Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Clinical and Genetic Characteristics of SCA27B: A Global Systematic Review and Meta- Analysis

Farsana Mustafa
All India Institute of Medical Sciences
Ayush Agarwal
All India Institute of Medical Sciences
Ajay Garg
All India Institute of Medical Sciences
Mohammed Faruq
CSIR - Institute of Genomics and Integrative Biology (IGIB)
Achal Kumar Srivastava
All India Institute of Medical Sciences
Divyani Garg
divyanig@gmail.com

All India Institute of Medical Sciences

Research Article

Keywords: SCA27B, LOCA, Episodic, Downbeat Nystagmus, FGF14

Posted Date: April 7th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9257134/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at The Cerebellum on June 26th, 2026. See the published version at https://doi.org/10.1007/s12311-026-02043-w.

Abstract

Background

Spinocerebellar ataxia 27B (SCA27B) has been recognised as a major cause of sporadic late-onset cerebellar ataxias, accounting for 9–61% of previously unexplained cases.

Objectives

To describe clinical, radiological and genetic spectrum of SCA27B through a systematic review of the global literature.

Methods

A systematic literature search of PubMed, Embase (Ovid), Ovid Medline and Scopus was conducted. Studies including genetically confirmed SCA27B patients were selected. Individual patient and aggregate data were extracted, pooled and summarised.

Results

A total of 45 studies including 1364 patients were analysed. The pooled mean age at onset was 53.9 ± 14.7 years. Cerebellar ataxia (pooled prevalence 0.91; 95% CI: 0.78–0.97), oculomotor abnormalities [excluding nystagmus] (0.74; 95% CI: 0.64–0.82), overall nystagmus (0.67; 95% CI: 0.57–0.75), downbeat nystagmus (0.48; 95% CI: 0.34–0.63), dysarthria (0.46 [0.38–0.54]), episodic symptoms (0.38 [0.29–0.48]), vertigo/dizziness (0.34 [0.29–0.39]), and tremors (0.31 [0.19–0.47]) were the most frequent clinical features. Substantial heterogeneity was present across outcomes. Genotype-phenotype correlation analysis showed that ≤ 249 repeats were associated with significantly higher odds of downbeat nystagmus (OR = 0.56, p = 0.002), nystagmus (OR = 0.45, p = 0.002) and pyramidal signs (OR = 0.25, p < 0.001). Larger expansions (≥ 250 repeats) were significantly linked to episodic manifestations (OR = 1.54, p = 0.049) and broader oculomotor involvement (OR = 3.70, p < 0.001).

Conclusions

SCA27B is a common and genetically defined cause of late-onset cerebellar ataxia with a heterogeneous phenotype. Vestibular and episodic features often precede gait ataxia. Recognition of key clues, including downbeat nystagmus, oculomotor abnormalities, episodic symptoms and triggers, is essential to facilitate timely diagnosis and appropriate genetic testing.

Introduction

Molecular testing is negative in approximately 75% of late-onset cerebellar ataxias (LOCAs), largely attributable to limitations of standard next-generation sequencing analysis in detecting certain sequence variations, such as tandem repeat expansions.[1] The use of advanced bioinformatics tools and long-read sequencing has become essential for diagnosing cases in which genetic forms of LOCA are suspected.[2] Spinocerebellar ataxia 27B (SCA 27B) is a dominantly inherited cerebellar ataxia characterized by heterozygous or homozygous (GAA)-(TTC) repeat expansion in intron 1 of fibroblast growth factor 14 (*FGF14*) gene. SCA27B has emerged as an important cause of adult-onset, inherited cerebellar ataxia, representing 9-61% of previously unexplained cases across different patient cohorts.[2] Clinical hallmarks include slowly progressive cerebellar ataxia with early episodic manifestations, double vision, downbeat nystagmus (DBN) and vertigo or dizziness.[3] A cohort study of 118 individuals with sporadic LOCAs found pathogenic *FGF14* GAA expansions in 12.7% (15/118), suggesting that SCA27B may commonly occur even in the absence of an apparent family history.[4]

Screening for *FGF14* GAA repeat expansions involves a multi-step workflow that includes fluorescent long-range polymerase chain reaction (PCR), bidirectional repeat-primed PCR followed by agarose gel electrophoresis of the long- range PCR products and confirmation with Sanger sequencing.[3] Current evidence suggests that pathogenicity is associated with expansions of at least 250 GAA repeats, although reduced or incomplete penetrance has been reported for repeat lengths within the 250- 300 range.[5]

As cohorts and cases continue to be increasingly reported worldwide, synthesizing global evidence is critical to delineate the consolidated spectrum of SCA27B, to aid diagnostic uncertainty and guide appropriate genetic testing strategies. This systematic review summarizes current global literature on demographics, clinical manifestations and genetic characteristics of SCA27B.

Methods

Search strategy

A systematic literature search was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. [6] PubMed, Ovid Medline, Embase (Ovid), and Scopus were searched from database inception to 26 January 2026. The study protocol was prospectively registered with PROSPERO (CRD420251246545). The search strategy combined controlled vocabulary (eg., *MeSH* and *Emtree*) and free-text keywords relating to the genetic cause (*FGF14* GAA repeat expansion) and the associated phenotype (spinocerebellar ataxia 27B / SCA27B/ episodic ataxia / adult-onset cerebellar ataxia). Detailed search strategy is provided in Supplement S1.

Eligibility Criteria

Studies were included if they met the following criteria:

1. Population

Studies that involved human participants of any age with genetically confirmed SCA27B, defined by the presence of a pathogenic GAA–TTC repeat expansion in intron 1 of the *FGF14* gene, confirmed by repeat-primed PCR, long-range PCR, or long-read sequencing. Studies based solely on clinical suspicion without molecular confirmation were excluded.

2. Scope of Reporting

Eligible studies reported data in at least one of the following domains:

- Clinical features: age at onset; episodic versus progressive ataxia; cerebellar, oculomotor, or vestibular manifestations; gait or coordination impairment; pyramidal or extrapyramidal signs; amyotrophy; autonomic features; natural history or progression rate.
- Investigations: Neuroimaging findings; electrophysiological studies; vestibular or ocular motor assessments; GAA repeat expansion size.
- Treatment and outcomes: therapeutic interventions, documented clinical response or long-term functional outcomes.

3. Study Design
Case reports, case series, cohort studies (prospective or retrospective), registry-based studies, cross-sectional studies, and natural history studies were eligible. Diagnostic screening or genetic prevalence studies were included only if individual or aggregate clinical data were provided for confirmed SCA27B cases. We also included a seven-patient dataset from our group (manuscript under peer review at the time of analysis). Only peer-reviewed, full-text articles published in English were included.

Screening

Two reviewers independently reviewed the screened titles and abstracts, followed by full-text assessment for eligibility (FM/DG). Disagreements were resolved by consensus.

Outcomes

The following data were extracted from the included studies: Author and year of publication, age at onset of symptoms, age at presentation, sex, family history, symptoms at onset, occurrence of vestibular symptoms, dysarthria, oculomotor features (excluding nystagmus), nystagmus (all types), downbeat nystagmus, pyramidal signs, cerebellar ataxia, tremors, amyotrophy, extrapyramidal symptoms, dysautonomia, triggers, GAA repeat size, nerve conduction studies, neuroimaging findings and treatment details.

Statistical analysis

Statistical analyses were performed using R (R Foundation for Statistical Computing, Vienna, Austria), with proportional meta-analyses done using the metafor package.[7,8] A proportional meta-analysis was performed to estimate the pooled prevalence of individual clinical features in patients with SCA27B. Random-effects models were used for all analyses, with proportions stabilized using the Freeman–Tukey double arcsine transformation to account for studies with extreme values. Results were reported as pooled prevalence with 95% confidence intervals (CI), supported by reproducible outputs including forest plots, Q-tests and funnel plots. Heterogeneity was quantified using Tau and I^2 estimates, and potential publication bias was assessed using fail-safe N, Egger's regression, and Kendall's tau, strengthening the statistical validity of the phenotypic profile generated.[8,9]In studies where only aggregate data were reported, summary level information was captured. For studies presenting outcomes as median with interquartile range, mean and standard deviation(SD) were estimated using the combined methods described by Luo et al[10] and Wan et al which provide validated approaches for converting medians and interquartile range(IQR) values to means and standard deviations under the assumption of an approximately normal distribution, applying the formula IQR = 1.35 × SD.[11]

Genotype-phenotype correlation analysis

Across the included studies, there was significant heterogeneity in the reporting of *FGF14* GAA repeat expansion length. Studies used different reporting methods, including aggregated medians, broad ranges and pre-defined categorical thresholds (e.g., ≥ 250 repeats), frequently without providing individual patient-level data or clearly differentiating between monoallelic and biallelic expansions in the provided summary statistics. Due to these inconsistencies, repeat length was examined using categorical groupings for pooled analysis. Data were dichotomized into two clinically meaningful subgroups based on the longest reported allele: a high-repeat group (≥ 250 GAA repeats) and a low-repeat group (≤ 249 GAA repeats). The ≥ 250 repeat threshold was decided based on its established role as the diagnostic cutoff for a fully penetrant pathogenic expansion in SCA27B, thereby maintaining clinical relevance in the comparative analysis. The presence or absence of clinical findings was treated as categorical data. 2x2 contingency tables were constructed to assess the associations between repeat category and presence of symptoms. As several outcomes were infrequent and yielded expected cell counts below five, Fisher's exact test was applied to compare proportions between groups. The odds ratio (OR) and 95% confidence intervals (CI) were calculated to estimate the effect size of the repeat length on each clinical feature. A two-sided *p*-value of < 0.05 was considered statistically significant.

Publication bias assessment

Publication bias was evaluated using multiple complementary statistical methods to detect small effect size of the studies and potential selective reporting. Funnel plot visual inspection was done for each clinical outcome included in meta-analysis and quantitative assessments were done using Kendall's rank correlation test (Begg's test) and regression-based Egger-type tests to evaluate asymmetry in the funnel plot. Rosenthal's Fail-Safe N (file-drawer analysis) was also calculated to estimate the number of

hypothetically missing null-effect studies required to render the pooled effects statistically non-significant. These methods together provide a robust evaluation of publication bias combining visual, statistical and sensitivity-based perspectives.

Results

The PRISMA flow diagram is depicted in Fig. 1. Individual patient level data/aggregated data of a total of 1364 patients from 45 articles were reviewed (Supplement S2, S3 and S4). Global distribution of reported SCA27B cases is shown in Fig. 2. Across all included studies, the pooled mean age at onset was 53.97 ± 14.87 years. The male-to-female ratio was 582 (42.6%) to 538 (39.4%), while sex was not reported for 244 individuals (17.8%). The pooled prevalence of various clinical and laboratory features are reported below.

Cerebellar ataxia

Cerebellar ataxia was evaluated across 23 studies, and the random-effects model showed a pooled prevalence of 0.91 (95% CI: 0.78–0.97), confirming cerebellar ataxia as the predominant clinical feature in SCA27B (Fig. 3) although details regarding midline or appendicular involvement were not reported uniformly. Substantial variability was observed across cohorts, indicated by high heterogeneity (I^2 = 88.1%, Tau^2 = 6.4692, $p < 0.0001$).

Oculomotor abnormalities [excluding nystagmus]

Oculomotor abnormalities [excluding nystagmus] were evaluated across 17 studies and the random-effects model showed a pooled prevalence of 0.74 (95% CI: 0.64–0.82). The forest plot (Fig. 4) shows high prevalence estimates across most cohorts, highlighting the prominence of impaired eye movement control within the clinical spectrum of SCA27B. Substantial heterogeneity was observed (I^2 = 87.5%, Tau^2 = 0.0464, $p < 0.0001$).

Overall nystagmus

The pooled random effects estimate points out that nystagmus is a common clinical manifestation in SCA27B, with a pooled prevalence of 0.67(95% CI: 0.57–0.75) across 25 studies. The forest plot (Fig. 5) shows a wide range of prevalence values, indicating that although nystagmus was frequently observed, its presence varied substantially between cohorts. Substantial heterogeneity was observed (I^2 = 58.9%, Tau^2 = 0.8948, $p < 0.0001$).

Downbeat Nystagmus

DBN was evaluated across 22 studies and the random-effects model demonstrated a pooled prevalence of 0.48 (95% CI: 0.34–0.63) (Fig. 6). Significant heterogeneity was noted (I^2 = 82%, Tau^2 = 1.9466, $p <$

0.001).

Dysarthria

Dysarthria was evaluated across 21 studies and the random-effects model showed a pooled prevalence of 0.46 (95% CI: 0.38–0.54) (S5). Substantial heterogeneity was noted (I^2 = 80.9%, Tau^2 = 0.0289, $p < 0.001$).

Episodic symptoms

Episodic symptoms were evaluated across 25 studies, with a pooled prevalence of 0.38 (95% CI: 0.29–0.48) based on a random-effects model (S6). Significant heterogeneity was observed (I^2 = 85.9%, Tau^2 = 0.0441, $p < 0.0001$).

Tremor

Tremors were evaluated across 13 studies and the random-effects model showed a pooled prevalence of 0.31 (95% CI: 0.19–0.47), confirming tremor as a relatively common clinical manifestation in SCA27B. Reported prevalence estimates varied widely across studies (S7). Reported tremor phenotypes comprised intention tremor, postural tremor, and dystonic tremor, indicating that tremor in SCA27B is heterogeneous rather than restricted to a single motor phenotype. Substantial heterogeneity was observed (I^2 = 91.3%, Tau^2 = 1.6947, $p < 0.0001$).

Vertigo and dizziness

Vertigo was evaluated across 21 studies and a random-effects model showed a pooled proportion of 0.34 (95% CI: 0.29–0.39), indicating that approximately 34% of individuals with SCA27B experience vertigo as a clinical symptom. Substantial heterogeneity among studies (I^2 = 62.2%, $p < 0.0001$) was noted suggesting important variability in cohort characteristics, reporting methodology and disease severity (Tau^2 = 0.0121). The forest plot (S8) showed that most studies reported proportions above the pooled estimate, although several outlier cohorts demonstrate either notably high or low prevalence.

Dysautonomia

Dysautonomia was assessed across 10 studies, with the random-effects model showed a pooled prevalence of 0.21 (95% CI: 0.16–0.27) (S9). Mild to moderate heterogeneity was observed across studies (I^2 = 33.2%, τ^2 = 0.0036, $p = 0.1421$), suggesting some variability between cohorts that did not reach statistical significance.

Pyramidal Involvement

Pyramidal signs were evaluated across 13 studies and the random-effects model showed a pooled prevalence of 0.20 (95% CI: 0.06–0.38). Prevalence estimates varied widely across studies, as shown in the forest plot (S10). Substantial heterogeneity was observed, consistent with the variability among cohorts (I^2 = 95.3%, Tau^2 = 0.1443, $p < 0.0001$).

Amyotrophy and extrapyramidal symptoms

Estimates for amyotrophy were based on three studies (k = 3), with a pooled prevalence of 0.03 (95% CI: 0.00–0.08) using a random-effects model. Similarly, estimates for extrapyramidal symptom were derived from two studies (k = 2), yielding a pooled prevalence of 0.13 (95% CI: 0.00–0.37). For both the outcomes, the small number of contributing studies resulted in wide confidence intervals, showing a high degree of statistical imprecision. As a result, heterogeneity metrics should be interpreted cautiously, as the limited sample may not provide sufficient power to reliably detect between- study variability (S11).

Radiology

Radiological data was available for 41 out of 45 studies(91.1%), out of which cerebellar atrophy was noted in in 457 out of 782 patients of the cohort, although a definitive pooled analysis could not be done due to non-uniform data reporting across the included studies. (S3). Within the subset of studies that specifically evaluated individual radiological abnormalities, pontine atrophy was observed in 39 of 188 patients (20.7%), midbrain atrophy in 13 of 135 cases (9.6%), and hemispheric white matter hypersignals in 117 of 199 patients (58.8%). Middle cerebellar peduncle (MCP) atrophy was reported in 8 of 86 patients (9.3%), while cervical medullary atrophy was observed in 3 of 32 patients (9.4%). Pons hypersignals were identified in 3 of 86 cases (3.5%) and MCP hypersignals in 2 of 86 cases (2.3%). Notably, no cases showed the “hot cross bun” sign. These figures reflect trends within the subset of studies that specifically screened for these radiological markers.

Nerve conduction studies

Nerve conduction study (NCS) abnormalities were variably reported and were often described as a length-dependent process. Sensory–motor axonal neuropathy emerged as the most prominent electrophysiological finding, identified in 42 of 120 patients (35%) within cohorts that provided detailed data. In contrast, demyelinating features were uncommon, observed in only 2 of 63 evaluable cases (3.2%). Due to substantial heterogeneity in reporting across studies, these findings likely reflect investigative patterns within specific reporting subgroups rather than true pooled prevalence.[4,5]

Repeat size

Estimates for the proportion of individuals with less than 250 repeats were derived from seven studies with 222 participants. Using a random-effects model, the estimated pooled prevalence was 0.98 (95% CI: 0.13–1.00). Moderate heterogeneity was observed (I^2 = 51.1%, p = 0.056). The wide confidence interval and extremely broad prediction interval (0.00–1.00) reflected substantial inconsistency and statistical imprecision between studies, likely influenced by small sample sizes and the presence of studies reporting extreme proportions (0% or 100%).

Estimates for the proportion of individuals with repeats greater than 250 were derived from 27 studies including 941 participants. The pooled prevalence using a random effects model was estimated as 1.00 (95% CI: 0.37–1.00). Statistical heterogeneity was negligible (I^2 = 0.0%, p = 0.9895), indicating

consistency across all studies. Despite the absence of statistical heterogeneity, the confidence interval (0.00–1.00) was wide, highlighting the imprecision related to the high frequency of studies reporting proportions of 100% and the inherent statistical instability when pooling near-boundary proportions.

Genotype- Phenotype correlations

Association analyses between repeat lengths (≥ 250 vs ≤ 249) and clinical features was assessed. Higher odds in the ≤ 249 group were identified for downbeat nystagmus (OR = 0.556, 95% CI: 0.38–0.81; p = 0.0016), overall nystagmus (OR = 0.45, 95% CI: 0.25–0.76; p = 0.0017), pyramidal signs (OR = 0.25, 95% CI: 0.16–0.39; p < 0.001). Higher odds for episodic symptoms (OR = 1.54, 95% CI: 0.99–2.45; p = 0.049), oculomotor signs (excluding nystagmus) (OR = 3.70, 95% CI: 2.39–5.83; p < 0.001) were observed in the ≥ 250 group.

No significant associations were observed for amyotrophy, cerebellar ataxia, dysarthria, dysautonomia, tremor, vertigo, extrapyramidal symptoms, or trigger-related features (p > 0.05) (S4). These genotype-phenotype correlations are visually summarized in a heatmap (S15), which demonstrates the direction and magnitude of effect sizes across clinical features according to repeat length category.

Publication bias assessment

Evidence of funnel-plot asymmetry was limited to a small subset of outcomes. Vertigo/dizziness showed significant asymmetry on both Begg's test (Kendall's τ = 0.374, p = 0.005) and Egger's test (Z = 2.234, p = 0.025). In addition, oculomotor abnormalities also showed strong evidence of asymmetry (Begg's test: Kendall's τ = −0.532, p < 0.001; Egger's test: Z = − 4.607, p < 0.001). In contrast, no significant asymmetry was noted for tremors, pyramidal symptoms, nystagmus, downbeat nystagmus, cerebellar ataxia, episodic symptoms, dysarthria or dysautonomia (Begg/Egger p-values > 0.05). These findings indicate the presence of small-study effects, likely reflecting the influence of case reports, case series and retrospective cohort designs within the included literature and suggest a non-trivial risk of publication bias for these specific clinical features. Rosenthal's Fail-Safe N values were consistently large across outcomes (in the thousands), suggesting that a substantial number of missing null studies would be required to negate the statistical significance of the pooled findings. These high values do not eliminate the possibility that effect estimates may be inflated in outcomes showing funnel-plot asymmetry, in the presence of the predominance of smaller observational studies within the available literature. Funnel plots and publication-bias statistics are provided in S16-S26.

Discussion

The classic phenotypic description of SCA27B cases is a slowly progressive pan-cerebellar syndrome with oculomotor signs and episodic symptoms. In most previously published series, SCA27B has been reported to present predominantly in the 5-7th decades and is recognised as a major cause of sporadic LOCA.[4] The only prior systematic review by Hirschfeld et al. reported a mean age of onset of 57.4 years among 776 patients. Similarly, in the study by Wirth et al., the mean age at inclusion of 15 individuals

with SCA27B was 72.4 ± 6.3 years, however the mean age of onset was 67.5 ± 7 years.[4] The pooled mean age at onset of 55 ± 14.8 years in the global data likely reflects the inclusion of a greater number of recently documented cases worldwide, indicating that as awareness and diagnostic testing expand, earlier presentations are also increasingly being identified. This highlights an important shift in the evolving epidemiological trends in SCA27B and points out the need to consider this diagnosis even in younger individuals presenting with unexplained cerebellar syndromes.[12] Across most of the published SCA27B cohorts including our review and the one by Hirschfeld et al, the sex distribution is consistently close to equal, with a slight male predominance.[12]

SCA27B is an autosomal dominant ataxia with frequent familial clustering, with segregation of the *FGF14* GAA expansion in multigenerational pedigrees in at least two generations.[11] In most studies, around 20–40% of genetically confirmed SCA27B probands are labelled sporadic at first assessment, despite the underlying autosomal dominant mechanism.[4] Biallelic *FGF14* GAA expansions have also been reported, though these appear to represent a more severe variant within the SCA27B spectrum.[12] Family history was reported in nearly one-third of the patients in the current review. Detailed history and examination of relatives can unmask mildly affected family members which helps in converting “sporadic probands” into autosomal dominant pedigrees. Late-onset SCA27B may imply that transmitting parents may die before symptom onset or remain only mildly affected, potentially contributing to the under-recognition of familial disease.

In the present review, vertigo and dizziness were recognized as frequent manifestations of SCA27B, often preceding the onset of overt cerebellar ataxia. In several international cohorts, individuals have reported recurrent episodes of vertigo, oscillopsia or non-positional dizziness preceding the development of imbalance, sometimes by years, frequently resulting in initial misdiagnoses such as vestibular neuritis or benign paroxysmal positional vertigo.[1, 2,4]

Cerebellar ataxia remains the core clinical feature, supported by our meta-analysis demonstrating a pooled prevalence of 91%. While our quantitative analysis evaluated ataxia as a broad diagnostic category, the largest published datasets detail a pattern where axial and gait ataxia are prominent,[2] indicated by greater impairment in stance and lower limbs compared to appendicular ataxia.[2,4] Dysarthria is a major component of this midline cerebellar involvement, which we identified in 46% of cases in our pooled analysis.

Nystagmus is a prominent oculomotor manifestation in SCA27B, with DBN appearing to be particularly characteristic. Previous studies have reported DBN in up to 70% of affected individuals.[13] In the present meta-analysis, while nystagmus was present in two-third patients, DBN specifically was identified in nearly half, underscoring its diagnostic relevance. Other cerebellar oculomotor abnormalities such as impaired visual fixation, suppression of the vestibulo-ocular reflex (VOR), diametric saccades and abnormal saccadic pursuit were identified in 74% patients in our metanalysis. The constellation of DBN, cerebellar oculomotor signs, reduced VOR suppression, vertiginous symptoms and visual disturbances

frequently occurred at or near symptom onset, suggesting early preferential involvement of the cerebellar flocculus and paraflocculus in SCA27B.[2]

Apart from ataxia and oculomotor, some other neurological features may occur less frequently. Large international cohorts have consistently shown that pyramidal involvement is not a primary clinical hallmark of SCA27B. In the French-Canadian cohort and pooled French cohorts analysed by Bonnet et al, gait and appendicular ataxia together with cerebellar oculomotor abnormalities were observed in above 90% of cases, whereas pyramidal and extrapyramidal features were each reported in fewer than 20% of patients. These findings suggest that corticospinal tract signs are relatively uncommon compared with cerebellar manifestations.[3,14] This pattern is reflected in our meta-analysis as well, where pyramidal involvement was present in only one-fifth. Tremor can occur in SCA27B, although it is generally attributable to the underlying cerebellar dysfunction and is reported infrequently in larger cohorts. Pellerin et al. noted postural upper-limb tremors happens in approximately 10–27% of cases across cohorts, typically manifesting as a mild action or postural tremor rather than a classic parkinsonian resting tremor.[2] Tremor was observed in 31% of the subjects included in the present meta-analysis.

Taken together, these findings points out that the predominant clinical profile of SCA27B is a pan-cerebellar syndrome with prominent oculomotor and vestibular abnormalities. Features suggestive of broader multisystem involvement such as dysautonomia, significant extrapyramidal signs or dystonia are more typically associated with conditions like multiple system atrophy–cerebellar type (MSA-C) and are reported less frequently in SCA27B. However, dysautonomia and extrapyramidal signs were prevalent in 21% and 13% of patients in the pooled analysis respectively. Dysautonomia and extrapyramidal signs can be present in SCA27B, particularly in more advanced or multisystem presentations. [15] Therefore, the presence of these clinical findings should not discourage diagnostic consideration of SCA27B; rather, clinicians should recognize that the disorder displays a broader phenotypic spectrum than previously appreciated, even if these additional features are comparatively less prevalent.

Interestingly, some patients with SCA27B reported a febrile illness around the time of symptom onset, with fever at onset documented in 1.3% of patients. Most such reports originated from the Asian Indian cohort, indicating that data from the wider literature remain very limited. However, there is no published evidence identifying fever as a definitive or consistent trigger in SCA27B, and it may be worthwhile to explore how febrile triggers contribute to ‘unmasking’ or ‘triggering’ the disease. Owing to the scarcity and inconsistency of available data, a meta-analysis could not be performed for triggers causing ataxia. In contrast, more established triggers included fatigue, alcohol, emotional stress, and physical exertion, which were reported more consistently across multiple cohorts.

Episodic symptoms in SCA27B manifesting as transient worsening of cerebellar ataxia, vertigo, dizziness, diplopia or dysarthria lasting minutes to days, distinguish it from other progressive cerebellar ataxias and are triggered by stress, infections, alcohol, caffeine or metabolic factors.[15] These paroxysmal features, reported in 13–80% across cohorts, often precede permanent progressive ataxia and can guide targeted FGF14 GAA repeat testing, as these features are less common in other SCAs.[16]

In our meta-analysis, episodic symptoms were found in 38% of cases, slightly lower than the 41.9% (296/707) reported by Hirschfeld et al, a variation that may reflect differences in cohort composition and reporting practices. FGF14 is expressed in the nervous system, mainly in the cerebellar granule cells and Purkinje cells. FGF14 regulates the spontaneous rhythmic firing of Purkinje cells by regulating voltage-gated sodium channels to the initial segment of the axon. In GAA-FGF14 related cerebellar ataxias, episodic presentation of these symptoms may be observed as ion channel kinetics are involved.[1]

Symptoms suggestive of peripheral neuropathy are rarely seen in SCA27B. Only one patient in the Asian Indian case series had axonal sensorimotor neuropathy, and a detailed diagnostic evaluation for other causes of neuropathy were negative. Theuriet et al similarly reported that the prevalence of neuropathy among individuals with SCA27B was comparable to that of the elderly general population, suggesting that these neuropathies are predominantly non-specific, length-dependent axonal processes attributable to age-related factors or comorbid risk factors rather than the underlying genetic disorder.[17] As additional cases are documented in literature understanding of the true relationship between SCA27B and peripheral neuropathy may evolve. Current evidence remains insufficient to establish a definitive association.

Neuroimaging in SCA27B most commonly shows cerebellar atrophy, with a predilection for the vermis, reported in up to 94% of cases and relatively less involvement of the cerebellar hemispheres. [18] The anterior and superior posterior lobes tend to be disproportionately affected, a pattern that correlates with the high frequency of DBN.[3] Signal changes involving the superior cerebellar peduncles (SCP), particularly T2/3D-FLAIR hyperintensity, have been recognized as another emerging imaging feature of diagnostic value, occurring in approximately 60–70% of reported cases.[19] Although these radiological findings were extracted in our review, the heterogeneity in reporting formats and absence of consistently quantifiable parameters across studies limited the ability to cumulatively analyse them.

Our systematic review represents the most comprehensive data to date on the clinical, radiological and genetic characteristics of SCA27B. In our meta-analysis, cerebellar ataxia and oculomotor abnormalities emerged as the key clinical features of SCA27B. Episodic symptoms and vertigo were also frequent, emphasizing that paroxysmal vestibulo-cerebellar manifestations are central to the phenotype rather than incidental features. Dysarthria occurred in approximately half of cases whereas tremor and pyramidal signs were less common and extrapyramidal features, amyotrophy and dysautonomia remained infrequent.

Genotype–phenotype correlations revealed distinct clinical patterns across repeat length categories, with shorter expansions (≤ 249 repeats) showing significantly higher odds of DBN, nystagmus, and pyramidal signs, whereas larger expansions (≥ 250 repeats) were significantly associated with episodic manifestations and oculomotor involvement. Core clinical manifestations of this disorder including cerebellar ataxia, dysarthria, tremor, and vertigo as well as rare features like amyotrophy and dysautonomia, showed no significant association with repeat-length subgroups. Core ataxic syndrome is an expansion independent baseline c symptom of this disease. These results support a genotype–

phenotype relationship in SCA27B, where expansion size may differentially modulate ocular motor, pyramidal and episodic symptom clusters rather than acting as a binary pathogenic determinant.

Substantial heterogeneity across the studied outcomes likely reflects true clinical variability, as well as methodological differences between studies, including case ascertainment, symptom definitions, disease duration, and referral patterns favouring more severe phenotypes. These factors support the use of a random-effects model for analysis and are consistent with expectations given the predominance of retrospective case series in the published literature. Although publication bias analyses showed small-study effects for several features, very large fail-safe N values confirm the robustness of these associations despite possible overestimation of absolute symptom prevalence. The inclusion of a larger number of published cases than previous reviews strengthen the reliability of our pooled estimates and allows a broader characterisation of the phenotypic variability. This analysis highlights emerging diagnostic patterns, including younger age of onset, episodic symptoms and characteristic oculomotor abnormalities. Key strengths include the use of a standardized proportional meta-analytic framework across all outcomes, application of variance-stabilizing transformations to accommodate extreme proportions and consistent chronological handling of multiple cohorts originating from the same studies, all of which enhance comparability across phenotypic domains. Furthermore, adherence to PRISMA methodology, independent screening of studies, and incorporation of both individual-level and aggregate data further reinforce the robustness and transparency of the review.

Several limitations should be acknowledged. Most included studies were observational case series or case reports, limiting causal inference and contributing to heterogeneity in reported outcomes. Individual-level data were unavailable, preventing adjustment for disease duration or derivation of genotype-phenotype correlations and some studies required estimation of means from medians, resulting in potential imprecision. While our review focuses broadly on the SCA27B spectrum, it is important to note that biallelic *FGF14* variants have also been reported. We were unable to analyse this specific subgroup as a separate category. Many of the included studies reported genetic data using aggregated medians or broad ranges, without differentiating between monoallelic and biallelic expansions in the provided summary statistics. Neuroimaging, electrophysiology and treatment reporting were inconsistent and therapeutic data were largely sparse and observational, precluding meaningful evaluation of treatment effects. Finally, publication bias could not be reliably assessed for outcomes reported in only a few studies.

Despite these limitations, this meta-analysis provides the most comprehensive quantitative synthesis to date of the clinical spectrum of SCA27B and may aid clinicians in recognizing both common and less frequent manifestations of the disease. Future prospective multicentre data with harmonised reporting is essential to clarify genotype- phenotype correlations, radiological features and treatment responsiveness.

Conclusion

SCA27B is an increasingly recognized as a cause of adult-onset cerebellar ataxia with a broader and more heterogeneous clinical spectrum than previously described. Our combined case series and meta-analysis showed that onset may occur earlier than reported in previous literature and that episodic symptoms, vertigo and distinctive oculomotor abnormalities particularly DBN commonly precede progressive gait ataxia, contributing to diagnostic delay. Further research is needed to expand understanding of genotype-phenotype variability, multisystem involvement, and treatment responses as more cases are identified.

Declarations

Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript: A. Writing of the First Draft, B. Review and Critique.

F.M.: 1B, 1C, 2A, 2B, 3A

D.G: 1A, 1B, 2C, 3B

A.A: 1B, 1B, 1C, 3B

A.G.: 1B, 3B

M.F.: 1B, 1C, 3B

A.K.S.: 1B, 2C, 3C

Acknowledgements

None

Disclosures

Ethical compliance statement:

The study was approved by the institutional review board. An informed consent was obtained from all the patients included in the study. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

Funding sources and conflict of interest:

This work was partly supported by ICMR 5/4–5/5Ad-hoc/Neuro/220/NCD-I (GAP240). All authors report no financial disclosures. There are no conflicts of interest relevant to this work.

Financial disclosures for the previous 12 months: The authors declare that there are no additional disclosures to report.

Clinical trial number: not applicable.

Data Availability

The data analysed in this study can be obtained from the corresponding authors upon reasonable request.

References

1. Pellerin D, Danzi MC, Wilke C, Renaud M, Fazal S, Dicaire MJ, Scriba CK, Ashton C, Yanick C, Beijer D, Rebelo A. Deep intronic FGF14 GAA repeat expansion in late-onset cerebellar ataxia. N Engl J Med. 2023;388(2):128–41.
2. Pellerin D, Danzi MC, Renaud M, Houlden H, Synofzik M, Zuchner S, et al. Spinocerebellar ataxia 27B: A novel, frequent and potentially treatable ataxia. Clin Transl Med. 2024;14(1):e1504.
3. Bonnet C, Pellerin D, Roth V, Clément G, Wandzel M, Lambert L, et al. Optimized testing strategy for the diagnosis of GAA-FGF14 ataxia/spinocerebellar ataxia 27B. Sci Rep. 2023 June;15:13:9737.
4. Wirth T, Clément G, Delvallée C, Bonnet C, Bogdan T, Iosif A, et al. Natural History and Phenotypic Spectrum of GAA- *FGF14* Sporadic Late-Onset Cerebellar Ataxia (SCA27B). Mov Disord. 2023;38(10):1950–6.
5. Wirth T, Bonnet C, Delvallée C, Pellerin D, Bogdan T, Clément G, et al. Does Spinocerebellar ataxia 27B mimic cerebellar multiple system atrophy? J Neurol. 2024;271(4):2078–85.
6. Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ. 2021;372.
7. R Core Team. (2024). R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/
8. Viechtbauer W. Conducting meta-analyses in R with the metafor package. J Stat Softw. 2010;36(3):1–48.
9. Schwarzer G, Carpenter JR, Rücker G. meta: An R package for meta-analysis. J Stat Softw. 2015;64(3):1–34.
10. McGrath S, Zhao X, Steele R, Thombs BD, Benedetti A. DEPRESsion Screening Data (DEPRESSD) Collaboration. Estimating the sample mean and standard deviation from commonly reported quantiles in meta-analysis. Stat Methods Med Res. 2020;29(9):2520–37.
11. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol. 2014;14(1):135.

12. Hirschfeld AS, Misiorek JO, Dabrowska M, Muszynski J, Gerhart BJ, Zenczak M et al. Spinocerebellar ataxia 27B (SCA27B)-a systematic review and a case report of a Polish family. J Appl Genet. 2025.
13. Abou Chaar W, Eranki AN, Stevens HA, Watson SL, Wong DY, Avila VS, et al. Clinical, Radiological and Pathological Features of a Large American Cohort of Spinocerebellar Ataxia (SCA27B). Ann Neurol. 2024;96(6):1092–103.
14. Pellerin D, Danzi M, Renaud M, Houlden H, Synofzik M, Zuchner S, Brais B. GAA-FGF14-Related Ataxia. GeneReviews®[Internet]. 2024 Jan 25.
15. Wilke C, Pellerin D, Mengel D, Traschütz A, Danzi MC, Dicaire MJ, et al. GAA-FGF14 ataxia (SCA27B): phenotypic profile, natural history progression and 4-aminopyridine treatment response. Brain J Neurol. 2023;146(10):4144–57.
16. Foucard C, Belley M, Sangare A, Bonnet C, Renaud M, Roze E. Paroxysmal ataxia: a characteristic feature of FGF14 repeat expansion (SCA27B). Neurology: Genet. 2023;10(1):e200118.
17. Theuriet J, Paulet L, Acket B, Ory-Magne F, Belbachir H, Chanson JB, Bouhour F, Laurencin C, Froment Tilikete C, Lardeux P, Clement G. Neuropathy in GAA-FGF14 Late-Onset Cerebellar Ataxia (SCA27B): Prevalence and Characteristics. Eur J Neurol. 2025;32(7):e70247.
18. Chen S, Ashton C, Sakalla R, Clement G, Planel S, Bonnet C, Lamont PJ, Kulanthaivelu K, Nalini A, Houlden H, Duquette A. Involvement of the superior cerebellar peduncles in GAA-FGF14 ataxia. Neurology: Genet. 2025;11(2):e200253.
19. Kartanou C, Mitrousias A, Pellerin D, Kontogeorgiou Z, Iruzubieta P, Dicaire MJ, et al. The FGF14 GAA repeat expansion in Greek patients with late-onset cerebellar ataxia and an overview of the SCA27B phenotype across populations. Clin Genet. 2024;105(4):446–52.
20. Iruzubieta P, Pellerin D, Bergareche A, Albajar I, Mondragón E, Vinagre A, et al. Frequency and phenotypic spectrum of spinocerebellar ataxia 27B and other genetic ataxias in a Spanish cohort of late-onset cerebellar ataxia. Eur J Neurol. 2023;30(12):3828–33.
21. Indelicato E, Fleszar Z, Pellerin D, Nachbauer W, Zuchner S, Traschütz A, et al. GAA-FGF14 Expansions and CACNA1A Variants: Phenotypic Overlap and Diagnostic Implications. Mov Disord. 2025;40(10):2262–8.
22. Satolli S, Rossi S, Vegezzi E, Pellerin D, Manca ML, Barghigiani M, et al. Spinocerebellar ataxia 27B: a frequent and slowly progressive autosomal-dominant cerebellar ataxia-experience from an Italian cohort. J Neurol. 2024;271(8):5478–88.
23. Hirschfeld AS, Misiorek JO, Dabrowska M, Muszynski J, Gerhart BJ, Zenczak M et al. Spinocerebellar ataxia 27B (SCA27B)-a systematic review and a case report of a Polish family. J Appl Genet. 2025.
24. Pinheiro-Barbosa R, Cissé C, Bastos P, Leung C, Traon AP le, Kermorgant M et al. How to distinguish spinocerebellar ataxia 27B from late onset cerebellar ataxia: insights from a case-control study. J Neurol. 2024;272(1):45.
25. Miyatake S, Doi H, Yaguchi H, Koshimizu E, Kihara N, Matsubara T, et al. Complete nanopore repeat sequencing of SCA27B (GAA-FGF14 ataxia) in Japanese. J Neurol Neurosurg Psychiatry. 2024;95(12):1187–95.

26. Mendes Ferreira V, Magriço M, Meira B, Barbosa R. Spinocerebellar Ataxia Type 27B (SCA27B): A Hereditary Ataxia in Portugal. Acta Med Port 2025 June 2;38(6–7):408–11.
27. Rettenmaier LA, Chen JYH, MacMore J, Gupta AS, Lin CC, Stephen CD et al. Spinocerebellar Ataxia Type 27B can be Suspected Based on Clinical Phenotype: The Massachusetts General Hospital Ataxia Center Experience. Cerebellum Lond Engl. 2025 July 18;24(5):133.
28. Kytövuori L, Pellerin D, Kärppä M, Sipilä JOT, Dicaire MJ, Iruzubieta P, et al. FGF14 (GAA•TTC) repeat expansion-related ataxia SCA27B is common in Northern Finland. Parkinsonism Relat Disord. 2025;137:107943.
29. Shirai S, Mizushima K, Fujiwara K, Koshimizu E, Matsushima M, Miyatake S et al. Case series: Downbeat nystagmus in SCA27B. J Neurol Sci [Internet]. 2023 Nov 15 [cited 2025 Nov 4];454. Available from: https://www.jns-journal.com/article/S0022-510X(23)00310-6/abstract
30. Prasad GP, Makarova A, Kathirvel K, Gulsuner S, Walsh T, Parthaje S, et al. Unstable FGF14 GAA repeat expansions in Indian ataxia patients: a broader phenotype and involvement of modifier loci? J Hum Genet. 2025;70(11):589–95.
31. Iruzubieta P, Pellerin D, Ashton C, Villa F, Renaud M, Dicaire MJ, et al. Delineating the pathogenic threshold and phenotypic spectrum of SCA27B: findings from a large French–Canadian cohort. J Neurol. 2025 Sept;20(9):636.
32. Mitrotti P, Vegezzi E, Zangaglia R, Palmieri I, Dicaire MJ, Gana S, et al. Bilateral Dentate Nuclei Hyperintensities and Response to 4-Aminopyridine in a Patient With Childhood-Onset GAA-FGF14-Related Ataxia. Neurol Genet. 2024;10(6):e200208.
33. Novis LE, Frezatti RS, Pellerin D, Tomaselli PJ, Alavi S, Della Coleta MV, et al. Frequency of GAA-FGF14 Ataxia in a Large Cohort of Brazilian Patients With Unsolved Adult-Onset Cerebellar Ataxia. Neurol Genet. 2023;9(5):e200094.
34. Chen S, Ashton C, Sakalla R, Clement G, Planel S, Bonnet C et al. Neuroradiological findings in GAA-FGF14 ataxia (SCA27B): more than cerebellar atrophy. medRxiv. 2024;2024.02.16.24302945.
35. Pellerin D, Heindl F, Wilke C, Danzi MC, Traschütz A, Ashton C, et al. GAA-FGF14 disease: defining its frequency, molecular basis, and 4-aminopyridine response in a large downbeat nystagmus cohort. EBioMedicine. 2024;102:105076.
36. Ignjatijevic A, Boorsma F, Wierenga E, Vansenne F, Verschuuren-Bemelmans CC, de Vries J, et al. High Prevalence of the Intronic GAA-FGF14 Repeat Expansion in Dutch Patients With Late-Onset Ataxia. Neurol Genet. 2025;11(2):e200244.
37. Chukwuocha I, Pellerin D, Shanmugarajah P, Tsironis T, Foster E, Hoggard N, et al. Clinical characteristics, cerebellar MR spectroscopy and response to 3,4-diaminopyridine in spinocerebellar ataxia 27B: the Sheffield Ataxia Centre experience. J Neurol. 2025;272(10):681.
38. De T, Sharma P, Upilli B, Vivekanand A, Bari S, Sonakar AK, Srivastava AK, Faruq M. Spinocerebellar ataxia type 27B (SCA27B) in India: insights from a large cohort study suggest ancient origin. Neurogenetics. 2024;25(4):393–403.

39. Koutsis G, Kartanou C, Kontogeorgiou Z, Koniari C, Mitrousias A, Pellerin D et al. Screening for SCA27B, CANVAS and other repeat expansion disorders in Greek patients with late-onset cerebellar ataxia suggests a need to update current diagnostic algorithms. J Neurol Sci [Internet]. 2024 Dec 15 [cited 2025 Nov 16];467. Available from: https://www.jns-journal.com/article/S0022-510X(24)00445-3/abstract
40. Pellerin D, Seemann J, Traschütz A, Brais B, Ilg W, Synofzik M. Reduced Age-Dependent Penetrance of a Large FGF14 GAA Repeat Expansion in a 74-Year-Old Woman from a German Family with SCA27B. Mov Disord. 2024;39(10):1892–4.
41. Borsche M, Thomsen M, Szmulewicz DJ, Lübbers B, Hinrichs F, Lockhart PJ, et al. Bilateral vestibulopathy in RFC1-positive CANVAS is distinctly different compared to FGF14-linked spinocerebellar ataxia 27B. J Neurol. 2024;271(2):1023–7.
42. Halstuk O, Dayan R, Silverstein S, Fellig Y, Saada A, Harel T, et al. Low prevalence of SCA27B in adult-onset cerebellar ataxia cohort of Jewish ancestry. Parkinsonism Relat Disord. 2024 Sept;126:107067.
43. Milovanović A, Dragaševic-Mišković N, Thomsen M, Borsche M, Hinrichs F, Westenberger A, et al. RFC1 and FGF14 Repeat Expansions in Serbian Patients with Cerebellar Ataxia. Mov Disord Clin Pract. 2024;11(6):626–33.
44. Ariello LE, Gold DR, Mu W, Schubert MC, Allen C, Paul A, et al. Ocular Motor and Vestibular Profile in Spinocerebellar Ataxia Type 27B: Toward a Practical Bedside Diagnostic Framework. Cerebellum Lond Engl. 2025 Sept;4(5):149.
45. Coulette S, Lecler A, Le Cossec C, Philibert M, Gaymard B, Delmaire C, et al. Video-Oculography as a Key Diagnostic Tool for SCA27B: A Real-Life Experience. Eur J Neurol. 2025 June;32(6):e70228.
46. Wong TH, Manuputty J, van Seeters T, Kamsteeg EJ, van de Warrenburg B. Delayed Progression of Ataxia with a Static Cerebellar Lesion- Consider SCA27B. Cerebellum Lond Engl. 2025;24(2):32.
47. Kakumoto T, Orimo K, Matsukawa T, Mitsui J, Ishihara T, Onodera O, et al. Frequency of FGF14 intronic GAA repeat expansion in patients with multiple system atrophy and undiagnosed ataxia in the Japanese population. Eur J Hum Genet. 2025;33(3):325–33.
48. Livanos I, Votsi C, Michailidou K, Pellerin D, Brais B, Zuchner S, et al. The FGF14 GAA repeat expansion is a major cause of ataxia in the Cypriot population. Brain Commun. 2025;7(1):fcae479.
49. Gold DR, Bery AK, Moukheiber E, Mu W, Abreu NJ, Fein AS et al. Causes of Diplopia, Strabismus Patterns, and Ocular Motor Features in Patients With Spinocerebellar Ataxia Type 27B. J Neuroophthalmol. 2022;10.1097/WNO.0000000000002364.
50. Mohren L, Erdlenbruch F, Leitão E, Kilpert F, Hönes GS, Kaya S et al. Identification and characterisation of pathogenic and non-pathogenic FGF14 repeat expansions. Nat Commun. 2024 Sept 3;15(1):7665.
51. Mori Y, Miyatake S, Kunieda K, Yoshikura N, Hayashi Y, Higashida K, et al. A cerebellar ataxia patient harboring 229 pure GAA repeat units in FGF14 presenting with grip myotonia. Neurol Clin Neurosci. 2024;12(6):366–8.

52. Ouyang R, Wan L, Pellerin D, Long Z, Hu J, Jiang Q et al. The genetic landscape and phenotypic spectrum of GAA-FGF14 ataxia in China: a large cohort study. eBioMedicine [Internet]. 2024 Apr 1 [cited 2025 Nov 24];102. Available from: https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(24)00112-9/fulltext
53. Ando M, Higuchi Y, Yuan J, Yoshimura A, Kojima F, Yamanishi Y, et al. Clinical variability associated with intronic FGF14 GAA repeat expansion in Japan. Ann Clin Transl Neurol. 2024;11(1):96–104.
54. Jiménez-Huete A, Patiño-García A, Guillén EF, Porta JM, Martin-Bastida A, Suárez-Vega V, et al. Brain 18F-FDG PET findings and sequential vestibular testing in SCA27B: a case report. J Neurol. 2024;271(2):1015–8.
55. Seemann J, Traschütz A, Ilg W, Synofzik M. 4-Aminopyridine improves real-life gait performance in SCA27B on a single-subject level: a prospective n-of-1 treatment experience. J Neurol. 2023;270(11):5629–34.
56. Ashton C, Indelicato E, Pellerin D, Clément G, Danzi MC, Dicaire MJ, Bonnet C, Houlden H, Züchner S, Synofzik M, Lamont PJ. Spinocerebellar ataxia 27B: episodic symptoms and acetazolamide response in 34 patients. Brain Commun. 2023;5(5):fcad239.
57. Bustamante ML, Miranda M, Pellerin D, Barreto M, Silva C, Miranda AC, Pizarro-Galleguillos B, Azaldegui O, Besa V, Canals F, Contreras ME. Repeat Expansions in a Chilean Cohort with Adult-Onset Cerebellar Ataxia. Cerebellum. 2025;25(1):3.
58. Van Prooije TH, Pennings M, Maas RP, de Vries J, Verschuuren-Bemelmans C, Odekerken V, Darweesh SK, Huisman M, Oosterloo M, Buijink A, van de Wardt J. Clinical, Genetic, and Imaging Characteristics of SCA27B: Insights from a Large Dutch Cohort. Mov Disord. 2026 Jan 8.

Figures

Figure 1: PRISMA flow chart

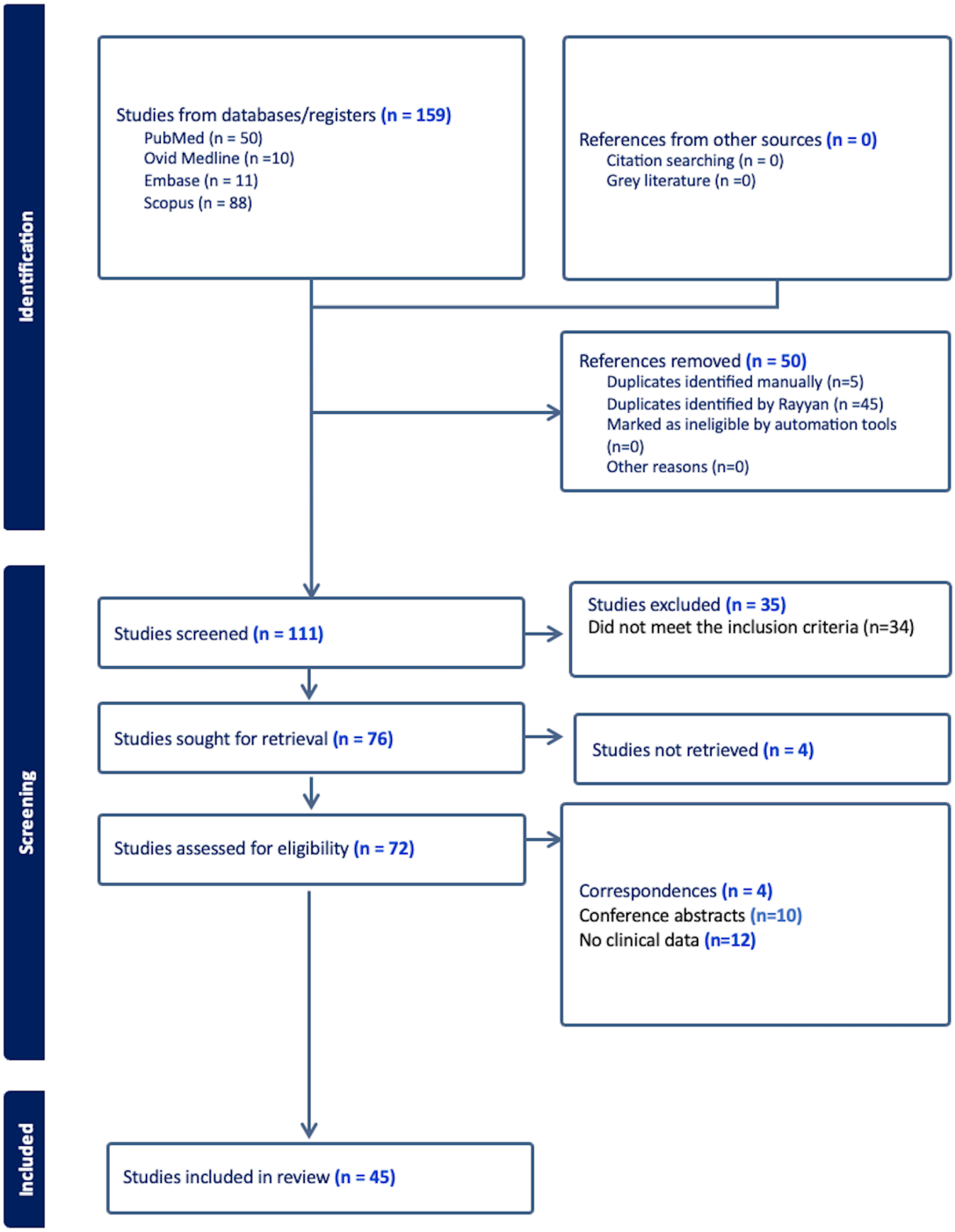

Figure 1

PRISMA flow chart of studies included in the systematic review

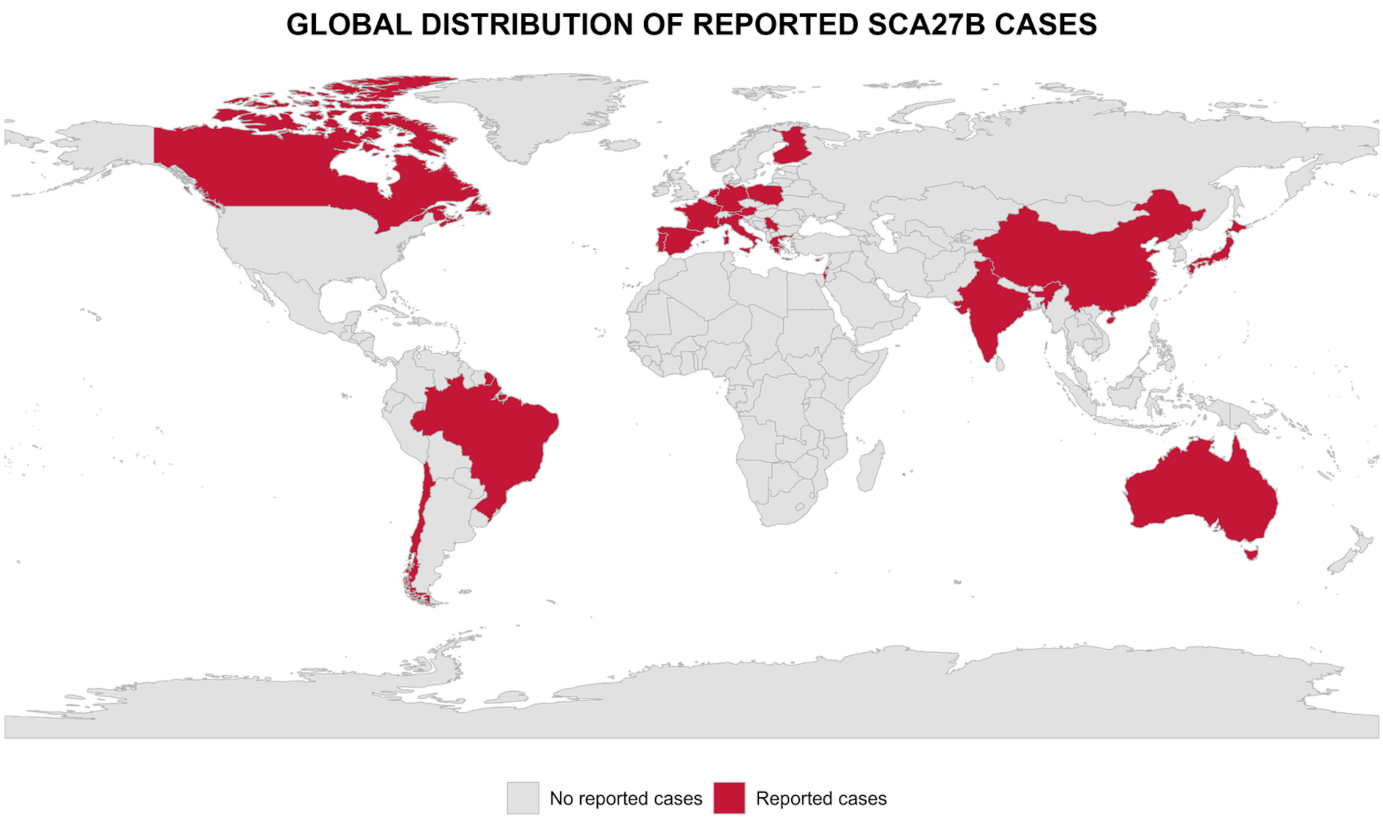

Figure 2

Map showing global distribution of reported cases of SCA7B

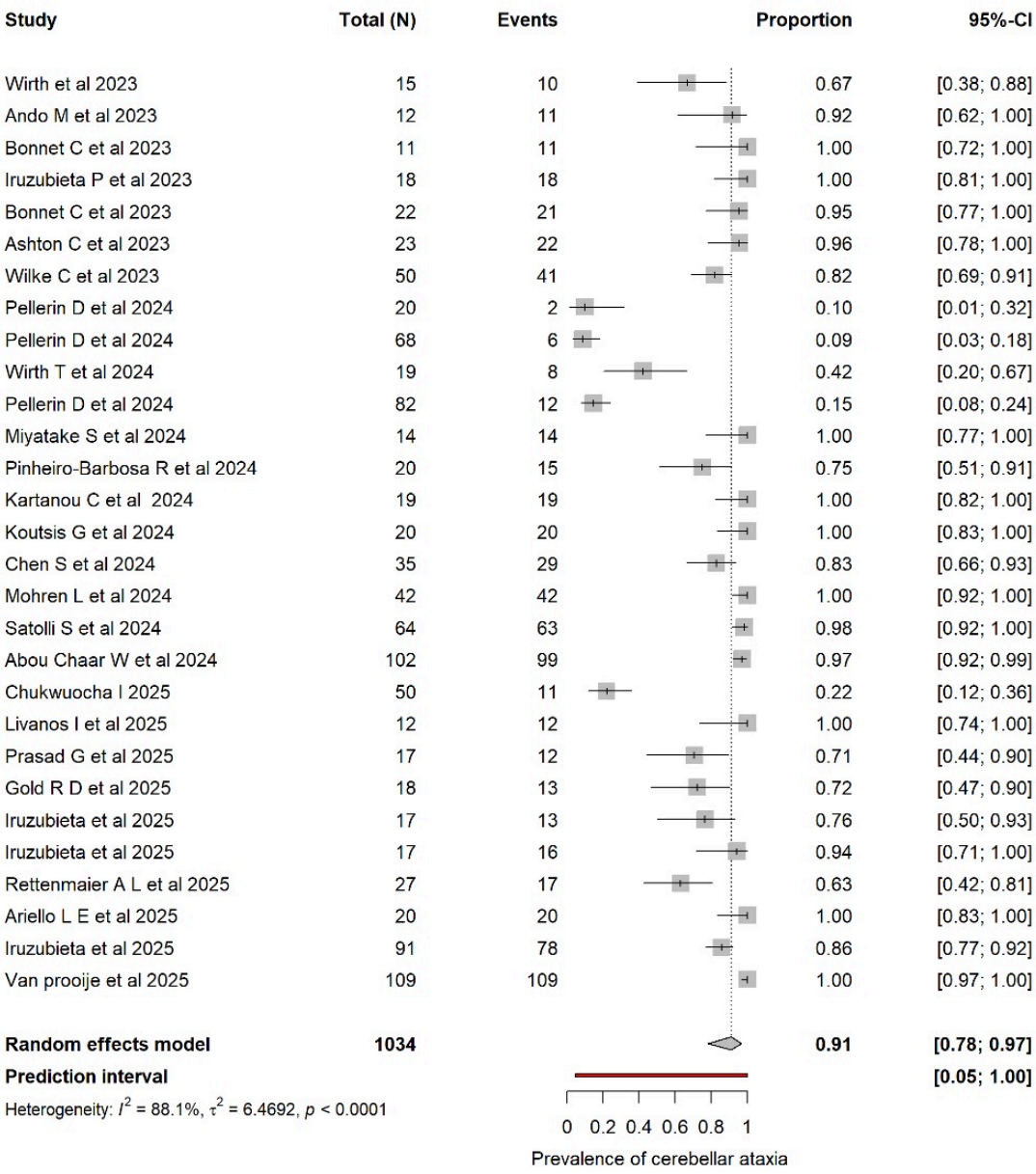

Figure 3

Forest plot showing individual study estimates and the pooled random-effects proportion of cerebellar ataxia in SCA27B (0.82; 95% CI: 0.67–0.93). Squares represent study-level prevalence estimates with 95% confidence intervals, while the diamond represents the pooled summary estimate. Substantial heterogeneity was observed across studies (I^2 = 95.7%, Tau^2 = 0.1676, p < 0.0001).

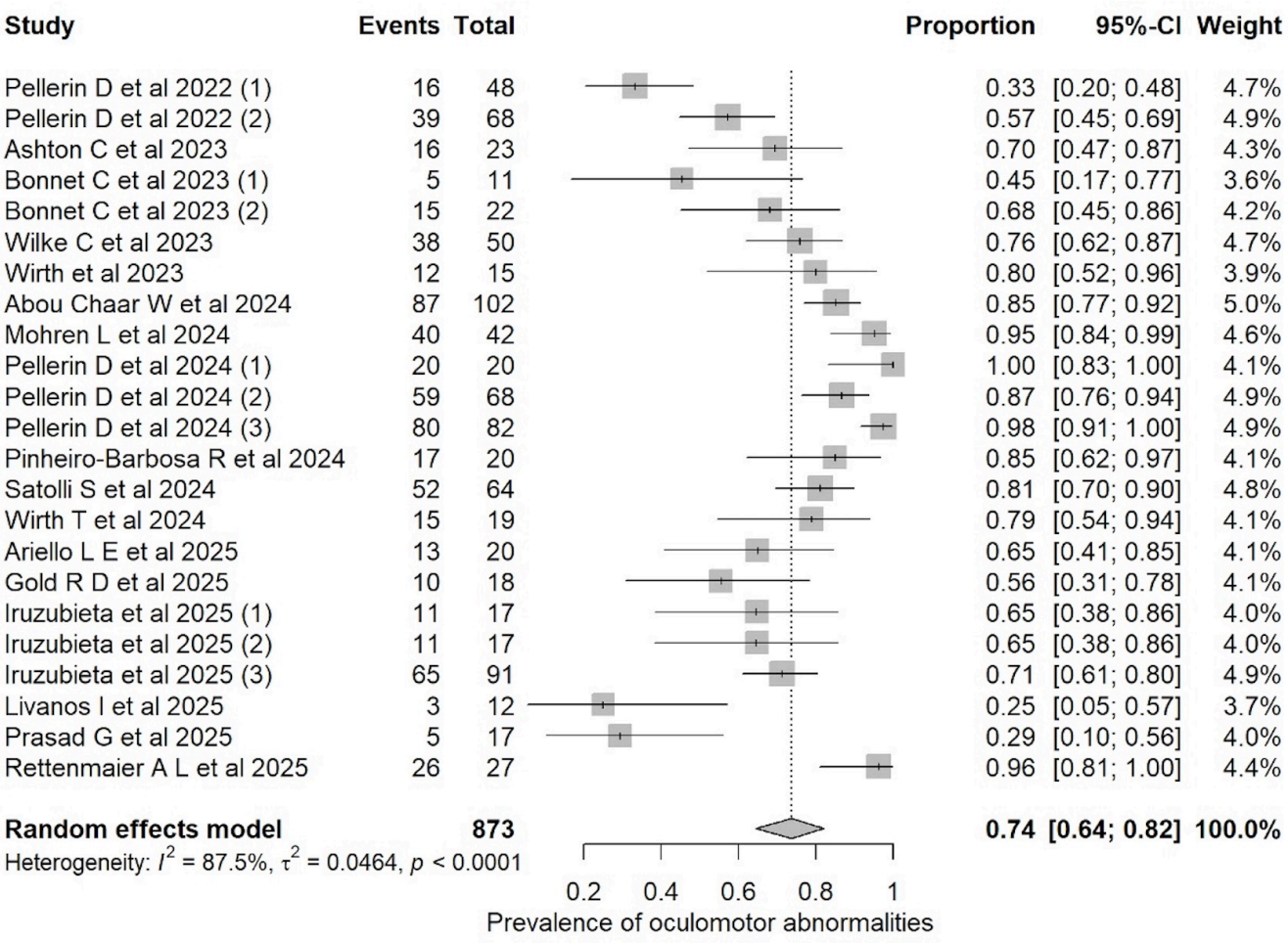

Figure 4

Forest plot showing individual study estimates and the pooled random-effects proportion of oculomotor abnormalities (excluding nystagmus) in SCA27B (0.74; 95% CI: 0.64–0.82). Squares represent study-level prevalence estimates with 95% confidence intervals, while the diamond represents the pooled summary estimate. Substantial heterogeneity was observed across studies (I^2 = 87.5%, Tau² = 0.0464, p < 0.0001).

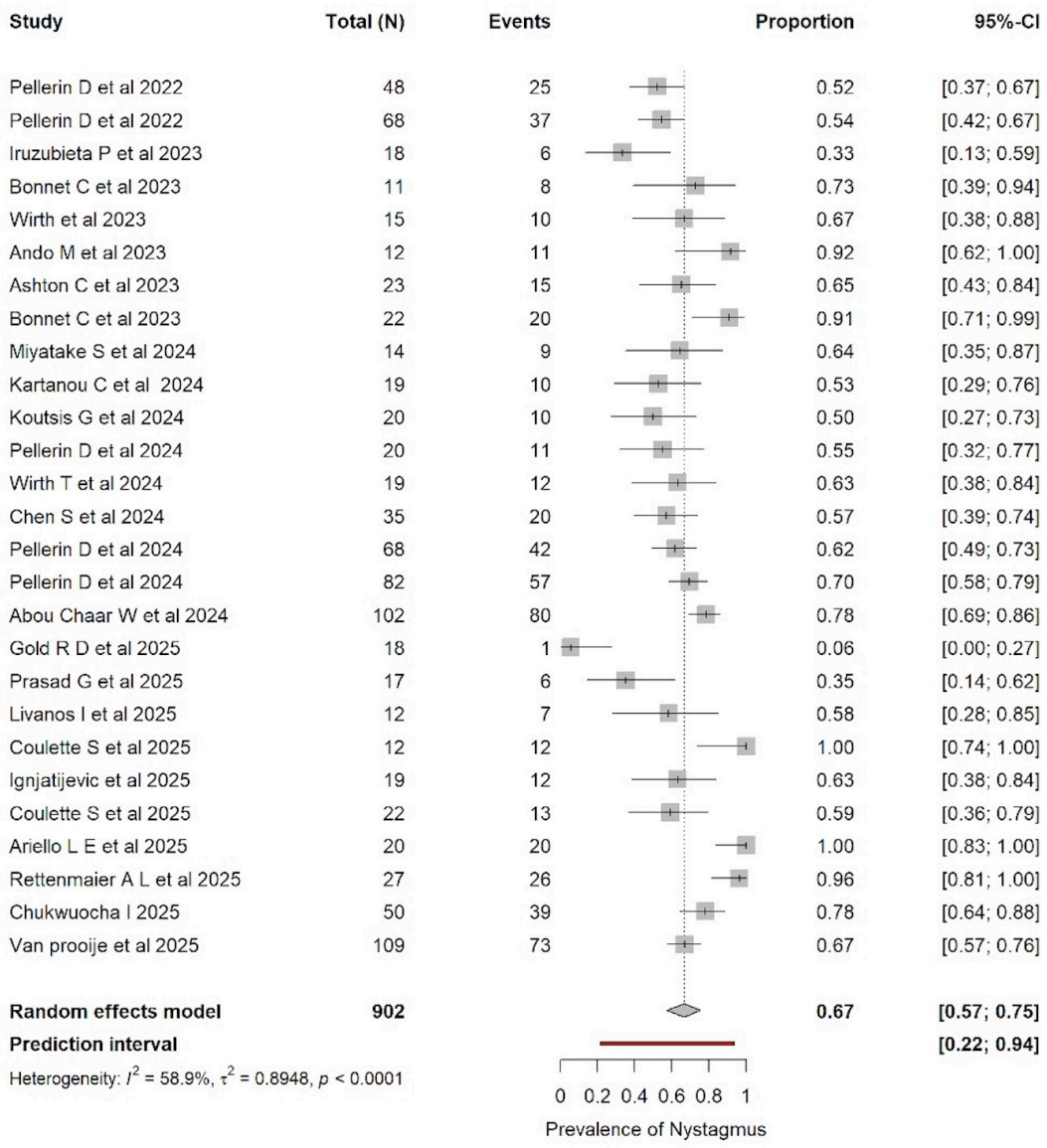

Figure 5

Forest plot showing individual study estimates and the pooled random-effects proportion of nystagmus in SCA27B (0.66; 95% CI: 0.58–0.74). Squares represent study-level prevalence estimates with 95% confidence intervals, while the diamond represents the pooled summary estimate. Substantial heterogeneity was observed across studies (I^2 = 81.6%, 208; Tau^2 = 0.0365, p <0.0001).

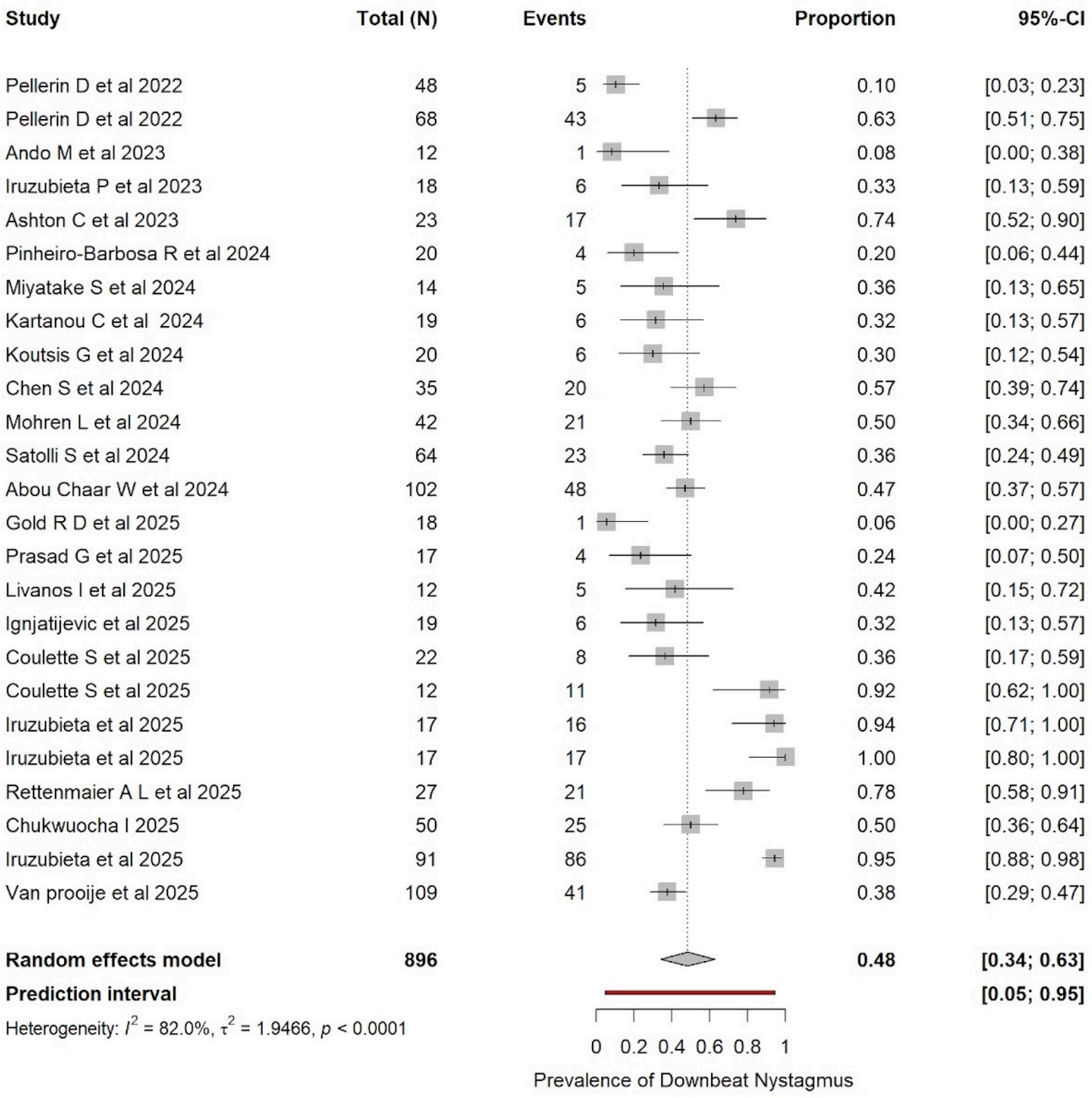

Figure 6

Forest plot showing individual study estimates and the pooled random-effects proportion of downbeat nystagmus in SCA27B (0.49; 95% CI: 0.36–0.62). Squares represent study-level prevalence estimates with 95% confidence intervals, while the diamond represents the pooled summary estimate. Substantial heterogeneity was observed across studies (I^2 = 91.8%, Tau^2 = 0.0774, p <0.001).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplement.docx