ALGORITHM TO PREDICT DIAGNOSTIC SUCCESS RATE OF WHOLE-EXOME SEQUENCING IN INDIVIDUALS WITH DYSTONIA

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EUROPEAN REFERENCE NETWORKS
FOR RARE, LOW PREVALENCE AND COMPLEX DISEASES

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ERN-RND is a European Reference Network established and approved by the European Union. ERN-RND is a healthcare infrastructure which focuses on rare neurological diseases (RND). The three main pillars of ERN-RND are (i) network of experts and expertise centres, (ii) generation, pooling and dissemination of RND knowledge, and (iii) implementation of e-health to allow the expertise to travel instead of patients and families.

ERN-RND unites 64 of Europe's leading expert centres as well as 4 affiliated partners in 24 member states and includes highly active patient organizations. Centres are located in Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Poland, Slovenia, Spain and Sweden.

The following disease groups are covered by ERN-RND:

- Ataxias and Hereditary Spastic Paraplegias
- Atypical Parkinsonism and genetic Parkinson's disease
- Dystonia, Paroxysmal Disorders and Neurodegeneration with Brain Ion Accumulation
- Frontotemporal Dementia
- Huntington's Disease and other Choreas
- Leukodystrophies

Specific information about the network, the expert centres and the diseases covered can be found on the network website www.ern-rnd.eu.

Recommendation for clinical use:
The European Reference Network for Rare Neurological Diseases endorsed this algorithm to predict diagnostic success rate of whole-exome sequencing in individuals with dystonia. The Reference Network recommends the use of the guidelines.

DISCLAIMER

Clinical practice guidelines, practice advisories, systematic reviews and other guidance published, endorsed or affirmed by ERN-RND are assessments of current scientific and clinical information provided as an educational service.

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METHODS

The endorsement process has been performed by the Disease group for Dystonia, paroxysmal disorders and NBIA of ERN-RND.

Consent on endorsement was given by the entire Disease Group on: 20.09.2023

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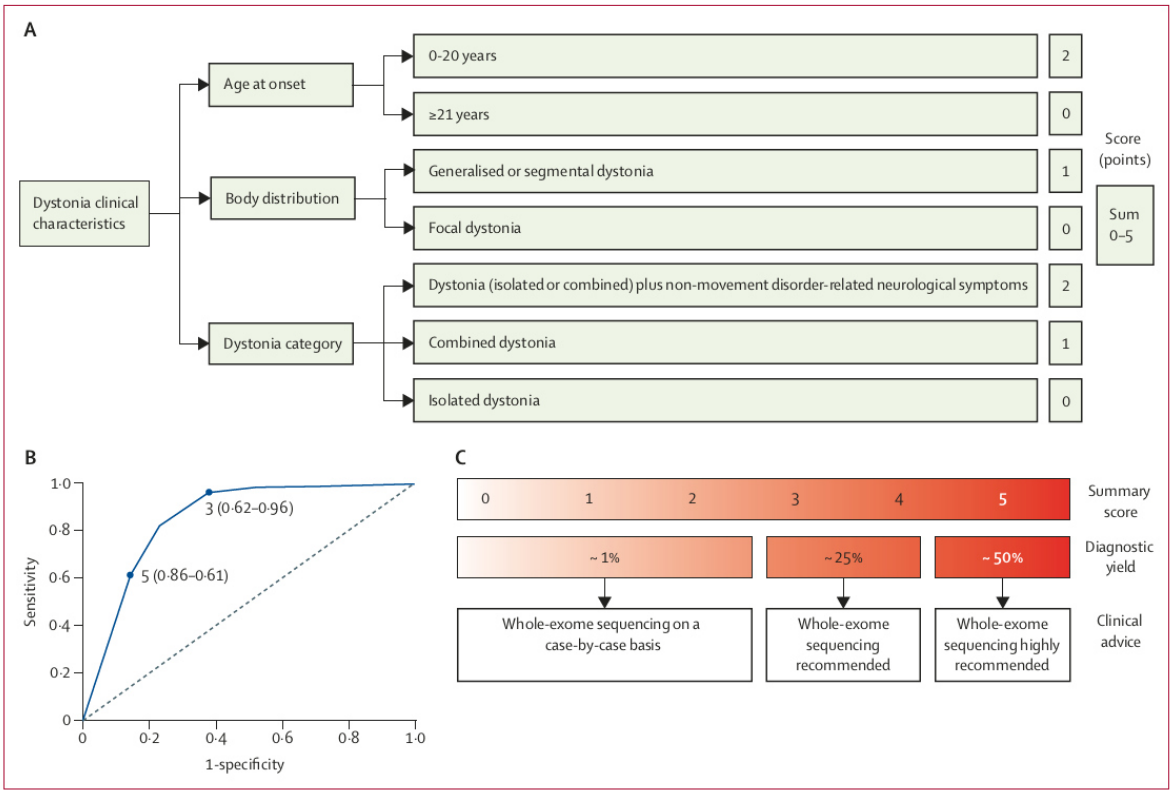

Figure 3: **Proposed algorithm to predict diagnostic success rate of whole-exome sequencing in individuals with dystonia**
(A) Schematic overview of the proposed scoring system. We selected as scoring parameters clinical predictors of a diagnostic whole-exome sequencing finding, as determined by multiple logistic regression analysis (appendix pp 52–53). The assigned scoring points add up to yield a summary score, ranging from 0 to 5. (B) Receiver operating characteristic curve plot for the proposed score with indication of the specificities and sensitivities at the thresholds postulated in part C. A summary score threshold of 3 points implies a small number (4%) of individuals are erroneously excluded from whole-exome sequencing and an acceptable number (38%) are erroneously included. (C) Summary scores (0–5), proportions of the subgroups with a diagnostic variant (diagnostic yield), and proposed recommendations for the clinical application of whole-exome sequencing in individuals with dystonia.

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for rare or low prevalence complex diseases

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