

REVIEW

Unravelling the Global Tapestry of Genetic Ataxias: Epidemiology and Genetic Testing Approaches

Malco Rossi, MD, PhD,^{1,2} Christopher D. Stephen, MB, ChB, FRCP, SM,³ Joana Damásio, MD, PhD,^{4,5,6} José Luiz Pedrosa, MD, PhD,⁷ Sheng-Han Kuo, MD,^{8,9} Chi-Ying R. Lin, MD, MPH,¹⁰ Oluwadamilola Ojo, MD,^{11,12} Shaimaa El-Jaafary, MD,¹³ Woong-Woo Lee, MD, PhD,¹⁴ Harutyun Madoev, MSc,¹⁵ Orlando G.P. Barsottini, MD, PhD,⁷ Achal Kumar Srivastava, MD, DM,¹⁶ Christine Klein, MD,¹⁵ and Bart P. van de Warrenburg, MD, PhD^{17*}

ABSTRACT: The landscape of genetic ataxias is influenced by migration, population genetics, consanguinity, and founder effects, resulting in significant regional variation. Within the expanding domain of genetic ataxias, knowledge of regional epidemiology is scarce, particularly outside of North America and Europe. Understanding the epidemiology of genetic ataxias, together with deep phenotyping and knowledge of the appropriate ancillary studies, is crucial for the development and deployment of diagnostic testing strategies. This review offers a comprehensive, data-driven overview of 2932 articles with regional epidemiological estimates

and the occurrence and prevalence of 548 genes associated with ataxia across 122 countries. Regional differences in epidemiology and phenotypic spectra are highlighted, driving an approach that incorporates complementary diagnostic test results and how these may inform cost-effective, region-specific genetic testing. All data are also publicly available as an online database, the MDSGene Global Genetic Ataxia Resource, accessible at <https://www.mdsgene.org/ataxia.html>. A phenotype-guided, tailored, and sequential testing approach is proposed, based on regional prevalence, to assist clinicians worldwide in diagnosing individuals with

¹Sección de Movimientos Anormales, Departamento de Neurología, Fleni, Buenos Aires, Argentina; ²Instituto Fleni-CONICET (INEU) Buenos Aires, Buenos Aires, Argentina; ³Ataxia Center, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, USA; ⁴Neurology Department, Centro Hospitalar Universitário de Santo António, Porto, Portugal; ⁵Genetic Epidemiology and Epigenetics, UMIB-Unit for Multidisciplinary Research in Biomedicine, ICBAS, School of Medicine and Biomedical Sciences, University of Porto, Porto, Portugal; ⁶CGPP – Center for Predictive and Preventive Genetics, IBMC – Institute for Molecular and Cell Biology, i3S – Instituto de Investigação e Inovação em Saúde Universidade do Porto, Porto, Portugal; ⁷Department of Neurology, Ataxia Unit, Universidade Federal de São Paulo, São Paulo, Brazil; ⁸Department of Neurology, Columbia University Medical Center, New York, New York, USA; ⁹Initiative of Columbia Ataxia and Tremor, Columbia University Irving Medical Center, New York, New York, USA; ¹⁰Alzheimer's Disease and Parkinson's Disease Centers, Department of Neurology, Baylor College of Medicine, Houston, Texas, USA; ¹¹College of Medicine, University of Lagos, Lagos, Nigeria; ¹²Lagos University Teaching Hospital, Lagos, Nigeria; ¹³Neurology Department, Kasr Al-Ainy School of Medicine, Cairo University, Cairo, Egypt; ¹⁴Department of Neurology, Nowon Eulji Medical Center, Eulji University, Seoul, Korea; ¹⁵Institute of Neurogenetics, University of Lübeck, Lübeck, Germany; ¹⁶Department of Neurology, All India Institute of Medical Sciences, New Delhi, India; ¹⁷Department of Neurology, Radboud University Medical Center, Nijmegen, The Netherlands

*Correspondence to: Prof. Bart P. van de Warrenburg, Department of Neurology, Radboud University Medical Center, Nijmegen, The Netherlands; E-mail: bart.vandewarrenburg@radboudumc.nl

Malco Rossi and Christopher D. Stephen contributed equally to this study.

Relevant conflicts of interest/financial disclosures: J.D., J.L.P., C.-Y. R.L., W.-L.L., H.M., O.G.P.B., and A.K.S. report no conflict of interest. M.R. has served on an advisory board for Biogen and has received honoraria for talks from the International Parkinson and Movement Disorder Society and Biogen. C.D.S. has provided scientific advisory for SwanBio Therapeutics and received research funding from Sanofi-

Genzyme for a study of video oculography in late-onset GM2 gangliosidosis and a National Institutes of Health (NIH) grant (K23 NS118045). His institution has received financial support from Sanofi-Genzyme, SwanBio Therapeutics, Encora Therapeutics and Biogen, and previously Biohaven, for the conduct of clinical trials. He has received honoraria from the American Academy of Neurology and the International Parkinson and Movement Disorders Society. He has received grant support from NIH K23 NS118045. S.-H.K. has served on an advisory boards for Biogen, Praxis Precision Medicines, and Yoda Pharmaceuticals. O.O. is a co-investigator on grants from the National Institute of Health and Care Research, UK (Transforming Parkinson's Care in Africa NIHR133391) and has received honoraria for talks from the International Parkinson and Movement Disorders Society, GBA1-Canada (G-Can), and travel support from the International Parkinson and Movement Disorders Society, Global Parkinson's Genetics Program (GP2), and G-Can. S.E.-J. has received honoraria for talks from the International Parkinson and Movement Disorder Society, and has a successful grant application for 2024–2025 pilot awards for global health leaders. C.K. has served as a medical advisor to Centogene, Takeda, and the Lundbeck Foundation and has received speakers' honoraria from Bial and royalties from Oxford University Press and Georg Thieme Verlag. B.v.d.W. served on advisory boards and/or provided paid consultancy to Biogen, Vico Therapeutics, and Biohaven; receives research support from Hersenstichting, ZonMw, Dutch Research Council, FARA, and Christina Foundation; and receives royalties from BSL/Springer-Nature.

Funding agencies: This study was partially supported by the National Institutes of Health/National Institute of Neurological Disorders and Stroke K23 NS118045 (C.D.S.). MDS Gene is supported by the University of Lübeck and the University of Toronto.

Received: 19 March 2025; **Revised:** 1 June 2025; **Accepted:** 30 June 2025

Published online 19 July 2025 in Wiley Online Library
([wileyonlinelibrary.com](https://www.wileyonlinelibrary.com)). DOI: 10.1002/mds.30302

presumed genetic ataxia, of which at least 45 causes are treatable. This approach is particularly important in underserved regions, but also in developed countries where health systems limit access to genetic testing, improving the cost-effectiveness and feasibility of genetic testing in these areas. Future screening studies in high-income settings should adopt a more comprehensive approach, integrating broader genetic testing

that covers the full range of genetic ataxias. Capacity building for genetic screening in underserved regions, particularly in Africa, South America, and the Middle East, should be prioritized. © 2025 International Parkinson and Movement Disorder Society.

Key Words: algorithm; epidemiology; genetic ataxia; genetic testing; prevalence

Cerebellar ataxia can be idiopathic, acquired, or genetic, the latter including Mendelian and mitochondrial inheritance.¹ In over 140 genetic entities, ataxia is a predominant and/or consistent feature, sometimes combined with other movement disorders.^{1,2} Ataxia manifests as part of a more complex phenotype across more than 400 other genetic disorders.^{1,2} Clinical and genetic heterogeneity result in substantial diagnostic challenges.^{2,3} Genetic diagnosis often requires more than one testing method, such as combining next-generation sequencing (NGS) with repeat expansion testing.⁴ The prevalence of genetic ataxias varies considerably regionally and by ethnicity.^{5,6} Knowledge of epidemiology, phenotypic spectra, and ancillary test characteristics facilitates early diagnosis and management, particularly where genetic testing is not universally available or accessible. This is particularly relevant for ataxias for which there are pathogenesis-directed treatments, which may have regional predilections.⁷ Guidance for tailored and sequential genetic testing approaches is important for cost-effectiveness and feasibility, particularly in underserved regions with barriers to accessing genetic testing or even in developed countries where health systems limit access to genetic testing.^{8,9} In this narrative review, we discuss how regional epidemiology and phenotypic spectra, paired with ancillary testing, inform rational, region-specific genetic testing approaches.

Methods

Literature Search Strategy and Eligibility Criteria

We performed a comprehensive search of PubMed from inception to September 2024, including publications in English, Spanish, Portuguese, German, or other languages with an English language abstract. Search terms included: “ataxia,” “spinocerebellar,” “SCA,” “prevalence,” “incidence,” “epidemiology,” “name of country,” and “genetic.” During the peer review process, publications on ATX-*FGF14* (SCA27B) and ATX-*RFC1* were updated to May 2025, given the growing number of reports highlighting the high prevalence of these disorders in various regions. Relevant additional publications found in reference lists of the publications

were also included. The expert opinion of coauthors was considered in instances of sparse or conflicting data. Inclusion criteria were publications providing geographical data on patients with genetically confirmed cerebellar ataxia, including case reports, case series, and ataxia cohort studies. Supporting data are shown in Data S1 and S2 as well as in the International Parkinson and Movement Disorder Society Genetic mutation database (MDSGene Global Genetic Ataxia Resource; <https://www.mdsgene.org/ataxia.html>) that systematically collects demographic, clinical, and genetic information on patients with movement disorders.

Results

Worldwide Distribution

Genetic ataxias have been reported in most countries. In some regions, only case reports/series were available; while in others, large ataxia cohort studies have been conducted to determine overall or relative frequencies (Fig. 1).

Autosomal Dominant Cerebellar Ataxia (ADCA)

Data up to 2013 estimated an average global prevalence of autosomal dominant cerebellar ataxia (ADCA) at 2.7/100,000.¹⁰ Prevalence rates vary across regions, with certain ADCAs showing high prevalence in specific areas of countries like Japan (19.2/100,000 for ATX-ATXN3 in Gosei), Cuba (47.9/100,000 for ATX-ATXN2 in Holguin), Brazil (165.7/100,000 for ATX-ATXN3 in General Camara, Rio Grande do Sul), Portugal (835.2/100,000 for ATX-ATXN3 in Flores Island, Azores), and Australia (743/100,000 for ATX-ATXN3 in Groote Eylandt Archipelago).^{5,6,11} Over 50 ADCA subtypes have been reported, with spinocerebellar ataxia (SCA) ATX-ATXN3 (SCA3) the most prevalent globally, followed by ATX-*FGF14* (SCA27B), ATX-ATXN1 (SCA1), ATX-ATXN2 (SCA2), ATX-*CACNA1A* (SCA6), ATX-ATXN7 (SCA7), and ATX-ATXN8 (SCA8) (Fig. 2). However, roughly 35% of ataxias are genetically undiagnosed in ataxia cohort studies (Fig. 2, Data S1), with higher undiagnosed rates in Türkiye, Russia, Finland, and Argentina. Estimating relative frequencies of ADCA

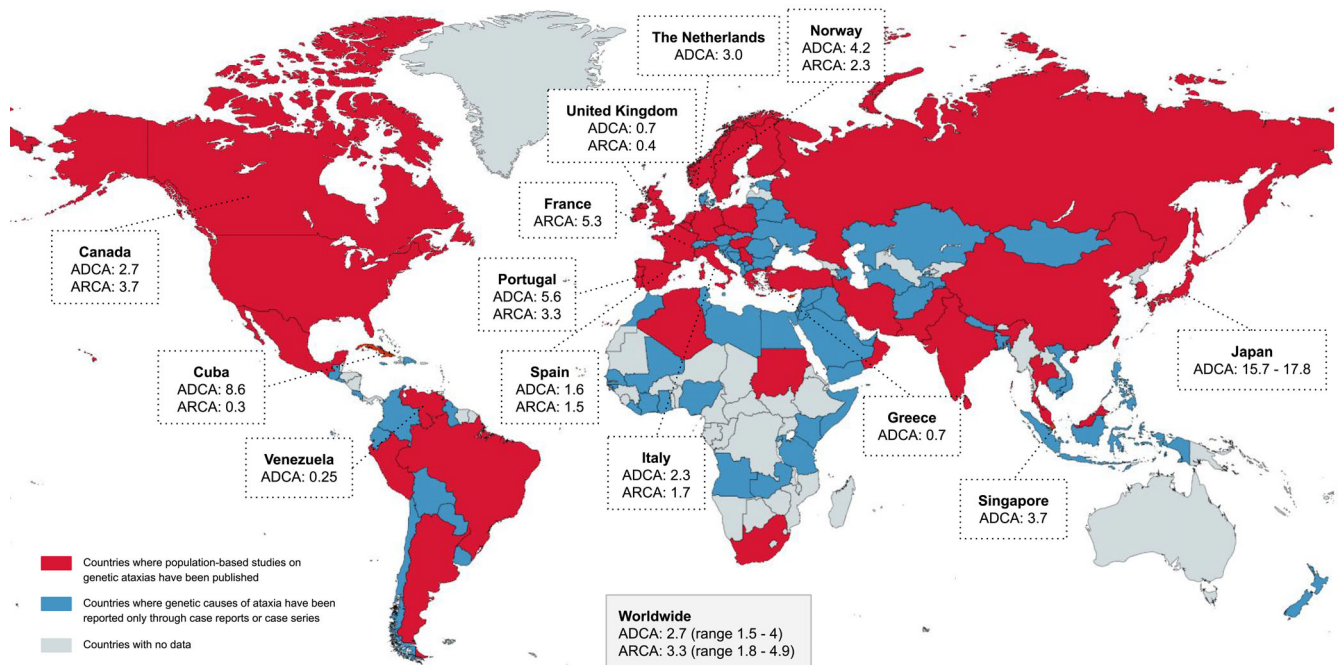


FIG. 1. Worldwide distribution and different prevalences of the genetic ataxias. The numbers represent prevalence rates per 100,000. ADCA, autosomal dominant cerebellar ataxia; ARCA, autosomal recessive cerebellar ataxia. [Color figure can be viewed at wileyonlinelibrary.com]

subtypes is limited by screening biases related to population sample sources and sizes, ages, availability, accessibility, types of genetic testing, and number of genetic ataxias investigated.^{5,6,11}

Autosomal Recessive Cerebellar Ataxias (ARCA)

The average global prevalence of autosomal recessive cerebellar ataxias (ARCA) was estimated at 3.3/100,000,¹⁰ with higher rates in France, Portugal, and Canada, which may not only be related to genuinely higher rates of ARCA in these countries but could also be related to methodological factors, such as the extent (total number of genes included) of screening studies. Friedreich ataxia (ATX-FXN) is the most frequent genetic ataxia worldwide, with a global prevalence of 2–4/100,000, a carrier rate of 1:60 to 1:100, and estimated incidence of 1:29,000.^{10,12} ATX-FXN predominates in European Caucasians, and other ethnicities in India, Türkiye, and Algeria (Figs S10 and S11), while occurrence in Amerindian, sub-Saharan African, and many Asian populations is presumed to be virtually absent or anecdotal.¹³ In Europe, a possible southwest-to-northeast prevalence gradient exists,¹⁴ with prevalence highest in Spain (1:21,000),¹⁵ France, and Ireland, and lowest in Scandinavia (1:750,000 in Finland).¹⁶ In a South American study of 1338 presumed ARCA patients, ATX-FXN (57%) was the most frequent cause, followed by ATX-RFC1 (8%), and ATX-ATM (7%).¹⁷ In a European study of 677 non-ATX-FXN patients with suspected ARCA, ATX-SACS

(7.7%) was most frequent, followed by ATX-SPG7 (6.1%), ATX-SETX (4%), ATX-SYNE1 (4%), ATX-RFC1 (3.8%), and ATX-ATM (3.8%).¹⁸ Other ARCA with a worldwide distribution are listed in Table 1.

X-Linked Ataxias

Premutation *FMR1* CGG-repeat expansions, causing Fragile X-associated Tremor/Ataxia Syndrome (FXTAS), is the most frequent X-linked ataxia (Figs 1 and S12), predominantly affecting males, and rarely fully manifesting in females.¹⁹

Mitochondrial-Inherited Ataxias

Mitochondrial-inherited ataxias are rare globally, with *MT-ATP6* variants reported most frequently (0.5%–5.3% in unselected adult ataxia screening studies) (Tables S2 and S8).

Regional Differences Between and Within Continents

A total of 2932 articles providing geographical information on patients with genetic ataxia were included. Of these, 140 provided epidemiological data from Africa, 547 from the Americas, 724 from Asia, 336 from the Middle East, 91 from Oceania, and 1094 from Europe.

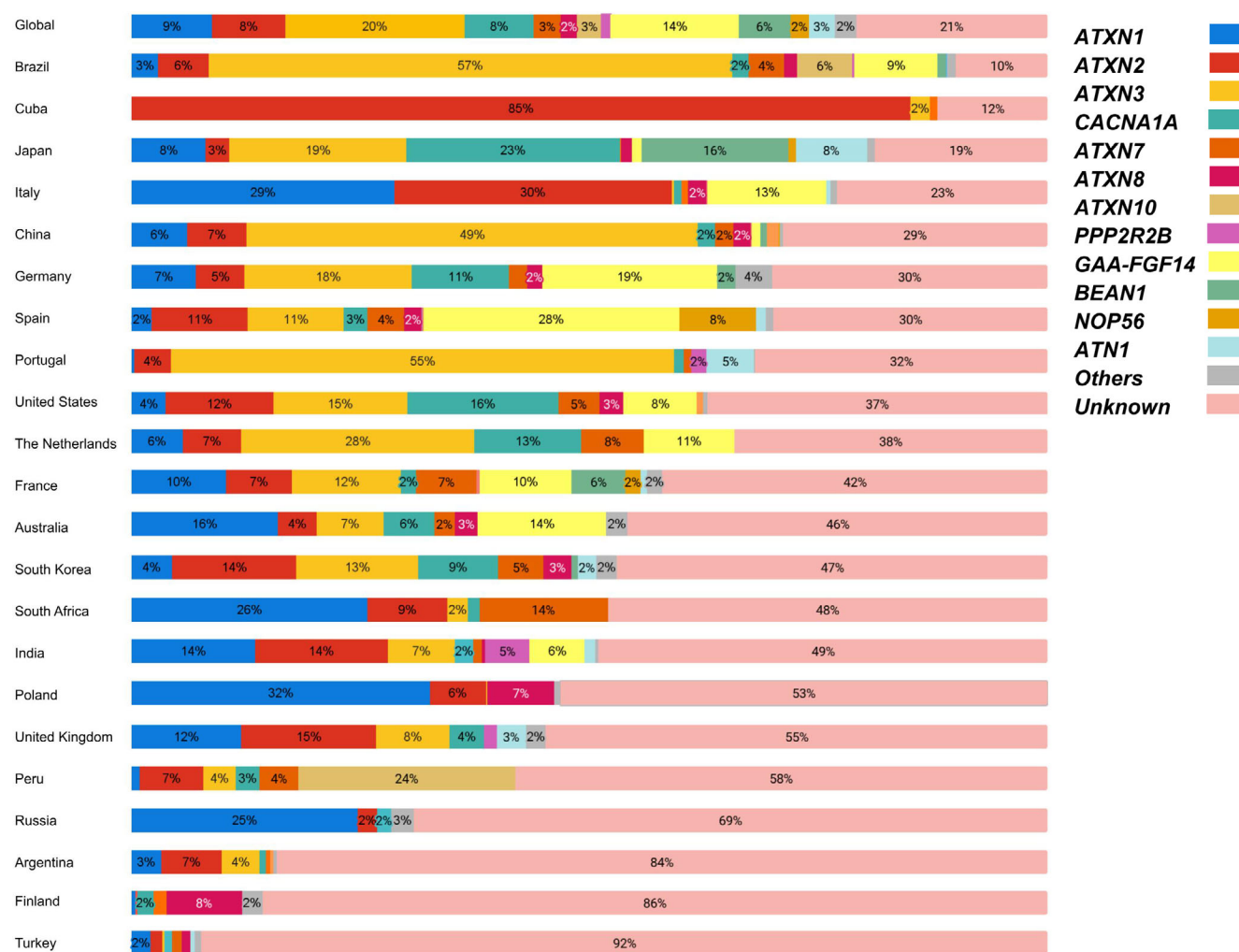


FIG. 2. Global relative frequencies of the most common autosomal dominant cerebellar ataxias. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com/doi/10.1002/md.30302)]

Africa

African populations have high genetic diversity, and low linkage disequilibrium among loci, given their long evolutionary history.²⁰ High consanguinity within specific subpopulations increases the occurrence of certain genetic ataxias.²¹ However, scant data exist, with genetic ataxia reported in a few African countries, mostly from case reports/series, with limited epidemiological or large screening studies (Fig. S8, Table S14). In South Africa, the annual incidence of polyglutamine ADCAs was estimated at 20.2/100,000 per year.²² This is almost certainly an underestimation, as genetic testing in remote areas and low-income communities was limited by absent infrastructure and financial constraints.²² South African screening studies found ATX-ATXN1, ATX-ATXN7, and ATX-ATXN2 as the most common ADCAs, with most patients being of Black African or mixed descent.²² ATX-ATXN7 is prevalent in indigenous Bantu people from South Africa and Zambia, where both groups share a common

haplotype.²³ A genetic ataxia unrelated to European ethnicity or European migration to Africa was demonstrated by a Tuareg family (a Berber ethnic group) in Mali with ATX-FXN.²⁴ ATX-FXN is mainly reported in North African countries (Table S14). In a large Algerian ARCA screening study, ATX-FXN was the most frequent cause (30%), followed by ATX-TTPA and ATX-SETX (11% each).²¹

America

In the United States and Canada, ATX-ATXN1, ATX-ATXN2, ATX-ATXN3, ATX-CACNA1A, ATX-ATXN7, ATX-FXN, ATX-SYNE1, and HSP/ATX-SPG7 are the most common genetic ataxias, constituting 27%–61% among screening studies (Fig. 2, Table S11). The prevalence of ADCA in Canada is in the range 2.25–2.67/100,000, with a higher prevalence in Ontario (Table S12), whereas the prevalence of ARCA in Eastern Quebec is 3.73/100,000. Historical events have shaped the

TABLE 1 Frequency of most common autosomal recessive cerebellar ataxia (*ARCA*) genes across the globe

Country	ANO10	APTX	ATM	FXN	POLG	RFC1	SACS	SETX	SPG7	SYNE1	TTPA
Algeria	–	3.6	–	29.5	–	–	4.8	10.8	–	0.6	11.4
Australia	2.5–3.6	–	–	0–2.5	–	0–29.4	–	–	2.5–3.6	–	–
China	0.4–1.8	–	1.8	0	0	0.5	3.8–11.1	5.6–15.4	0.4	0.9–9.2	1.8
India	1	0.6	0.6–2	2.3–28.6	–	0.1	0.6–7.1	2.6–6.1	–	1	2
Japan	–	1.3–1.6	3.6–34.9	0	–	1.8–10.8	–	0.3–1.6	–	–	–
Russia	2.1	–	4.2	18.8	2.1–14.9	–	–	4.2	–	–	–
South Korea	1.3	0.1–2.6	0.2–1.3	–	–	–	–	–	2.6	2.6–3.2	–
Taiwan	–	–	–	0	0	–	–	–	–	–	–
Iran	–	3.1	8.6	3.1	0.6	–	7.4–9	–	–	–	0.6
Turkey	0.2	0.1–6	4	0–37.5	–	1.1–14	0.5–7.7	0.8–4	0.8	1.7	–
Europe ^a	2.1	1.6	3.8	–	2.4	3.8	7.7	4	6.1	4	0.7
Finland	–	–	1	0–2.1	6.3	5.2	3.1	–	0	–	–
France	1.6–4.8	1.1–6.2	1.5–4.2	1–39	0.7	1.5–15	1–8.7	1–15.1	1.9–4.3	2.1–12.5	0.7,1.1
Germany	–	1.2–1–8	–	2–26.8	0	4–88	–	2.4–8	–	–	–
Ireland	1.5	0.5	2	34.7	1	–	1	1	10.7	–	–
Italy	–	6.4–11.1	3.8	6.3–12.2	0	14.5	–	–	2.3	–	3.8
Norway	–	–	6.4	2.3–6.7	–	–	1.9	2.3	3.8	–	0.6
Portugal	5.3	1.4	1.6	11.2	5.3	–	0.7	1.2–5.3	–	5.3	0.8
Spain	0.4–0.6	–	1.2	0.7–18.2	0.3–1.4	–	0.8	1.5–4.1	0.8–10.5	0.6–10.9	0.3–0.8
United Kingdom	–	–	–	1.7–2.7	–	0–71	17.1	–	5.7–18.6	–	–
Canada	1.8	0.6	1.2	1.2–3.3	0.6–0.8	0.6	1.8–2.9	1.1–1.6	0.4–12.5	1.1–17.8	–
United States	1.3–1.8	0.6	1.2	11.4	0.6	3.2	1.8–2.5	1.3	2.6–5.3	0–5.3	–
South America ^b	0.3	–	7	57	1	8	4	3	–	2	1
Argentina	–	0.6	0.9	6.4–10.8	–	–	0.3	0.6	–	0.6	–
Brazil	1	1–1.3	2.2–15.1	6–17.3	–	3.4–8.6	0.9–4.8	1.3–3.2	1.1–5.2	2.6–4.8	1.1–1.3

Note: Frequencies are shown as percentages extracted from ataxia cohort studies. Ranges were provided when two or more frequencies for a single gene per country were available. Cohort studies characteristics are shown in Data S1.

^aPMID: 37027459.

^bPMID: 35507441.

regional gene pools of the French-Canadian population, leading to an increased frequency of ATX-SYNE1, ATX-SACS, and ATX-SETX in certain regions, such as Quebec.²⁵ ATX-SYNE1, initially identified in the Quebec Beauce region, accounts for 17.8% of ATX-FXN-negative ataxias from Eastern Quebec, contrasting with global frequencies of 0.6%–13%. A broader phenotypic spectrum in ATX-SYNE1 is reported in non-Canadian patients, including motor neuron and respiratory dysfunction.²⁶ ATX-SACS (ARSACS), originally identified in the Quebec Charlevoix-Saguenay-Lac-Saint-Jean region and with a prevalence of 0.43/100,000 in Eastern Quebec, occurs worldwide, with relative global prevalences between 0.3% and 21% in non-ATX-FXN ARCA.²⁷ ATX-SETX, originally described in a large French-Canadian family, is also present in the indigenous peoples of Canada,²⁸ representing 1.1%–1.6% of Canadian non-ATX-FXN ARCAs but 3%–4% in screening studies in Europe and South America (Table S11). Importantly, a high frequency of 39% for ATX-FGF14 (SCA27B) has been found in the French-Canadian population,²⁹ although this is now increasingly recognized as a particularly common ADCA worldwide (Fig. S14).^{30–33} Other rare genetic ataxias first described in Canada include ATX-ELOVL4,³⁴ and among Dariusleut Hutterites ATX-VLDLR (a congenital, non-progressive cerebellar ataxia with developmental delay) and ATX-DNAJC19 (an early-onset non-progressive ataxia with dilated cardiomyopathy, testicular dysgenesis, and growth failure).³⁵

In Mexico, ATX-FXN is common (9%–21% of unselected familial or sporadic ataxia), while ATX-ATXN2, ATX-ATXN7, and ATX-ATXN10 represent the most frequent ADCAs, with ATX-ATXN1, ATX-ATXN3, and ATX-CACNA1A being uncommon. The Mexican state of Veracruz has an unusually high ATX-ATXN7 prevalence (14.3/100,000; 423.5/100,000 in Tlaltetela municipality). ATX-FMR1 accounts for 10% of individuals with cerebellar ataxia who have tested negative for the common ADCAs or ATX-FXN (Table S11).

In Central America and the Caribbean, only scant data involving isolated cases from a few regions exist (Table S11, Fig. S6). Cayman ataxia, caused by ATCAY variants and characterized by hypotonia present from birth, varying degrees of psychomotor delay, and cerebellar syndrome, was initially considered restricted to Grand Cayman Island but was subsequently reported in Pakistan, Iran, and Türkiye.³⁶ ATX-ATXN2 has an unusually high prevalence of 7.5/100,000 in Cuba (47.9/100,000 in Holguín province),³⁷ representing 84.7% of ADCAs, followed by ATX-ATXN3 in 2% (Fig. 2).

In South America, ATX-ATXN3 is highly prevalent in southern Brazil, owing to historical Azorean immigration.³⁸ The next most common ADCAs are ATX-ATXN2, ATX-ATXN1, and ATX-ATXN10.⁶ In

comparison, ATX-ATXN2 is the most frequent ADCA in Argentina, ATX-ATXN7 in Venezuela, and ATX-ATXN10 in Peru (Fig. 2). ATX-FXN is the most frequent ARCA in South America, without relevant prevalence differences of other ARCAs between countries (Table S11).

Asia

The genetic landscape of ataxia in Asia is diverse and complex (Fig. S2). There are ataxia cohort studies in several countries, and a significant proportion of undiagnosed cases (Table S5). ATX-ATXN3 and ATX-ATXN2 are the most common ADCAs in Asia (Fig. 2). ATX-ATXN3 is highly prevalent in China, Taiwan, and in some regions of Japan (19.2/100,000 in the Gosei area of Toyama) (Fig. S3). In contrast, ATX-ATXN1 is the most frequent ADCA in Sri Lanka and Russia (48/100,000 in the Sakha population of Eastern Siberia), with ATX-ATXN2 the most prevalent in India, South Korea, and in ethnic Malay from Singapore. In Thailand, ATX-TBP (SCA17) should be considered in individuals who have tested negative for ADCAs.³⁹ In Japan, relative frequencies of ATX-CACNA1A, ATX-BEAN1 (SCA31), and ATX-ATN1 (DRPLA) are higher than in other countries.⁵ ATX-CACNA1A and ATX-BEAN1 are phenotypically similar in the screened cohorts, both presenting as late-onset, relatively pure cerebellar ataxias, with hearing loss observed in ATX-BEAN1.⁴⁰ ATX-ATN1, characterized by heterogeneous movement disorders in adults, and myoclonic epilepsy in juvenile-onset cases, is more prevalent (up to 21% of ADCAs) in Japan, followed by South Korea (4%), and rare in other Asian countries.⁵

Regional differences in the prevalence of ADCAs also exist in India (Fig. S4). Notably high regional prevalences in India include ATX-PPP2R2B (SCA12) in the Agarwal community in north-western regions, ATX-ATXN2 in north-eastern regions, ATX-ATXN3 in Telangana, and ATX-ATXN1 in Bangalore and South India. The largest Indian ataxia screening study identified ATX-PPP2R2B (8.7%), and ATX-ATXN2 (8.6%) as the most prevalent ADCAs, followed by ATX-ATXN1 (4.9%), and ATX-ATXN3 (3%), with ATX-ATXN7 being relatively rare (0.5%), confined to one ethnic group from Haryana region.⁴¹ Few ATX-PPP2R2B cases in non-Agarwal communities have been reported from southern India, and are ultra-rare globally (Table S5).

ARCAs are underreported in Asia, except in Pakistan, which has relatively high consanguinity rates (Table S5). ATX-FXN is mostly reported in Russia and India, whereas data from China, Taiwan, Japan, and Singapore report 0% prevalence, with isolated cases reported in other Asian countries (Tables S5 and S6). In screening studies in South Korea, ARCAs

include HSP/ATX-SPG7, ATX-APTX, and ATX-SYNE1, with a frequency of approximately 3% each. Within unselected early-onset cerebellar ataxia in India, the most common non-ATX-FXN ARCA were ATX-SACS (7.1%), ATX-SETX (6.1%), ATX-ATM (2.0%), and ATX-TTPA (2.0%). In China, the most frequent ARCA include ATX-SETX (5.6–15.4%), ATX-NPC1 (11.5%), ATX-SACS (11.1%), ATX-CYP27A1 (7.7%), ATX-SYNE1 (9.2%), and ATX-ADCK3 (9.2%).

Middle East

Population studies predominantly originate from Türkiye and Iran, with scant reports from other countries. The proportion of undiagnosed cases ranges from 25% to 90% (Table S8). ATX-ATXN3 has been reported among Jewish Israeli families originating from Yemen, with an estimated prevalence of 29/100,000.⁴² Several ARCA have been described, given high rates of consanguinity, and genetic diversity, possibly related to the location at the crossroads between Eastern and Western civilizations along the ancient Silk Road.⁴³ In Türkiye, ATX-FXN is the most prevalent ARCA, followed by ATX-ATM, ATX-SACS, and PLA2G6. Among ADCAs, ATX-ATXN1 and ATX-ATXN2 are the most common. In Iran, the most common ARCA were PLA2G6 (11.7%), ATX-ATM (8.6%), ATX-SACS (7.4%), ATX-FXN (3.1%), and ATX-APTX (3.1%). PLA2G6-associated neurodegeneration, which has a wide phenotypic spectrum, is common among the Iranian Fars ethnicity but otherwise rare, while ATX-SACS is more prevalent in Azeri Iranians.⁴³ In Iraqi Jewish children, the presence of ataxia, early-onset optic atrophy, later-onset spasticity, chorea, and intellectual disability suggests Costeff syndrome.⁴⁴ An ancestral founder effect within Arab populations was found for RUBCN variants causing “Salih ataxia” (childhood-onset, slowly progressive ataxia, seizures, and intellectual disability).⁴⁵ Spinocerebellar Ataxia with Axonal Neuropathy Type 1 (childhood/early adulthood-onset ataxia, sensorimotor axonal neuropathy, pes cavus), caused by TDP1 variants, was described in consanguineous families from Saudi Arabia and Oman, probably sharing an ancestral founder haplotype.⁴⁶ The “dysequilibrium syndrome,” a rare, typically non-progressive ataxia, with intellectual disability, and quadrupedal gait related to VLDLR, CA8, ATP8A2, or WDR81 variants, is described in several families from Türkiye, Iran, Iraq, Oman, Saudi Arabia, Syria, and the United Arab Emirates.⁴⁷

Oceania

Most genetic ataxias have been reported in Australia and New Zealand, with screening studies conducted in Australia. The most common ADCA in Australia is ATX-ATXN1, followed by ATX-ATXN3, ATX-

CACNA1A, and ATX-ATXN2 (Fig. 2). Other than ATX-ATXN3 noted in aboriginal Australians, genetic ataxias in the native Māori population of New Zealand and the Cook Islands include ATX-RFC1 (with the (AAAGG)10-25(AAGGG)exp RFC1 pathogenic repeat configuration),⁴⁸ ATX/HSP-SACS, HSP/ATX-SPG7, ATX-ITPR1, and APOB variants (Table S19).

Europe

Several large screening studies provide data on relative prevalences and regional differences (Tables S2–S4, Fig. S1A,B). ATX-ATXN3 is highly prevalent in the Portuguese Azores (43/100,000), and 971/100,000 in Flores Island. ATX-ATXN3 is the most prevalent ADCA in Germany and the Netherlands, ATX-ATXN1 in Italy and Poland, ATX-CACNA1A (SCA6) in the northeast of England, while ATX-ATXN2 predominates in Italy. Other ADCAs are restricted to certain regions, including ATX-NOP56 (SCA36) in the Costa da Morte region in Galicia, Spain, ATX-DAB1 (SCA37) in southern Portugal and Spain, and ATX-ATXN8 in Finland. ATX-ATN1, typically associated with Japanese ancestry, has been reported in Italy, South Wales, and Portugal. Recently, a GGC-repeat expansion in ZFH3, associated with the SCA4 locus, causing gait ataxia, sensorimotor neuropathy, dysautonomia, and slow saccades, was identified in Swedish families.⁴⁹

Regarding ARCA, ATX-FXN is frequent in the Aegean islands, the Paphos district of Cyprus, the northern Spain Basque region, Italy, and France. Screening studies revealed relative frequencies of 5.3% for ATX-SYNE1 and 1.8% for ATX-STUB1.^{26,50} In Portugal, ataxia with oculomotor apraxia related to APTX, SETX, and PNKP variants (prevalence 0.4/100,000), are collectively the most frequent ARCA after ATX-FXN.⁵¹ In the North Sea region, particularly the Netherlands, MYC/ATX-GOSR2 is an early-onset ataxia with delayed motor milestones, areflexia, stimulus-sensitive myoclonus, and myoclonic seizures.⁵² In Finland, ATX-RFC1 and POLG variants are the most common ARCA, while Salla disease (ATX-SLC17A5), a sialic acid storage disorder reported in Finnish families (early-onset ataxia, hypotonia, developmental delay, and short stature) is rarer.⁵³

The MDSGene Global Genetic Ataxia Resource

Complete data on the regional differences between and within continents and countries can be found in the MDSGene Global Genetic Ataxia Resource (<https://www.mdsgene.org/ataxia.html>).

Diagnostic Approach to Genetic Ataxias

Establishing the final diagnosis of genetic ataxia can be challenging despite recent advancements in

comprehensive testing options.⁵⁴ Advanced genetic techniques, such as long-read sequencing, have identified novel genetic ataxias, including exonic repeat expansions in the *THAP11* (SCA51) and *ZFH3* (SCA4) genes, and intronic repeat expansions in the *RFC1* and *FGF14* genes.⁴ *ATX-RFC1*, causing Cerebellar Ataxia with Neuropathy and Vestibular Areflexia Syndrome (CANVAS), has been found in up to 88% of CANVAS cohorts and between 0% and 16% in unselected ataxia screening studies, being more common in Europe and Australia (Data S1). It is important to state that *ATX-FGF14* due to GAA repeat expansions (presenting with downbeat nystagmus, and episodic manifestations including gait and limb ataxia, visual disturbances, vertigo, or dysarthria, frequently responding to 4-aminopyridine), is an increasingly common, late-onset ADCA. *ATX-FGF14* has a prevalence of up to 61%, particularly in Canada and Western Europe, appearing rare in China and Japan.⁵⁵

In most wealthy countries, the ataxia diagnostic approach involves comprehensive genetic testing, including whole genome sequencing (WGS), whole exome sequencing (WES), or multigene panel testing, including repeat expansions. Advanced techniques, including long-read sequencing, are available in some reference laboratories, or for research purposes. Short-read genome sequencing is a well-established technology already employed by diagnostic commercial laboratories, whereas long-read sequencing with adaptive sampling provides significant advantages for detecting and characterizing repeat expansions but still requires optimization before it can be implemented in clinical settings.⁵⁶ However, in most regions, genetic testing is significantly limited by reduced access to trained personnel/manpower with further limitations from financial barriers, poor healthcare infrastructure, and absent testing facilities, leading to unequal access for patients and clinicians.^{8,9}

Age at Onset, Phenotype, and Ancillary Tests Facilitate a Targeted Genetic Testing Strategy

Age at onset is of moderate relevance for the diagnosis. In general, most ARCAs are early-onset, whereas ADCAs typically occur later. There are, however, many exceptions, for example, *ATX-RFC1*⁵⁷ typically presents in adulthood; whereas other ARCAs, such as late-onset GM2 gangliosidosis (*ATX/HSP-HEXA/HEXB*), very late-onset *ATX-FXN*, *HSP/ATX-SPG7*, and *ATX-SACS* (usually characterized by early disease onset) can also occasionally manifest in (late) adulthood.⁵⁸ Similarly, some of the ADCAs can have an early onset, particularly in the setting of repeat expansion disorders with large expansions.⁵⁹

Characteristic clinical features may indicate specific diagnoses (Table S20). Region-specific phenotypic

heterogeneity can also guide workup. ARSACS should be considered in early-onset cerebellar ataxia even without retinal hypermyelination or spasticity in regions other than Quebec.⁶⁰ Additionally, many *ATX-ATXN2* patients in India may not have characteristic slow saccades.⁶¹ In *ATX-ATXN10*, seizures are frequent in most patients; however, most Brazilian patients do not develop seizures, potentially related to the Amerindian-Belgian connection.⁶² Asians with *ATX-ATXN3* have a later onset age compared with Caucasians and African Americans, while African Americans exhibit more severe ataxia when controlling for CAG repeat length and disease duration, and more commonly have parkinsonism.^{63,64}

Laboratory findings can add diagnostic specificity, and suggested first-tier tests are shown in Table S21. Alpha-fetoprotein is a reliable biomarker of ARCAs *ATX-ATM* and *ATX-SETX*, with slightly elevated levels in *ATX-APT*, *ATX-PNKP*, *ATX-TDP1*, and *ATX-ARV1*.⁶⁵ Reduced serum vitamin E levels suggest *TTPA*, *MTTP*, *VLDLR*, and *APOB* variants.⁶⁶ Second-tier tests are shown in Table S22. Characteristic neuroimaging patterns can also facilitate diagnosis, for example, linear pontine hypointensities in ARSACS, or the middle cerebellar peduncle sign in FXTAS (Table S23).

In complex disorders without predominant ataxia, diagnosis often requires broad genetic testing. Given their rarity, a targeted genetic testing approach based on clinical manifestations and ancillary testing can be a cost-effective diagnostic strategy (Table 2). NGS, with analysis of copy number variations (CNVs), should be a first-line approach in pediatric ataxia with intellectual disability and global developmental delay.⁶⁷ A wider genetic testing diagnostic approach includes NGS, with multigene panels, WES, WGS, analysis of mtDNA, and CNVs.⁶⁸ However, common repeat-expansion ataxias (polyglutamine ADCAs, *ATX-FGF14*, *ATX-FXN*, *ATX-RFC1*, and *ATX-FMR1*) are insufficiently covered with these non-targeted approaches, and should be tested according to clinical suspicion. In adult-onset ataxia without clinical or ancillary diagnostic clues, initial testing should include screening for the most common repeat-expansion ataxias, given their high prevalence.⁶⁹ Multigene panels, including repeat-expansion ataxias, are preferred but not universally available or affordable.

Genetic Testing: A Tiered Approach Based on Regional Prevalence

Prioritizing genetic testing based on ethnic origin or geographical location is important, especially with limited resources, or where health systems in developed countries limit access to genetic testing (Table S1). A novel genetic testing approach based on clinical judgment, which can be applied in various countries, is

TABLE 2 Targeted genetic testing strategy guided by clinical symptoms and key findings from ancillary tests

Phenotype besides ataxia	Laboratory findings	Neuroimaging patterns	Targeted gene/s
Intention tremor, cognitive decline, behavioral disturbances, parkinsonism, neuropathy, dysautonomia over the age of 50 years	—	Middle cerebellar peduncle sign: hyperintensities in middle cerebellar peduncles (usually in association with corpus callosum splenium, or periventricular white matter hyperintensities)	<i>FMR1</i>
Episodic ataxia, downbeat nystagmus, vestibular dysfunction, diplopia, oscillopsia	—	Superior cerebellar peduncles atrophy and hyperintensity	<i>FGF14</i>
Chronic cough, downbeat nystagmus, vestibular dysfunction, neuropathy, parkinsonism, dysautonomia over the age of 35 years	—	Occasional spinal cord atrophy	<i>RFC1</i>
Dysarthria, absent deep tendon reflexes, impaired proprioception, fixation instability, and variably present features such as scoliosis, pes cavus, optic atrophy, hearing loss, diabetes mellitus, and cardiomyopathy	—	Spinal cord atrophy without cerebellar atrophy Spinal cord hyperintense signaling of dorsal part on inversion recovery images	<i>FXN</i>
Friedreich ataxia-like, ^a pigmentary retinopathy	Vitamin E (↓ levels)	Spinal cord hyperintense signaling of dorsal part on inversion recovery images	<i>TTPA</i>
Friedreich ataxia-like, ^a chronic diarrhea, pigmentary retinopathy, liver disease	Vitamin E, cholesterol, apolipoprotein B (↓ levels), ↑ liver transaminases, anemia, acanthocytosis	—	<i>MTTP</i>
Conjunctival telangiectasias, dystonia, immune deficiency, predisposition to malignancy	α-Fetoprotein (↑ levels: ≈200 μg/L)	Spinal cord atrophy	<i>ATM</i>
Friedreich ataxia-like, ^a oculomotor apraxia, neuropathy, dystonia, chorea	α-Fetoprotein (↑ levels: 5–20 μg/L), cholesterol (↑ levels), albumin (↓ levels)	—	<i>APTX</i>
Friedreich ataxia-like, ^a oculomotor apraxia, strabismus, hypogonadism, neuropathy, dystonia, chorea	α-Fetoprotein (↑ levels: 15–65 μg/L), gonadotrophin (↓ levels)	—	<i>SETX</i>
Friedreich ataxia-like, ^a prominent myelinated fibers radiating from the edges of the optic disc, spastic gait, neuropathy	—	Superior cerebellar vermis atrophy; posterior mid-body corpus callosum thinning; bilateral hypointense pontine striations; hyperintense peri thalamic rims, enlarged pons	<i>SACS</i>
Juvenile cataracts, tendon xanthomas, xanthelasmata, chronic diarrhea, prominent early psychosis or bipolar affective disorder-like symptoms, dystonia, parkinsonism, seizures, neuropathy	Cholestanol and urinary hydroxylated bile alcohols (↑ levels), cholesterol: (↓ levels)	Bilateral heterogeneous hyperintensities of the dentate nuclei with a central hypointensity in the deep cerebellar nuclei related to deposition of hemosiderin and focal calcifications	<i>CYP27A1</i>

(Continues)

TABLE 2 Continued

Phenotype besides ataxia	Laboratory findings	Neuroimaging patterns	Targeted gene/s
Liver disease, Kayser–Fleischer rings, dystonia, parkinsonism, early psychosis or bipolar affective disorder-like symptom	24-hr cupruria (↑ levels); ceruloplasmin (↓ levels); hemolytic anemia; liver transaminases (↑ levels)	Bilateral hyperintensities in the putamen, caudate nuclei, thalamus, internal and external capsules, midbrain, middle cerebellar peduncles, and cerebellum; hypointensities in globus pallidus; T1-hyperintensity of the globus pallidus; cerebral, cerebellar, putamen and pons atrophy; central pontine myelinolysis; ‘face of the giant panda’; ‘double panda sign’; ‘face of the miniature panda’	<u>ATP7B</u>
Vertical supranuclear gaze palsy, intellectual disability, dystonia, gelastic cataplexy, seizures, prominent treatment-resistant psychiatric syndromes (depression, psychosis, bipolar disorders), liver disease ^b	Oxysterols (↑ levels), Filipin staining test	–	<u>NPC1</u>
Liver disease, diabetes mellitus, pigmentary retinopathy, dystonia	Copper and ceruloplasmin (↓ levels), anemia with ferritin (↑ levels), glycemia (↑ levels)	Hypointensities in dentate nucleus and basal ganglia, spinal cord hyperintense signaling of dorsal part on inversion recovery images	<u>CP</u>
Abnormal dentition, hypogonadotropic hypogonadism, intellectual disability, tremor	Gonadotrophin (↓ levels)	Bilateral hyperintensity along the superior cerebellar peduncles ranging from the dentate nucleus up to the midbrain just below the red nucleus	<u>POLR3A</u>
Episodic ataxia, dystonia, seizures, spasticity, microcephaly with facial dysmorphism, occasional intellectual disability	Lactate and pyruvate in serum and CSF (↑ levels)	Leigh syndrome-like pattern: bilateral pallidal, caudate, and putaminal hyperintensities with (occasional) cavitations. Corpus callosum agenesis (complete or partial) or dysgenesis	<u>PDHA1</u>
Developmental delay, intellectual disability, dystonia, seizures	L-2-hydroxyglutaric acid in urine, serum, and CSF (↑ levels)	Leigh syndrome-like pattern; bilateral hyperintensities of dentate nuclei commonly combined with mild cerebellar atrophy; hypointensities in dentate nucleus, and basal ganglia	<u>L2HGDH</u>
Developmental delay, macrocephaly, spasticity, epilepsy	–	Megalencephaly with large frontotemporal subcortical cavitations and leukoencephalopathy	<u>MLC1</u>
Pigmentary retinopathy, cataracts, hearing impairment, peripheral neuropathy, skin manifestations, cardiac disease	Phytanic acid (↑ levels)	Hypointensities in the dentate nucleus and basal ganglia	<u>PHYH</u>
Stroke-like episodes, exercise intolerance, muscle weakness, seizures, tremor, dystonia, cataracts,	Creatine kinase and lactate (↑ levels)	Stroke-like hyperintensities	<u>ADCK3</u>

(Continues)

TABLE 2 Continued

Phenotype besides ataxia	Laboratory findings	Neuroimaging patterns	Targeted gene/s
optic atrophy, hearing impairment, diabetes mellitus			
Myoclonus, seizures, areflexia, scoliosis	Creatine kinase (↑ levels)	—	<i>GOSR2</i>
Intellectual disability, exercise intolerance, muscle weakness, peripheral neuropathy, seizures, hearing impairment, optic atrophy, gaze palsy, hypergonadotropic hypogonadism	Gonadotrophin (↑ levels)	Stroke-like hyperintensities; spinal cord atrophy	<i>TWNK</i>
Neuropathy, myopathy, seizures, pigmentary retinopathy, gaze palsy, ptosis, hearing impairment, stroke-like episodes, short stature, diabetes, cardiomyopathy	Lactate in serum, and CSF (↑ levels)	Stroke-like hyperintensities	<i>mtDNA</i>
Erythrokeratoderma	—	'Hot cross bun' sign (rare)	<i>ELOVL4</i>

Note: In bold: genes related to repeat expansion disorders; underlined: treatable ataxias with mechanism-directed treatments. All tests are serum biomarkers unless otherwise indicated. The genes listed here are intended to serve as a guide and other targeted approaches can be applied depending on clinical suspicion.

Abbreviation: CSF, cerebrospinal fluid.

^a'Friedreich ataxia-like' phenotype indicates a patient exhibits clinical manifestations that resemble Friedreich ataxia.

^bPhenotype of the childhood late-onset *NPC1*.

proposed in Figure 3. Considering costs and limited resources, a sequential genetic testing approach is recommended. In suspected ADCA patients, regional ADCA prevalence rates suggest initial testing of specific genetic ataxias; for example, ATX-*ATXN1* in Poland and Russia, ATX-*ATXN2* in Cuba, and ATX-*ATXN3* in Portugal, Brazil, and China (Fig. 3). Ethnicity also plays an important role, such as in Singapore, prioritizing ATX-*ATXN2* testing in ethnic Malay or Indian patients, and ATX-*ATXN3* and ATX-*ATXN2* in ethnic Chinese patients. In Brazil, ATX-*CACNA1A* and ATX-*ATN1* should be considered for patients with Japanese ancestry. Similar considerations include prioritizing ATX-*NOP56* testing in Spanish Galician populations, ATX-*ATXN7* in Veracruz, Mexico, ATX-*PPP2R2B* in Indian Agarwals, and other ataxias with founder effects (Fig. 3, Table S1).

Knowledge of regional epidemiology is also relevant for avoiding routine testing of ataxias that are absent or extremely rare in certain countries or populations. These include ATX-*ATXN3* in Cyprus, the Czech Republic, Finland, Greece, Poland, Russia, Serbia, and Türkiye, ATX-*BEAN1* in Caucasians, or ATX-*ATXN10* and ATX-*PPP2R2B* in European or East Asian populations. Furthermore, given the very low prevalence of ATX-*FXN* in certain Asian countries, such as China and Japan, routine testing for ATX-*FXN* is generally not recommended in suspected ARCA/de novo patients, unless the clinical presentation is strongly suggestive. In countries including

Cyprus or Oman, where screening studies indicate the absence of the most common ADCAs, a broad genetic testing approach is recommended. Furthermore, including certain repeat-expansion ADCAs in multigene panels (*TBP*, *ATXN8*, *ATXN10*, *PPP2R2B*, *NOP56*, *BEAN1*, *DAB1*, and *ATN1*) may be unnecessary, given global rarity or restriction to specific regions or countries.

Discussion

The landscape of genetic ataxias is influenced by migration, population genetics, consanguinity, and founder effects. The epidemiological data of 548 genetic ataxias across 122 countries that we present here inform the diagnostic approach of individuals with undiagnosed ataxia. Given regional differences, routine testing for all ADCAs may not be optimal for adult-onset sporadic or suspected ADCA cases, nor is ATX-*FXN* testing the best approach for every suspected ARCA. Sequential genetic testing can be more cost-effective, or the only diagnostic option in certain regions. The new standard of care for ataxia involving routine genetic testing is no longer merely a research curiosity but an essential requirement that empowers patients. Providing a diagnosis in ataxia patients has important implications for ending the diagnostic odyssey, genetic counseling, and disease management. Furthermore, early diagnosis is critical for ataxias with

Continent or Region	Country	Genes														
		A T X N 1	A T X N 2	A T X N 3	C A C N A 1 A	A T X N 7	A T X N 8	A T X N 10	P P P 2 R 2 B	T B P	N O P 5 6	F G F 1 4	B E A N 1	A T N 1	R F C 1	F X N
Oceania	Australia															
Africa	Algeria															
	South Africa															
Middle-East	Oman															
	Turkey															
Asia	China															
	India															
	Japan															
	Malaysia															
	Russia															
	Singapore															
	South Korea															
	Sri Lanka															
	Taiwan															
	Thailand															
America	Canada															
	Mexico															
	United States															
	Cuba															
	Argentina															
	Brazil															
	Peru															
	Venezuela															
Europe	Cyprus															
	Czech Republic															
	Finland															
	France															
	Germany															
	Greece															
	Ireland															
	Italy															
	Norway															
	Poland															
	Portugal															
	Serbia															
	Spain															
	The Netherlands															
	United Kingdom															

FIG. 3. Proposed first-tier genetic testing approach for common genetic ataxias based on regional prevalence rates. Green boxes: highly prevalent genetic ataxias that should be considered as a first-tier genetic testing approach. Red boxes: genetic ataxias with $\leq 1\%$ prevalence in one or more ataxia cohort studies and occurrence is either absent or in isolated cases. Blank boxes: no specific recommendation: a first-tier genetic testing approach is plausible due to variable prevalence rates in one or more ataxia cohort studies, or information is absent. Supporting information for ataxia cohort studies can be found in Data S1. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com/doi/10.1002/mds.30302)]

pathogenesis-directed treatment (Table S24), and for future gene-specific therapies, and the need to assemble clinical trial-ready cohorts.

Clinicians must consider clinical presentation, epidemiology, and regional variation of genetic ataxias when determining the most effective genetic testing strategy. A phenotype-guided, sequential testing approach based

on ancillary test results and regional prevalence, as described herein, facilitates cost-effective genetic testing in the setting of limited resources or access. It is important to highlight that genetic testing strategies should not be guided solely by the prevalence of specific genetic forms but must also consider thorough history-taking and the examination of family members and

relatives. Therefore, even in the absence of a clear familial pattern, routine testing of seemingly sporadic or suspected cases remains relevant.

This study has limitations. Although significant geographical disparities exist in genetic ataxias, differences in healthcare access have led to varying diagnostic rates. In many countries, data are limited or absent, often restricted to case reports of specific genetic ataxias, with reporting bias skewed toward more common causes. Few countries have conducted systematic screening studies, with the prevalence of most genetic ataxias unknown in many regions. Moreover, many large-scale prevalence studies focused on only a few genetic ataxias (primarily common polyglutamine ADCAs) or in specific age groups, with marked methodological heterogeneity. In addition, a key limitation of this review is the variability in methodologies across different studies, making direct comparisons of prevalence within a country, geographical region, or specific ethnicity challenging. Differences in genetic screening approaches, ranging from genome sequencing to targeted candidate gene screening, further complicate the interpretation of regional differences. As a result, conclusions regarding the underdiagnosis or relative frequency of specific ataxias in certain areas may be biased by study selection. Additionally, within-country variations, such as those observed in India, Brazil, or Japan, highlight the influence of sample size and sub-ethnic diversity, which may not always be captured in published studies. To address this, we provided comprehensive ataxia cohort studies' characteristics, such as sample size and genetic screening methods employed as Data S1 and S2. Although we leveraged the diverse native-speaking languages of our authorship, future work could include publications with a broader range of languages not covered in this review. We also encourage authors to make their data as accessible and readable as possible to ensure inclusion in future analyses.

Knowledge of the regional variation of the genetic ataxias is important not only for cost-effective genetic testing, facilitating appropriate diagnosis and tailored management for patients and clinicians but also for planning treatment trials through industry partners. However, current epidemiological data likely underestimate the true carrier frequency of ataxia-causing genes and the degree of reduced penetrance. A recent study analyzing whole-genome sequencing data from over 82,000 individuals found a higher frequency of repeat expansion disorder-related alleles, suggesting that the actual number of affected individuals may be two to three times higher than currently reported. Moreover, this study demonstrated that these disorders occur across all major ancestries, highlighting the need for more inclusive global diagnostic efforts.⁷⁰ In addition, as long-read sequencing technologies continue to decrease in cost and

become more widely accessible, they are expected to provide a more accurate and comprehensive understanding of the global prevalence of repeat expansion disorders.

The data in this review and its Data S1 and S2 are publicly available and searchable for all healthcare professionals and the scientific community as an online resource with various maps and filter options on the MDSGene Global Genetic Ataxia Resource (<https://www.mdsgene.org/ataxia.html>). Improving accessibility to genetic testing in underserved and underrepresented regions should be prioritized for ataxias, highlighting the need for international research initiatives such as GP2, the Global Parkinson's Disease Genetics Program.^{71,72} ■

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

M.R.: 1A, 1B, 1C, 2A.

C.D.S.: 1A, 1B, 1C, 2A.

J.D.: 1B, 1C, 2A, 2B.

J.L.P.: 1B, 1C, 2A, 2B.

S.-H.K.: 1B, 1C, 2A, 2B.

C.-Y.R.L.: 1B, 1C, 2A, 2B.

O.O.: 1B, 1C, 2A, 2B.

S.E.-J.: 1B, 1C, 2A, 2B.

W.-W.L.: 1B, 1C, 2A, 2B.

H.M.: 1A, 1B, 1C, 2A, 2B.

O.G.P.B.: 1B, 1C, 2A, 2B.

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

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

B.P.v.d.W.: 1A, 1B, 1C, 2B.

All authors contributed to the article and approved the submitted version.

Acknowledgments: The maps were created with [mapchart.net](https://www.mapchart.net). The authors take a neutral position with respect to territorial claims in published maps. Special gratitude is extended to Floriana Colombo, Daniela Grimberg, and Mónica Soria, the librarians at Fleni, for their crucial support in obtaining some of the publications that support the data presented here.

Financial Disclosures of All Authors (for the Preceding 12 Months): M.R.: Stock Ownership in medically related fields: None. Consultancies: None. Advisory Boards: Biogen. Partnerships: None. Honoraria: International Parkinson and Movement Disorder Society. Grants: None. Intellectual Property Rights: None. Expert Testimony: None. Employment: Servicio de Movimientos Anormales, Departamento de Neurología, Fleni. Contracts: None. Royalties: None. Other: None. C.D.S.: Stock Ownership in medically related fields: None. Consultancies: None. Advisory Boards: SwanBio Therapeutics. Partnerships: None. Honoraria: American Academy of Neurology and The International Parkinson and Movement Disorders Society. Grants: Sanofi-Genzyme; National Institutes of Health K23 NS118045. Intellectual Property Rights: None. Expert Testimony: None. Employment: Ataxia Center, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA. Contracts: None. Royalties: None. Other: None. J.D.: Stock Ownership in medically related fields: None. Consultancies: Biohaven. Advisory Boards: Biogen. Partnerships: None. Honoraria: None. Grants: None. Intellectual Property Rights: None. Expert Testimony: None. Employment: Neurology Department Centro Hospitalar Universitário de Santo António, Porto Portugal. Genetic Epidemiology and Epigenetics, UMIB-Unit for Multidisciplinary Research in Biomedicine, ICBAS, School of Medicine and Biomedical Sciences, University of Porto, Porto, Portugal. Contracts: None. Royalties: None. Other: None. J.L.P.: Stock Ownership in medically related fields: None. Consultancies: None. Advisory Boards: None. Partnerships: None. Honoraria: None. Grants: None. Intellectual Property Rights: None. Expert Testimony: None. Employment: Department of Neurology, Ataxia Unit, Universidade Federal de São Paulo, São Paulo, Brazil. Contracts: None. Royalties: None. Other: None. S.-H.K.: Stock Ownership in medically related fields: None. Consultancies: None. Advisory Boards: Biogen, Praxis Precision Medicines, and Yoda Pharmaceuticals. Partnerships: None. Honoraria: None. Grants: None. Intellectual Property Rights: None. Expert Testimony: None. Employment: Department of Neurology, Columbia University Medical Center, New York, New York, USA.

Contracts: None. Royalties: None. Other: None. C.-Y.R.L.: Stock Ownership in medically related fields: None. Consultancies: None. Advisory Boards: None. Partnerships: None. Honoraria: None. Grants: None. Intellectual Property Rights: None. Expert Testimony: None. Employment: Alzheimer's Disease and Parkinson's Disease Centers, Department of Neurology, Baylor College of Medicine, Houston, Texas, USA. Contracts: None. Royalties: None. Other: None. O.O.: Stock Ownership in medically related fields: None. Consultancies: None. Advisory Boards: None. Partnerships: None. Honoraria: International Parkinson and Movement Disorders Society, GBA1-Canada (G-Can). Grants: National Institute of Health and Care Research, UK (Transforming Parkinson's Care in Africa NIHR133391). Intellectual Property Rights: None. Expert Testimony: None. Employment: College of Medicine, University of Lagos, Idi-Araba, Lagos State, Nigeria. Contracts: None. Royalties: None. Other: Travel Support: International Parkinson and Movement Disorders Society, Global Parkinson's Genetics Program (GP2), and G-Can. S.E.-J.: Stock Ownership in medically related fields: None. Consultancies: None. Advisory Boards: None. Partnerships: None. Honoraria: International Parkinson and Movement Disorder Society. Grants: 2024–2025 pilot awards for global health leaders. Intellectual Property Rights: None. Expert Testimony: None. Employment: Neurology Department, Kasr Al-Ainy School of Medicine, Cairo University, Cairo, Egypt. Contracts: None. Royalties: None. Other: None. W.-W.L.: Stock Ownership in medically related fields: None. Consultancies: None. Advisory Boards: None. Partnerships: None. Honoraria: None. Grants: None. Intellectual Property Rights: None. Expert Testimony: None. Employment: Department of Neurology, Nowon Eulji Medical Center, Eulji University, Seoul, Korea. Contracts: None. Royalties: None. Other: None. H.M.: Stock Ownership in medically related fields: None. Consultancies: None. Advisory Boards: None. Partnerships: None. Honoraria: None. Grants: None. Intellectual Property Rights: None. Expert Testimony: None. Employment: University of Luebeck and University Hospital of Schleswig-Holstein. Contracts: None. Royalties: None. Other: None. O.G.P.B.: Stock Ownership in medically related fields: None. Consultancies: None. Advisory Boards: None. Partnerships: None. Honoraria: None. Grants: None. Intellectual Property Rights: None. Expert Testimony: None. Employment: Servicio de Movimientos Anormales, Departamento de Neurología, Fleni. Contracts: None. Royalties: None. Other: None. A.K.S.: Stock Ownership in medically related fields: None. Consultancies: None. Advisory Boards: None. Partnerships: None. Honoraria: None. Grants: None. Intellectual Property Rights: None. Expert Testimony: None. Employment: Department of Neurology, All India Institute of Medical Sciences, New Delhi, India. Contracts: None. Royalties: None. Other: None. C.K.: Stock Ownership in medically related fields: None. Consultancies: Centogene, Takeda, Lundbeck Foundation, Biogen. Advisory Boards: None. Partnerships: None. Honoraria: Bial. Grants: German Research Foundation (DFG), The Michael J. Fox Foundation for Parkinson's Research (MJFF), Aligning Science Across Parkinson's (ASAP). Intellectual Property Rights: None. Expert Testimony: None. Employment: University of Luebeck and University Hospital of Schleswig-Holstein. Contracts: None. Royalties: Oxford University Press. Other: None. B.P.v.d.W.: Stock Ownership in medically related fields: None. Consultancies: None. Advisory Boards: Biogen, Vico Therapeutics, and Biohaven. Partnerships: None. Honoraria: None. Grants: Hersenstichting, ZonMw, Dutch Research Council, FARA, and Christina Foundation. Intellectual Property Rights: None. Expert Testimony: None. Employment: Department of Neurology, Radboud University Medical Center, Nijmegen, Netherlands. Contracts: None. Royalties: BSL/Springer-Nature. Other: None.

Data Availability Statement

Data have been uploaded to the MDSGene Global Genetic Ataxia Resource (<https://www.mdsgene.org/ataxia.html>) and the visual display is shown in Figures S15 and S16.

References

- Lange LM, Gonzalez-Latapi P, Rajalingam R, Tijssen MAJ, Ebrahimi-Fakhari D, Gabbert C, et al. Nomenclature of genetic movement disorders: recommendations of the International Parkinson and Movement Disorder Society Task Force—an update. *Mov Disord* 2022;37(5):905–935.
- Rossi M, Anheim M, Durr A, Klein C, Koenig M, Synofzik M, et al. The genetic nomenclature of recessive cerebellar ataxias. *Mov Disord* 2018;33(7):1056–1076.
- Pedroso JL, Vale TC, França Junior MC, Kauffman MA, Teive H, Barsottini OGP, et al. A diagnostic approach to spastic ataxia syndromes. *Cerebellum* 2022;21(6):1073–1084.
- Vegezzi E, Ishiura H, Bragg DC, Pellerin D, Magrinelli F, Currò R, et al. Neurological disorders caused by novel non-coding repeat expansions: clinical features and differential diagnosis. *Lancet Neurol* 2024;23(7):725–739.
- van Prooije T, Ibrahim NM, Azmin S, van de Warrenburg B. Spinocerebellar ataxias in Asia: prevalence, phenotypes and management. *Parkinsonism Relat Disord* 2021;92:112–118.
- Teive HAG, Meira AT, Camargo CHF, Munhoz RP. The geographic diversity of spinocerebellar ataxias (SCAs) in the Americas: a systematic review. *Mov Disord Clin Pract* 2019;6(7):531–540.
- Stezin A, Pal PK. Treatable ataxias: how to find the needle in the haystack? *J Mov Disord* 2022;15(3):206–226.
- Gatto EM, Walker RH, Gonzalez C, Cesarini M, Cossu G, Stephen CD, et al. Worldwide barriers to genetic testing for movement disorders. *Eur J Neurol* 2021;28(6):1901–1909.
- Watson S, Ngo KJ, Stevens HA, Wong DY, Kim J, Song Y, et al. Cross-sectional analysis of exome sequencing diagnosis in patients with neurologic phenotypes facing barriers to clinical testing. *Neurol Genet* 2024;10(3):e200133.
- Ruano L, Melo C, Silva MC, Coutinho P. The global epidemiology of hereditary ataxia and spastic paraplegia: a systematic review of prevalence studies. *Neuroepidemiology* 2014;42(3):174–183.
- Rodríguez-Labrada R, Martins AC, Magaña JJ, Vazquez-Mojena Y, Medrano-Montero J, Fernandez-Ruiz J, et al. Founder effects of spinocerebellar ataxias in the American continents and the Caribbean. *Cerebellum* 2020;19(3):446–458.
- Sequeiros J, Martins S, Silveira I. Epidemiology and population genetics of degenerative ataxias. *Handb Clin Neurol* 2012;103:227–251.
- Labuda M, Labuda D, Miranda C, Poirier J, Soong BW, Barucha NE, et al. Unique origin and specific ethnic distribution of the Friedreich ataxia GAA expansion. *Neurology* 2000;54(12):2322–2324.
- Vankan P. Prevalence gradients of Friedreich's ataxia and R1b haplotype in Europe co-localize, suggesting a common Palaeolithic origin in the Franco-Cantabrian ice age refuge. *J Neurochem* 2013;126(Suppl. 1):11–20.
- Polo JM, Calleja J, Combarros O, Berciano J. Hereditary ataxias and paraplegias in Cantabria, Spain. An epidemiological and clinical study. *Brain* 1991;114(Pt 2):855–866.
- Juvonen V, Kulmala SM, Ignatius J, Penttinen M, Savontaus ML. Dissecting the epidemiology of a trinucleotide repeat disease—example of FRDA in Finland. *Hum Genet* 2002;110(1):36–40.
- Gama MTD, Braga-Neto P, Rangel DM, Godeiro C Jr, Alencar R, Embiruçu EK, et al. Autosomal recessive cerebellar ataxias in South America: a multicenter study of 1338 patients. *Mov Disord* 2022;37(8):1773–1774.
- Traschütz A, Adames-Gomez AD, Anheim M, Baets J, Falkenburger BH, Gburek-Augustat J, et al. Autosomal recessive cerebellar ataxias in Europe: frequency, onset, and severity in 677 patients. *Mov Disord* 2023;38(6):1109–1112.
- Berry-Kravis E, Abrams L, Coffey SM, Hall DA, Greco C, Gane LW, et al. Fragile X-associated tremor/ataxia syndrome: clinical features, genetics, and testing guidelines. *Mov Disord* 2007;22(14):2018–2030; quiz 2140.
- Campbell MC, Tishkoff SA. African genetic diversity: implications for human demographic history, modern human origins, and complex disease mapping. *Annu Rev Genomics Hum Genet* 2008;9:403–433.
- Hamza W, Ali Pacha L, Hamadouche T, Muller J, Drouot N, Ferrat F, et al. Molecular and clinical study of a cohort of 110 Algerian patients with autosomal recessive ataxia. *BMC Med Genet* 2015;16:36.
- Smith DC, Bryer A, Watson LM, Greenberg LJ. Inherited polyglutamine spinocerebellar ataxias in South Africa. *S Afr Med J* 2012;102(8):683–686.

23. Atadzhanov M, Smith DC, Mwaba MH, Siddiqi OK, Bryer A, Greenberg LJ. Clinical and genetic analysis of spinocerebellar ataxia type 7 (SCA7) in Zambian families. *Cerebellum Ataxias* 2017; 4(29):17.
24. Cissé CAK, Cissé L, Ba HO, Samassékou O, Simaga A, Taméga A, et al. Friedreich ataxia in a family from Mali, West Africa/Friedreich ataxia in a Malian family. *Clin Case Reports* 2021;9(5):e04065.
25. Dupré N, Bouchard JP, Brais B, Rouleau GA. Hereditary ataxia, spastic paraparesis and neuropathy in the French-Canadian population. *Can J Neurol Sci* 2006;33(2):149–157.
26. Synofzik M, Smets K, Mallaret M, Di Bella D, Gallenmüller C, Baets J, et al. SYNE1 ataxia is a common recessive ataxia with major non-cerebellar features: a large multi-centre study. *Brain* 2016;139(Pt 5):1378–1393.
27. Gomez CM. ARSACS goes global. *Neurology* 2004;62(1):10–11.
28. Mhanni AA, Hartley JN, Harward E, Spriggs E, Booth F. Ataxia with oculomotor apraxia type 2 in the Canadian aboriginal population. *Clin Genet* 2016;89(4):515–516.
29. Pellerin D, Danzi MC, Wilke C, Renaud M, Fazal S, Dicaire MJ, et al. Deep intronic FGF14 GAA repeat expansion in late-onset cerebellar ataxia. *N Engl J Med* 2023;388:128–141.
30. Ignjatijevic A, Boorsma F, Wierenga E, Vansenne F, Verschuuren-Bemelmans CC, de Vries J, et al. High prevalence of the intronic GAA-repeat expansion in Dutch patients with late-onset ataxia. *Neurol Genet* 2025;11(2):e200244.
31. 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):1092–1103. <https://doi.org/10.1002/ana.27060>
32. 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* 2024;467:123309.
33. Livanos I, Votsi C, Michailidou K, Pellerin D, Brais B, Zuchner S, et al. The GAA repeat expansion is a major cause of ataxia in the Cypriot population. *Brain Commun* 2025;7(1):fcae479.
34. Cadieux-Dion M, Turcotte-Gauthier M, Noreau A, Martin C, Meloche C, Gravel M, et al. Expanding the clinical phenotype associated with ELOVL4 mutation: study of a large French-Canadian family with autosomal dominant spinocerebellar ataxia and erythrodermatodermia. *JAMA Neurol* 2014;71(4):470–475.
35. Davey KM, Parboosingh JS, McLeod DR, Chan A, Casey R, Ferreira P, et al. Mutation of DNAJC19, a human homologue of yeast inner mitochondrial membrane co-chaperones, causes DCMA syndrome, a novel autosomal recessive Barth syndrome-like condition. *J Med Genet* 2006;43(5):385–393.
36. Bomar JM, Benke PJ, Slatery EL, Puttagunta R, Taylor LP, Seong E, et al. Mutations in a novel gene encoding a CRAL-TRIO domain cause human Cayman ataxia and ataxia/dystonia in the jittery mouse. *Nat Genet* 2003;35(3):264–269.
37. Velázquez-Pérez L, Medrano-Montero J, Rodríguez-Labrada R, Canales-Ochoa N, Campins Ali J, Carrillo Rodes FJ, et al. Hereditary ataxias in Cuba: a nationwide epidemiological and clinical study in 1001 patients. *Cerebellum* 2020;19(2):252–264.
38. Teive HAG, Moro A, Arruda WO, Raskin S, Teive GMG, Dallabrida N, et al. Itajaí, Santa Catarina-Azorean ancestry and spinocerebellar ataxia type 3. *Arq Neuropsiquiatr* 2016;74(10):858–860.
39. Choubunt L, Witoonpanich P, Hanchaiphiboolkul S, Bhidayasiri R, Jitkrisadakul O, Pongpakdee S, et al. Analysis of SCA8, SCA10, SCA12, SCA17 and SCA19 in patients with unknown spinocerebellar ataxia: a Thai multicentre study. *BMC Neurol* 2015; 15:166.
40. Yabe I, Matsushima M, Yoshida K, Ishikawa K, Shirai S, Takahashi I, et al. Rare frequency of downbeat positioning nystagmus in spinocerebellar ataxia type 31. *J Neurol Sci* 2015;350(1–2): 90–92.
41. Sharma P, Sonakar AK, Tyagi N, Suroliya V, Kumar M, Kutum R, et al. Genetics of ataxias in Indian population: a collative insight from a common genetic screening tool. *Adv Genet* 2022;3(2): 2100078.
42. Sharony R, Martins S, Costa IPD, Zaltzman R, Amorim A, Sequeiros J, et al. Yemenite-Jewish families with Machado-Joseph disease (MJD/SCA3) share a recent common ancestor. *Eur J Hum Genet* 2019;27(11):1731–1737.
43. Mahdih N, Heidari M, Rezaei Z, Tavasoli AR, Hosseinpour S, Rasulnejad M, et al. The genetic basis of early-onset hereditary ataxia in Iran: results of a national registry of a heterogeneous population. *Hum Genomics* 2024;18(1):35.
44. Anikster Y, Kleta R, Shaag A, Gahl WA, Elpeleg O. Type III 3-methylglutaconic aciduria (optic atrophy plus syndrome, or Costeff optic atrophy syndrome): identification of the OPA3 gene and its founder mutation in Iraqi Jews. *Am J Hum Genet* 2001;69(6): 1218–1224.
45. Seidahmed MZ, Hamad MH, AlBakheet A, Elmalik SA, Aldrees A, Al-Sufayan J, et al. Ancient founder mutation in RUBCN: a second unrelated family confirms Salih ataxia (SCAR15). *BMC Neurol* 2020;20(1):207.
46. Scott P, Al Kindi A, Al Fahdi A, Al Yarubi N, Bruwer Z, Al Adawi S, et al. Spinocerebellar ataxia with axonal neuropathy type 1 revisited. *J Clin Neurosci* 2019;67:139–144.
47. Boycott KM, MacDonald SK, Parboosingh JS. VLDLR Cerebellar Hypoplasia. *GeneReviews*®. Seattle, WA: University of Washington, Seattle; 1993.
48. Beecroft SJ, Cortese A, Sullivan R, Yau WY, Dyer Z, Wu TY, et al. A Māori specific RFC1 pathogenic repeat configuration in CANVAS, likely due to a founder allele. *Brain* 2020;143(9):2673–2680.
49. Chen Z, Gustavsson EK, Macpherson H, Anderson C, Clarkson C, Rocca C, et al. Adaptive long-read sequencing reveals GGC repeat expansion in ZFH3 associated with spinocerebellar ataxia type 4. *Mov Disord* 2024;39(3):486–497.
50. Synofzik M, Schüle R, Schulze M, Gburek-Augustat J, Schweizer R, Schirmacher A, et al. Phenotype and frequency of STUB1 mutations: next-generation screenings in Caucasian ataxia and spastic paraplegia cohorts. *Orphanet J Rare Dis* 2014;9:57.
51. Coutinho P, Ruano L, Loureiro JL, Cruz VT, Barros J, Tuna A, et al. Hereditary ataxia and spastic paraplegia in Portugal: a population-based prevalence study. *JAMA Neurol* 2013;70(6): 746–755.
52. Polet SS, Anderson DG, Koens LH, van Egmond ME, Drost G, Brusse E, et al. A detailed description of the phenotypic spectrum of North Sea progressive myoclonus epilepsy in a large cohort of seventeen patients. *Parkinsonism Relat Disord* 2020;72:44–48.
53. Lipponen J, Helisalmi S, Raivo J, Siitonen A, Doi H, Rusanen H, et al. Molecular epidemiology of hereditary ataxia in Finland. *BMC Neurol* 2021;21(1):382.
54. Chen Z, Tucci A, Cipriani V, Gustavsson EK, Ibañez K, Reynolds RH, et al. Functional genomics provide key insights to improve the diagnostic yield of hereditary ataxia. *Brain* 2023; 146(7):2869–2884.
55. Hengel H, Pellerin D, Wilke C, Fleszar Z, Brais B, Haack T, et al. As frequent as polyglutamine spinocerebellar ataxias: SCA27B in a large German autosomal dominant ataxia cohort. *Mov Disord* 2023;38(8):1557–1558.
56. Rafehi H, Fearnley LG, Read J, Snell P, Davies KC, Scott L, et al. A prospective trial comparing programmable targeted long-read sequencing and short-read genome sequencing for genetic diagnosis of cerebellar ataxia. *Genome Res* 2025;35(4):769–785. <https://doi.org/10.1101/gr.279634.124>
57. Cortese A, Reilly MM, Houlden H. RFC1 CANVAS/Spectrum disorder. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, eds. *GeneReviews*®. Seattle, WA: University of Washington, Seattle; 2020.
58. Paulus-Andres JA, Burnett MS. Three adult-onset autosomal recessive ataxias: what adult neurologists need to know. *Neurol Clin Pract* 2021;11(3):256–262.
59. Durr A. Autosomal dominant cerebellar ataxias: polyglutamine expansions and beyond. *Lancet Neurol* 2010;9(9):885–894.
60. Takiyama Y. Autosomal recessive spastic ataxia of Charlevoix-Saguenay. *Neuropathology* 2006;26(4):368–375.

61. Sonakar AK, Shamim U, Srivastava MP, Faruq M, Srivastava AK. SCA2 in the Indian population: unified haplotype and variable phenotypic patterns in a large case series. *Parkinsonism Relat Disord* 2021;89:139–145.
62. Teive HAG, Moro A, Moscovich M, Arruda WO, Munhoz RP, Raskin S, et al. Spinocerebellar ataxia type 10 in the south of Brazil: the Amerindian-Belgian connection. *Arq Neuropsiquiatr* 2015;73(8):725–727.
63. Gan SR, Figueroa KP, Xu HL, Perlman S, Wilmot G, Gomez CM, et al. The impact of ethnicity on the clinical presentations of spinocerebellar ataxia type 3. *Parkinsonism Relat Disord* 2020;72:37–43.
64. Subramony SH, Hernandez D, Adam A, Smith-Jefferson S, Hussey J, Gwinn-Hardy K, et al. Ethnic differences in the expression of neurodegenerative disease: Machado-Joseph disease in Africans and Caucasians. *Mov Disord* 2002;17(5):1068–1071.
65. Renaud M, Tranchant C, Koenig M, Anheim M. Autosomal recessive cerebellar ataxias with elevated alpha-fetoprotein: uncommon diseases, common biomarker. *Mov Disord* 2020;35(12):2139–2149.
66. Hentati F, El-Euch G, Bouhlal Y, Amouri R. Ataxia with vitamin E deficiency and abetalipoproteinemia. *Handb Clin Neurol* 2012;103:295–305.
67. Soliani L, Alcalá San Martín A, Balsells S, Hernando-Davalillo C, Ortigoza-Escobar JD. Chromosome microarray analysis for the investigation of deletions in pediatric movement disorders: a systematic review of the literature. *Mov Disord Clin Pract* 2023;10(4):547–557.
68. Coarelli G, Wirth T, Tranchant C, Koenig M, Durr A, Anheim M. The inherited cerebellar ataxias: an update. *J Neurol* 2023;270(1):208–222.
69. Wallace SE, Bird TD. Molecular genetic testing for hereditary ataxia: what every neurologist should know. *Neurol Clin Pract* 2018;8(1):27–32.
70. Ibañez K, Jadhav B, Zanovello M, Gagliardi D, Clarkson C, Facchini S, et al. Increased frequency of repeat expansion mutations across different populations. *Nat Med* 2024;30(11):3357–3368.
71. Global Parkinson's Genetics Program. GP2: the global Parkinson's genetics program. *Mov Disord* 2021;36(4):842–851.
72. Lim SY, Tan AH, Ahmad-Annuar A, Okubadejo NU, Lohmann K, Morris HR, et al. Uncovering the genetic basis of Parkinson's disease globally: from discoveries to the clinic. *Lancet Neurol* 2024;23(12):1267–1280. [https://doi.org/10.1016/S1474-4422\(24\)00378-8](https://doi.org/10.1016/S1474-4422(24)00378-8)

Supporting Data

Additional Supporting Information may be found in the online version of this article at the publisher's web-site.