

# Development of the ERN-RND Clinical Practice Guideline for *NKX2-1*-related disorders



DG/WG  
Chorea & HD

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## Introduction

- Clinical practice guideline for *NKX2-1*-related disorders (*NKX2-1*-RD), also known as Benign Hereditary Chorea or Brain–Lung–Thyroid Syndrome
- **Scope:** neurology, endocrinology, and respiratory care across the life course
- Developed within ERN-RND, in collaboration with ENDO-ERN and ERN-LUNG
- **Objective:** standardize diagnosis, treatment, and follow-up; provide algorithms, minimum datasets, and patient-centered tools (care pathway, checklists, leaflets)

## Results

Evidence base consolidated from five systematic reviews and two ERN surveys.

Draft recommendations cover:

- Diagnostic work-up and differential diagnosis.
- Management of chorea and other movement disorders.
- Thyroid dysfunction: screening, diagnosis, treatment, follow-up.
- Respiratory involvement: screening, prevention, and care.
- Long-term monitoring, MRI, cancer risk, and genetic testing.

Draft algorithms and minimum monitoring sets prepared.

Patient-facing materials and layout design in progress.

## Outlook

- Remaining work: finalize four pending PICO questions (signs/symptoms, MRI, cancer risk, genetics).
- Complete GRADE evidence profiles, recommendation wording, and external consensus review.
- Deliverables: full CPG text, clinician summary, patient leaflet, implementation KPIs.
- Funding: internal ERN-RND support.
- Expected completion: September 2026; update cycle planned every 4 years.

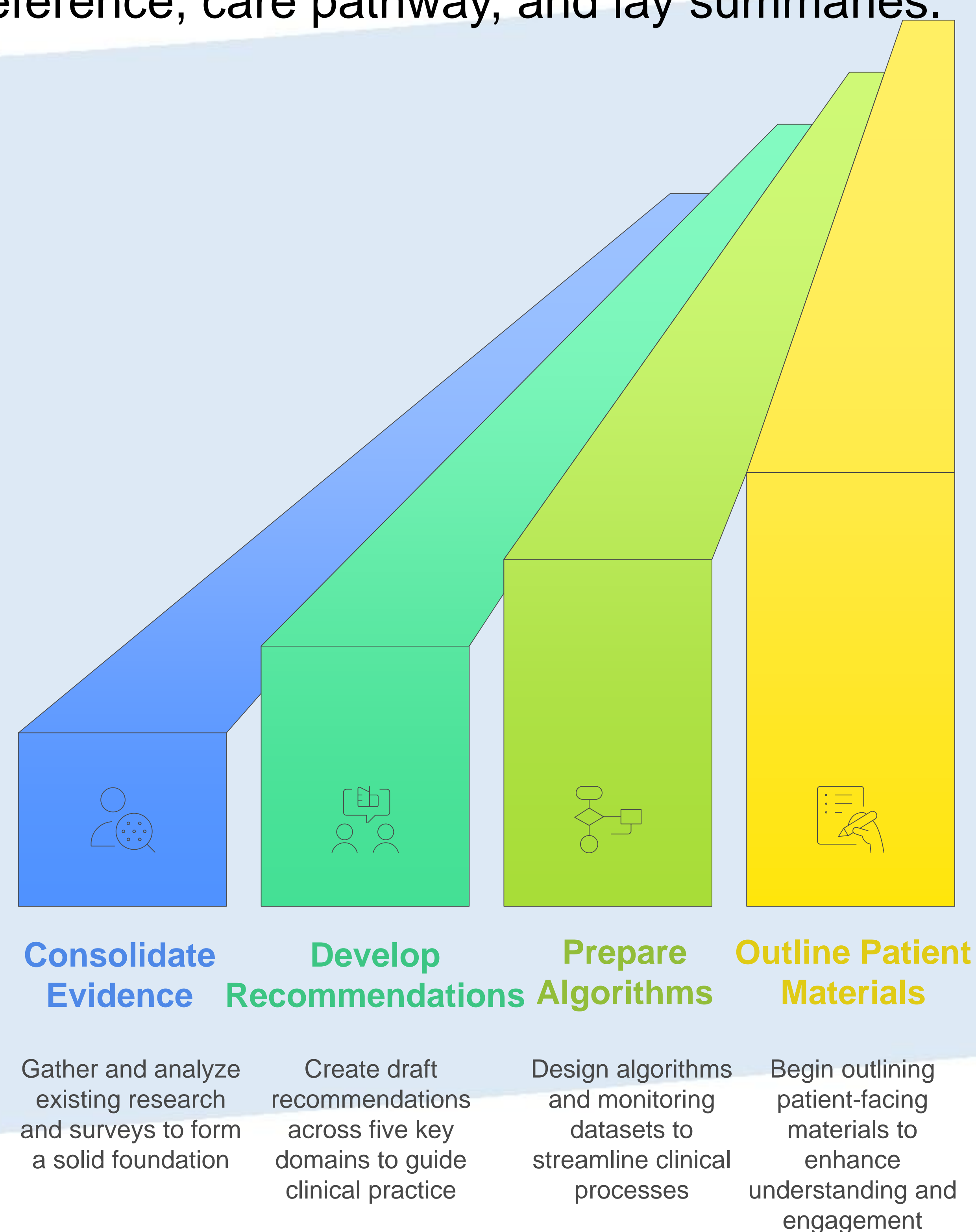
## Work Plan

**Governance:** multidisciplinary panel (neurology, pulmonology, endocrinology, genetics) + two patient representatives; conflicts of interest collected a priori.

**Methods:** systematic reviews and ERN surveys; PICO questions; GRADE evidence grading; AGREE II quality assurance.

**Equity:** attention to pediatric-specific issues, rare-disease context, and variability across EU healthcare systems.

**Dissemination tools:** professional quick-reference, care pathway, and lay summaries.



## Publications

1. Michel K et al. Respiratory and other organ manifestations in *NKX2-1*-related disorders: a systematic review. *Front Med (Lausanne)*. 2025 May 6;12:1507513.
2. Carmona-Hidalgo B et al. Systematic review of thyroid function in *NKX2-1*-related disorders: Treatment and follow-up. *PLoS One*. 2024 Oct 28;19(10):e0309064.
3. Carmona-Hidalgo B et al. Systematic review of thyroid function in *NKX2-1*-related disorders: Screening and diagnosis. *PLoS One*. 2024 Jul 11;19(7):e0303880.
4. Nou-Fontanet L et al. Insights from European Reference Network for rare neurological disorders study surveys on diagnosis, treatment, and management of *NKX2-1*-related disorders. *Eur J Paediatr Neurol*. 2024 Jul;51:110-117.
5. Nou-Fontanet L et al. Systematic review of drug therapy for chorea in *NKX2-1*-related disorders: Efficacy and safety evidence from case studies and series. *Eur J Neurol*. 2023 Dec;30(12):3928-3948.
6. Martín-Gómez C et al. Exploring the values, preferences, and information needs of patients with *NKX2-1*-related disorders: A qualitative study protocol. *PLoS One*. 2023 Feb 9;18(2):e0281573.

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