostic strategies, the overall modest discriminatory power of individual symptoms underscores the need for further research to develop innovative approaches for estimating pre-test clinical probability.

Contributorship

C.M McDermott was responsible for funding acquisition, developing the search strategy and eligibility criteria, data extraction, risk of bias assessment, statistical analysis, and manuscript drafting. A. Seminer and A. Mulihano contributed to data extraction. S. Comer contributed to risk of bias assessment and manuscript revision. C. Reddin, C. Judge, M.

Costello, M. Canavan, A. Smyth, and P. Hurley were responsible for manuscript revision. F. Krewer contributed to statistical analysis, manuscript drafting, and revision. M. J. O'Donnell provided supervision and contributed to manuscript drafting and revision.

Ethical approval

Not Applicable for this Systematic Review and Meta-Analysis

Inform consent

Not Applicable for this Systematic Review and Meta-Analysis

Guarantor

Prof. M.J. O'Donnell is the guarantor of this work and accepts full responsibility for the integrity and accuracy of the data and the content of this manuscript.

CRediT authorship contribution statement

Clodagh M McDermott: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Allie Seminer:** Data curation. **Sinéad Comer:** Investigation. **Alfredi Mulihano:** Data curation. **Catriona Reddin:** Writing – review & editing. **Conor Judge:** Writing – review & editing. **Maria Costello:** Writing – review & editing. **Michelle Canavan:** Writing – review & editing. **Andrew Smyth:** Writing – review & editing. **Paul Hurley:** Writing – review & editing. **Finn Krewer:** Writing – review & editing, Methodology, Formal analysis. **Martin J O'Donnell:** Writing – review & editing, Supervision, Methodology, Investigation, Conceptualization.

Declaration of competing interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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C.M McDermott, A. Seminer and A Mulihano were responsible for data collection. C.M McDermott and F. Krewer performed the analysis. All authors contributed to data interpretation and critical revision of the report.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jstrokecerebrovasdis.2025.108413.

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