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Recommendations for optimal interdisciplinary management and healthcare settings for patients with rare neurological diseases

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Abstract

Background In 2017, the German Academy for Rare Neurological Diseases (Deutsche Akademie für Seltene Neurologische Erkrankungen; DASNE) was founded to pave the way for an optimized personalized management of patients with rare neurological diseases (RND) in all age groups. Since then a dynamic national network for rare neurological disorders has been established comprising renowned experts in neurology, pediatric neurology, (neuro-) genetics and neuroradiology. DASNE has successfully implemented case presentations and multidisciplinary discussions both at yearly symposia and monthly virtual case conferences, as well as further educational activities covering a broad spectrum of interdisciplinary expertise associated with RND. Here, we present recommendation statements for optimized personalized management of patients with RND, which have been developed and reviewed in a structured Delphi process by a group of experts.

Methods An interdisciplinary group of 37 RND experts comprising DASNE experts, patient representatives, as well as healthcare professionals and managers was involved in the Delphi process. First, an online collection was performed of topics considered relevant for optimal patient care by the expert group. Second, a two-step Delphi process was carried out to rank the importance of the selected topics. Small interdisciplinary working groups then drafted recommendations. In two consensus meetings and one online review round these recommendations were finally consented.

Results 38 statements were consented and grouped into 11 topics: health care structure, core neurological expertise and core mission, interdisciplinary team composition, diagnostics, continuous care and therapy development, case

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conferences, exchange / cooperation between Centers for Rare Diseases and other healthcare partners, patient advocacy group, databases, translation and health policy.

Conclusions This German interdisciplinary Delphi expert panel developed consented recommendations for optimal care of patients with RND in a structured Delphi process. These represent a basis for further developments and adjustments in the health care system to improve care for patients with RND and their families.

Keywords Rare neurological diseases, Optimal care, Interdisciplinary management, Healthcare settings

Introduction

In Europe, a disease is considered “rare” when affecting <1 person in 2000. Although rare diseases (RDs) have—per definition—a low prevalence, the total number of patients with a RD is high, affecting about 3.5–5.9% of the population equating to 263–446 million people affected globally at any point in time [1]. The majority of RD have neurological manifestations including the central and peripheral nervous system and muscles [2]. In Germany alone, we estimate the number of patients with rare neurological diseases (RND) to amount to approximately 150,000 cases with 7000–8000 new cases manifesting each year. Care of patients with RND concerns a considerable fraction of the healthcare service provided by a national healthcare system [3]. Thus, suboptimal management of RND patients causes major healthcare problems [4].

The German Academy for Rare Neurological Diseases (Deutsche Akademie für Seltene Neurologische Erkrankungen; DASNE) is a German initiative aiming at paving the way for an optimized personalized management of patients with RND in all age groups. Instigated by the Centers for Rare Diseases in Lübeck and Tübingen, a dynamic national network for RND has been constituted comprising renowned experts in the fields of neurology, pediatric neurology, pediatrics, (neuro-)genetics and neuroradiology. DASNE has successfully implemented case presentations and multidisciplinary discussions both at yearly symposia and monthly virtual case conferences, as well as further educational activities covering a broad spectrum of interdisciplinary expertise associated with RND. [5]. The DASNE is associated with the German Reference Network (Deutsches Referenznetzwerk; DRN) for Rare Neurological Diseases, founded in 2021.

Taking into account both the magnitude of the healthcare challenge to provide optimal care for RND patients as well as the ambition of the DASNE and the German Reference Network for RND, precisely determining what optimal interdisciplinary management and healthcare settings for patients with rare neurological diseases mean is warranted. In the present study, following a structured Delphi process, we developed and reviewed 38 recommendation statements by an interdisciplinary expert

group composed of patient representatives, DASNE experts, as well as other healthcare professionals and managers. The development of the recommendations has been undertaken by thematic groups of experts (e.g. continuous care and therapy development, health policy) followed by a consensus meeting with the whole group of experts. Colleagues with different fields of expertise and backgrounds were involved. The recommendations were finalized in November 2021 and endorsed by the entire interdisciplinary expert group. Some are specific for RND, some are generically applicable also to other rare diseases. Furthermore, the specific areas, for which statements were developed, have a direct connection to care services or cover care related overarching topics such as health policy.

The aim of the recommendation is to refer to care for RND patients in general. Hence, specific recommendations for particular diseases or disease groups such as ataxias or leukodystrophies, are not covered in these statement recommendations.

The recommendations are conceived as action statements for the management and provision of clinical care, they are not merely political or contemplative. They refer to the structure of the care facility, ensuring neurological core expertise and core mission, composition of the interdisciplinary team, diagnostics, case conferences, continuous care and therapy development, translation, patient advocate groups, health policy, exchange/cooperation between rare disease centers and other partners in the health sector, and to databases. Research of RND is not addressed specifically. However, for RD the boundaries of what relates to care and what to research are often hard to define.

Results

37 experts, chosen for their involvement in DASNE, expertise in RND and representing the interdisciplinary team involved in RND care, collaborated to develop this recommendation. Involved expertise included neurology, pediatric neurology, human genetics, neuroradiology, neurorehabilitation, social counseling and patient advocacy groups as well as two directors of German rare disease centers. A Delphi-like consensus methodology was adopted. A systematic PubMed search yielded no results

as to similar studies specifically addressing the topic of this study.

Topics of relevance for optimal care of RND patients

An online collection of topics considered relevant for optimal patient care of RND patients was performed by the expert group. Next, a two-step Delphi process was performed to rank the importance of the selected topics. The two Delphi rounds revealed that none of the topics were rated as not important, the lowest median voting received on a Likert scale from 1 (not important) to 6 (most important) was 4. Table 1 shows the main topics as well as those subtopics that reached a median score ≥ 5 and were, thus, included in the further development of the statements. The full ranking results are given as Appendix 1. The selected eleven main topics reflect the full spectrum of topics that influence the quality of care provided to RND patients and include infrastructural, care as well as policy topics.

Consensus recommendations for optimal interdisciplinary management and healthcare settings for patients with RND

Small interdisciplinary working groups comprising three to five experts were formed and tasked to draft recommendations for the eleven main topics taking particularly considering the selected subtopics. In two subsequent consensus meetings and one online review round these recommendations were finally consented. Table 2 shows the main points of the consensus recommendations for optimal interdisciplinary management and healthcare settings for patients with RND.

Discussion

To the best of our knowledge, we have developed the first recommendations for optimal interdisciplinary management and healthcare settings for patients with rare neurological diseases on the basis of an adapted Delphi procedure involving a large interprofessional expert group. The recommendations can be taken as a guidance as to how and in which setting care for patients with RND should be provided. All recommendations were fully consented by our interprofessional expert group, which also included patient representatives. This level of agreement suggests that our recommendations provide important guidance for the development and delivery of high-quality RND care and we strongly recommend their use in realizing and planning the RND care provision.

Our consensus recommendations offer broader generalizability to all rare diseases. As far as we are aware of, no comparable study has been performed as yet for any rare disease. The recommendations highlight that the focus of RND care is on interprofessional and

interdisciplinary, patient-centered and expertise based informed care delivery. Common themes that were mentioned across more than one main topic and which could thus be deemed as the very essence for RND care provision were the following:

- Interdisciplinary and interprofessional care provision
- Continued medical education for RND experts and non-experts
- Importance of neurologic and neurogenetic expertise and expertise based decisions
- Empowered participation and contribution of patients and patient advocacy organizations
- Networking/cooperation between different players in the field of RND
- Digital infrastructure including digital patient records, which are accessible to the entire interdisciplinary and interprofessional team involved in the care of a RND patient as well as use of Orpha codes for coding of RND patients,
- Development of standard operating procedures for all RND related activities
- Adequate funding of care services and structures, and
- Structured and validated public information on RND expertise centers.

This study has several strengths. First, the resulting recommendations owe their credibility to the use of a modified Delphi procedure [6]. The authors have set clear standards for the conducting and reporting of the Delphi study, including the appointment of independent researchers to coordinate the study, the presence of a clear consensus criterion, clear descriptions of how the synthesis of responses in one survey round was used to design the subsequent round, and the review and approval of the final draft by an external board before publication and dissemination.

Second, the Delphi method allowed the involvement of a network of 14 interprofessional experts. These participants had various professional backgrounds and work settings. In the expert group, we also included six patient representatives. Our response rate of more than 80% indicates that the risk of selection bias is low. Third, the high degree of consensus in the expert groups regarding topic selection as well as derived recommendations contributes to the validity of our findings.

We acknowledge the following limitations of our study. For the study we performed we could not find an appropriate literature basis. Secondly, as healthcare for RND patients in Germany is currently changing, our recommendations might need to be updated considering the effects of these changes. Finally, recommendations need

Table 1 Main topics and subtopics with a median ≥ 5 in the second Delphi round

Structure of the care facility
Remuneration/available time
Spatial equipment incl. therapy rooms
Integration into the health care system/establishment of cross-sector care pathways
Ensuring neurological core expertise and core mission
Specialized training
Continued education and training
Promotion of young talent
Expertise for specific rare diseases/disease groups
Composition of the interdisciplinary team
Neurology, Neuropediatrics, Cognitive Neurology, Neurogenetics, Neuropathology
Neuroradiology/Nuclear Medicine
Speech therapy, occupational therapy, physiotherapy
Nursing care
(Neuro)Psychology
Psychosocial/social-medical counseling
Genetic counseling
Diagnostics
Next Generation Sequencing including reimbursement and evaluation
Case conferences
On site case conferences
Continuous care and therapy development
Interdisciplinary planning
Clinical trials
Standardized scales and scores
Quality of life
Translation
Patient advocacy organizations
Health policy
Social discourse on diagnostics and treatment costs
Political lobbying
Gene Therapy
Exchange and cooperation between rare disease centers and other partners in the health care sector
Exchange and cooperation between expertise centers for rare diseases
Cross-sectoral exchange and cooperation
Databases
Collaborative registries of rare disease centers
Registries focused on specific disease

validation in the actual healthcare setting. Whether the use of the recommendations will, in fact, improve care provision is a matter that warrants further study.

As future steps, we recommend the dissemination, and implementation of these recommendations for use

in practice and policy making. We also suggest evaluating the use of these recommendations in clinical practice, and their usefulness to change the healthcare system.

Table 2 Key points of consensus recommendations for optimal interdisciplinary management and healthcare settings for patients with RND

Heading of consensus statements	Key points of the corresponding consensus recommendation
Structure of the care facility (Statements 1–3)	Specialist out-patient clinics Interdisciplinary and interprofessional care, i.e. joint clinics of neurology / pediatrics / neuro-surgery / orthopedics / rehabilitation / occupational therapy and physiotherapy NAMSE and ERN-RND standards should be fulfilled Curriculum for RND including rotations to specialist out-patient clinics
Ensuring neurological core expertise and core mission (Statements 4–6)	Neurologic and neurogenetic expertise in RND Engagement of medical students / residents
Composition of the interdisciplinary team (Statements 7–11)	Interdisciplinary and interprofessional team including medicine (neurology, pediatric neurology, neurogenetics, neuropathology, neuroradiology), health care professions (speech therapy, occupational therapy, physiotherapy, (neuro)psychology), specialist nurses, psychosocial/social medical counseling CME and interprofessional education Patient centered approach with involvement of patients' relatives and representatives, and patient organizations; shared decision making Focus on goal-attainment and empowerment Networking with other de-centralized outpatient care (e.g. general practitioners, outpatient physiotherapy practices) including case conferences Availability of digital infrastructure
Diagnostics (Statements 12–13)	Interdisciplinary and interprofessional internal / regional / national / international case conferences that should be planned and documented according to SOPs Exome sequencing considered genetic analysis of choice; indication should be based on interdisciplinary case conferences with participation of human genetics Neuroradiology with expertise in the field of RND Clear and structured communication of results of diagnostic procedures Diagnostic endeavors targeted to possible therapeutic consequences
Case conferences (Statements 14–16)	Interdisciplinary and interprofessional case conferences according to SOPs SOPs should be harmonized across centers in the DRN for RND in collaboration with the DASNE Minimum requirements: three different specialties, mandatory participation of neurology Structured case presentations, documentation in the local hospital information / management system Format can be on-site or as video conference that should be easy-to-use and follow European data protection standards Remuneration according to number of disciplines involved External experts should receive personal compensation
Continuous care and therapy development (Statements 17–22)	Structured and validated information on centers in the Internet Early consultation of RND experts by practicing neurologists / general practitioners through remunerated participation in (online) case conferences that are credited with CME points Reducing budget restrictions for general practitioners for patients with rare diseases Interdisciplinary and interprofessional care networks for specific RND National registries / cohort studies to create trial-ready cohorts National platforms for communication and standardization of individual healing attempts
Translation (Statements 23–24)	Early diagnosis including newborn screening prerequisite for the development of targeted treatment Identification of biochemical biomarkers and neuroimaging parameters Development of recommendations for clinical description and clinically meaningful and appropriate outcome parameters
Patient advocacy organizations (Statements 25–27)	Shared informed decisions of treating physicians, affected patients and their families or carers Continuous care by experienced doctors with regular specialized consultations Emergency treatment and inpatient admissions in specialized centers
Health policy (Statements 28–30)	Expertise based decisions; communication of expertise to political and administrative decision makers with the involvement of patient organizations Across sector-care including cross-sector conferences and patient files with adequate remuneration for participants Interdisciplinary interprofessional care both for children / adolescents and adults. In adults, centers akin to social pediatric centers should be established, which are open for all chronic complex RND and not only for people with intellectual or multiple disabilities

Table 2 (continued)

Heading of consensus statements	Key points of the corresponding consensus recommendation
Exchange and cooperation between rare disease centers and other partners in the health care sector (Statements 31–36)	<p>Cooperation and mutual exchange between ERNs, the DRN, DASNE and non-ERN hospitals as well as patient organizations, e.g. with respect to patient registries</p> <p>Raising awareness for DRN-RND/ DASNE to non-specialist centers / private practices through established periodicals, web sites and educational events</p> <p>Development by the DRN-RND/ DASNE of clear and easy-to-use pathways to access centers for RND for physicians</p> <p>Training courses / CME for non-expert treating physicians, e.g. on the initiation of human genetic diagnostics</p>
Databases (Statements 37–38)	<p>Documentation of RND in the hospital information system in outpatient and inpatient settings at all care facilities using Orpha codes</p> <p>Uniform data collection of disease-identifying data (e.g. Orpha codes), health status data and disease progression data across all hospital clinical information systems</p> <p>Uniform deep data collection in the centers for RND for the identification of specific groups of RND to facilitate personalized treatment and research</p>

(CME Continuous medical education, DASNE Deutsche Akademie für Seltene Neurologische Erkrankungen (German Academy for rare neurological diseases), ERN European reference network; DRN Deutsches Referenznetzwerk (German reference network), RND Rare neurological diseases, SOP Standard operating procedure).

Conclusions

Our large interprofessional expert group came to a consensus on recommendations for RND. These recommendations represent an important first step in providing instructions and orientation with a view to the care that should be provided for RND patients. We hope these recommendations will have a catalytic effect to benefit patients and their relatives by changing the provision of care in the German healthcare system, thus contributing to improved quality of life for RND patients and other patients with rare diseases in Germany. Future implementation of these recommendation in care practice depends to a large extent on the systematic integration of specific care pathways and expertise networks such as the ERN-RND in the healthcare system as well as on respective resource allocation.

Methods

Determination of the most important topics

In May 2020, after studying the literature and finding no review or publication addressing the question of optimal interdisciplinary management and healthcare settings for patients with rare neurological diseases (RND), as a first step an interdisciplinary group of 34 experts including patient representatives was contacted and asked to propose topics that are important for optimal care of patients with rare neurological diseases.

Potential panel experts (including patient representatives) were identified through their involvement in DASNE or through the professional networks of the members of the taskforce. In the selection process, we aimed for an interdisciplinary group of RND experts. The

invited panelists were experts in RND research, practice, and policy, with backgrounds in medicine, social counseling, physiotherapy, ergotherapy, speech therapy and policy. Invited panelists also included five patient representatives from German patient advocacy organizations like the German Heredo-Ataxia Society.

In the letter that was used to contact the experts we explained the goal and the process of the study and asked an open question for topics that are important for the care of RND patients. The online questionnaire was answered by 17 experts that formed the expert panel for the ranking of the topics (see below). Subsequently, we structured these replies into main topics and subtopics. This process yielded 11 main topics each containing a number of subtopics.

Delphi round 1 and 2—ranking of topics

In June and July 2020, in the first Delphi round the determined main topics and subtopics were sent to the same expert panel through an online questionnaire. For the ranking of the main topics and subtopics, panelists were asked to rank the perceived importance of both main topics and related subtopics on a 6-point Likert scale (1 = least important to 6 = most important). The panelists' responses were used to calculate the levels of importance. Importance was indicated by a median score, which represents the 50th percentile value of opinions.

In August and September 2020, panelists received the median score of all topics together with the score they had given in the first Delphi round and were requested to re-assess their respective scoring. To maintain conformity between rounds, only those panelists who responded to the online questionnaire in the first Delphi round

(n=14) were asked to respond to the ranked topics in the second Delphi round. Again, panelists could indicate the perceived importance of both main topics and related subtopics on the same 6-point scale. All 14 panelists who responded in the first Delphi round, also responded in Delphi round 2. As we observed no major rating differences, especially with regard to downgrading but rather a ceiling effect, from round 1 to round 2, we decided to terminate the Delphi process after round 2.

Main topics were included in the recommendation development after round 2 if median ratings were ≥ 5 or if a subtopic received a median rating ≥ 5 . If a main topic did not receive a median rating ≥ 5 but a linked subtopic or different subtopics did, the recommendation development focused on the respective subtopic(s).

Formulation of recommendations on most important topics

The prioritized main topics were used to form small interdisciplinary working groups composed of three to five members of the expert group that were tasked to formulate draft recommendations relating to the identified topics. Working groups were formed on the following main topics: Structure of the care facility, ensuring neurological core expertise and core mission, composition of the interdisciplinary team, diagnostics, case conferences, continuous care and therapy development, translation, patient advocacy organizations, health policy, exchange and cooperation between rare disease centers and other partners in the health care sector and databases. We provided an example recommendation to inform the recommendation drafting and discussion in the working groups. To the working groups, we invited the initial larger expert group that we contacted in round 1. 37 experts contributed to the working groups and their respective drafting of recommendations and to the consensus process. All draft recommendations were received by May 2021 (Additional file 1).

Consensus on recommendations

In June and July 2021, we organized a consensus process consisting of three steps. All draft recommendations were presented, thoroughly discussed and adapted in two online consensus meetings, in which the entire expert panel participated.

After the two meetings we shared the current stage recommendations with the panel and accepted further comments for two weeks. The set of recommendations was then circulated and approved by the entire panel.

Appendix 1: Results of the Delphi process used for the ranking of the topics relevant for RND care provision

Main topics	Median vote Delphi round 1	Median vote Delphi round 2
Structure of the care facility	5	5
Ensuring neurological core expertise and core mission	6	6
Composition of the interdisciplinary team	5	5
Diagnostics	4	6
Continuous care and therapy development	4,5	5
Case conferences	4	4
Exchange and cooperation between rare disease centers and other partners in the health care sector	4,5	5
Patient advocacy groups	4	5
Databases	5	4,5
Translation	4,5	5
Health policy	4	4,5
Subtopics	Median vote Delphi round 1	Median vote Delphi round 2
<i>Structure of the care facility</i>		
Requirements planning	4,5	4
Quality criteria/certification	4	4
Remuneration/time	5	5
Spatial equipment incl. therapy rooms	5	5
Therapeutic supplies	4	4
Integration into the health care system/establishment of cross-sector care pathways	5	5
<i>Ensuring neurological core expertise and core mission</i>		
Specialized training	6	6
Continuing education and training	5	5
Promotion of young talent	6	6
Expertise for defined rare diseases/disease groups	6	6
<i>Composition of the interdisciplinary team</i>		
Neurology, Neuropediatrics, Cognitive Neurology, Neurogenetics, Neuropathology	6	6
Neuroradiology/Nuclear Medicine	5	5
Other medical specialties, e.g. cardiology, orthopedics	4	4
Speech therapy, occupational therapy, physiotherapy	5	5
Nursing care	5	5
(Neuro)Psychology	5	5

Subtopics	Median vote Delphi round 1	Median vote Delphi round 2
Psychosocial/social-medical counseling	5	5
Genetic counseling	5	5
Medical assistant	4	4
<i>Diagnostics</i>		
Special functional diagnostics, e.g. physiotherapy	4	4
Next Generation Sequencing (reimbursement, evaluation)	6	6
Prenatal/preimplantation diagnostics	4	4
<i>Continuous care and therapy development</i>		
Interdisciplinary planning	5	5
Clinical trials	5,5	5,5
Standardized scales and scores	5	5
Quality of life	5	5
<i>Case conferences</i>		
On site (structure and remuneration)	5	5
Digital (remote) case conferences (structure and remuneration)	4	4
<i>Exchange/cooperation between ZSEs and other partners in the health care sector</i>		
Exchange and cooperation between expertise centers for rare diseases	5,5	5,5
Between expert centres for rare disease and Psychiatry/Pain medicine	4	4
Between expert centres for rare diseases and medical centres for adults with multiple disabilities (joint consultation hours, remuneration)	4,5	4,5
Cross-sectoral exchange and cooperation	4,5	5
<i>Databases</i>		
Intra-rare disease centers	4	4
Inter-rare disease centers	5	5
Disease registry incl. biobanking, trial-readiness	6	6
Health insurance companies, making data available for research purposes	4	4
<i>Health policy</i>		
Social discourse on diagnostics and treatment costs	5	5
Political lobbying	5	5
Gene Therapy	5	5
International symbol for people with movement disorders (analogous to the sign for the blind) to prevent discrimination and stigmatization	4	4

Supplementary Information

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Additional file 1. Full formulation of recommendations for optimal interdisciplinary management and healthcare settings for patients with rare neurological diseases.

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Author contributions

HG and AM initiated the drafting of the recommendations and organized the meetings. CR supervised the project. HG, CR and AM wrote the manuscript and compiled all comments. HG, CR, TB, AB, KB, NB, EB, JE, KH, GH, IH, FJK, CK, TK, IKM, MK, KL, MM, TM, AN, AO, GR, KR, CS, LS, RS, JBS, JS, ES, GW, and AM participated in the meetings, drafted the recommendations and reviewed the manuscript. All authors approved the final Manuscript.

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Availability of data and materials

The data that support the findings of this study are available in the supplementary material at the end of the manuscript.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

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