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BRIDGING THE GAP: A CONCEPTUAL MODEL FOR TRANSITIONING NF1 PATIENTS FROM PEDIATRIC TO ADULT CARE IN RESOURCE-LIMITED SETTINGS

Abstract

Introduction: Neurofibromatosis type 1 (NF1) is a chronic autosomal dominant disorder requiring lifelong multidisciplinary oversight. International evidence shows that the transition from pediatric to adult care remains insufficiently standardized, despite the high risk of clinically significant complications during adolescence and early adulthood.

Materials and Methods: A systematic search was performed across PubMed, Scopus and Web of Science (2015–2025) using the keywords "Neurofibromatosis type 1 in adults," "transition care" and "clinical pathway NF1". English-language publications focusing on clinical and organizational aspects of transition were included.

Results: International recommendations emphasize early transition planning (starting at 14–16 years), risk-stratified follow-up, multidisciplinary surveillance, and structured transfer processes extending up to age 25. Key clinical risks during transition include tumor progression (e.g., plexiform neurofibromas, MPNST), neurocognitive impairments, vasculopathy, and skeletal deformities.

Discussion: The absence of established NF1 transition pathways in Kazakhstan may contribute to delayed diagnosis of complications and fragmented care. International practices highlight the necessity of coordinated, multidisciplinary management supported by structured planning, patient education, and continuity between pediatric and adult services. Implementation feasibility is influenced by resource constraints and limited specialist availability.

Conclusion: A stratified, structured transitional care model could improve early detection of NF1-related complications and strengthen continuity of care in Kazakhstan. Adoption of standardized transition pathways may enhance patient outcomes and support national rare disease strategies.

Keywords: patient care management, rare diseases, multidisciplinary care team, transitional care, care transition, neurofibromatosis type 1.

Introduction

Neurofibromatosis type 1 (NF1) is a chronic autosomal dominant disorder characterized by progressive multisystem involvement that require lifelong medical oversight [5, 15]. Despite significant global interest in improving outcomes for patients with rare genetic disorders, the transition from pediatric to adult healthcare services remains an underdeveloped and insufficiently standardized stage of care.

International studies emphasize that clinically significant complications are particularly common during the transitional period in patients with Neurofibromatosis Type 1. At this stage of life, there is an increased risk of developing malignant peripheral nerve sheath tumors, progressive skeletal deformities, chronic pain syndromes, pronounced cognitive impairments, and reproductive dysfunctions.

Studies indicate an important gap: practically applicable transition-of-care models specifically tailored to NF1 have not yet been developed [5, 25].

The aim of this review is to systematize the existing evidence on transitional care in NF1, identify key barriers and components of successful models, and evaluate their applicability in the context of healthcare systems with limited resources, including Kazakhstan.

Methodology

The previously reported lack of established transition-of-care models for NF1 served as the rationale for conducting a systematic literature search.

The search was performed across three major international databases – PubMed, Scopus, and Web of Science – for the period from 2015 to 2025. The following keywords and phrases were used: "Neurofibromatosis type 1 in adults," "transition care," and "clinical pathway NF1." Only English-language publications focusing on clinical and organizational aspects of the transition from pediatric to adult care, principles of multidisciplinary management, and risk stratification methods were included [5, 15, 25, 28]. In addition, official clinical protocols and guidelines from leading international organizations were reviewed, including the Children's Tumor Foundation (CTF) [6], EURORDIS [9], NHS England [20], the German NF1 competence network, and the NF Clinic Network (NIH, USA) [22].

This analysis aimed to synthesize international recommendations and evaluate their applicability within the healthcare system of the Republic of Kazakhstan. Based on these findings, an adapted conceptual model of transitional care was developed, incorporating recommended age stages, risk stratification, and the clinical transfer of patients from pediatric to adult services.

Review

The development of an adapted model of transitional care for NF1 in Kazakhstan requires integration of international practices with the specific characteristics of the national healthcare system. Given the rarity of NF1 and the limited experience in adult patient management, a stratified and structured approach to care coordination is essential [5].

In the Republic of Kazakhstan, patients with Neurofibromatosis Type 1 (NF1) are followed in pediatric services until the age of 18, after which responsibility for care shifts to adult healthcare providers [24]. At the same time, international guidelines define a more flexible age range for the transition period – 14 to 25 years – taking into account the clinical course of NF1, the patient's level of psychosocial maturity, and the readiness of the adult care system [20, 25, 28].

In accordance with international guidelines, transition should not occur at a fixed age but rather as a gradual and structured process initiated as early as 14 years. Early engagement of the patient facilitates the development of self-management skills, awareness of disease-specific needs, and responsibility for adhering to treatment recommendations [20, 25, 28].

Although 18 years remains the legal threshold for transfer of care, the transition process may extend beyond this age, particularly for individuals with cognitive or behavioral impairments, psychiatric comorbidities, or complex clinical pathways, which are frequent among NF1 patients [25, 28]. Given the elevated risk of severe complications – such as malignant transformation of plexiform neurofibromas, neuro-oncological or vascular disorders, chronic pain, and cognitive deficits – international organizations, including EURORDIS [9], the Children's Tumor Foundation [6], and the NIH Neurofibromatosis Network [22], recommend maintaining elements of pediatric support and multidisciplinary surveillance until the age of 25.

Diagnostic criteria for Neurofibromatosis type 1 (NF1) are consistent for both pediatric and adult patients, although their clinical presentation often varies with age. In 2021, the American College of Medical Genetics and Genomics (ACMG), in collaboration with the NIH and international experts, revised the diagnostic framework [11]. The diagnosis is established when at least two characteristic clinical features are present: multiple café-au-lait macules (≥6, with a diameter of ≥5 mm in children and ≥15 mm in adolescents and adults), two or more neurofibromas of any type or at least one plexiform neurofibroma, axillary or inguinal freckling. Additional hallmarks are optic pathway glioma, two or more Lisch nodules, other iris abnormalities, or typical osseous lesions (e.g., sphenoid wing dysplasia). A confirmed pathogenic NF1 gene variant or a first-degree relative with a definitive diagnosis of NF1 is also considered sufficient for establishing the diagnosis [11].

Thus, transitional care represents a distinct and structured process rather than a simple continuation of pediatric management. A consolidated overview of international transitional care recommendations is provided in Table 1.

Tumor manifestations of NF1 represent a principal and the most serious complication during the transition period, constituting a primary challenge for timely surveillance and effective clinical management. The most common tumor manifestations include plexiform neurofibromas, optic pathway gliomas, pheochromocytomas, gastrointestinal stromal tumors, breast cancer in young women, and hematologic malignancies such as juvenile myelomonocytic leukemia [11, 21].

Table 1 – International Recommendations for NF1 Transitional Care

Source	Year	Key Provisions	Applicability
European Reference Network for Rare Neurological Diseases (ERN-RND) [5].	2022	• Early transition planning (starting at age 14) • Individual transition plan (patient passport, cognitive function assessment, family involvement) • Appointment of a transition coordinator	• Include the transition plan in the outpatient record • Assign a transitional care physician between ages 14–16
NICE (UK), DraftRecommendations [11, 20].	2023	• Annual follow-up for symptomatic adults • Multidisciplinary approach (dermatologist, neurologist, oncologist, etc.) • Written handover of medical records • Involvement of primary care provider	• Protocol for interlevel data transfer • Include family physician in thecare scheme
Austrian NF1 adult surveillance form [26].	2025	• Baseline assessment at the point of transfer • Consideration of neurocognitive and social risks • Tumor prevention measures	• Screening template for transition • Regional protocol development for women's health and cognitive assessment
ConsensusStatement (USA) [6, 28].	2018	• Continuity of care into adulthood • Regular evaluation of cognitive and psychiatric issues • Inclusion of specialists in pain management, orthopedics, and rehabilitation • Importance of adult NF1 centers	• Create a referral roadmap with an expanded care team • Localize specialized centers for rare diseases
Note – compiled by the author based on the source (ERN-RND, NICE (UK), Draft Recommendations, The Austrian NF1 adult surveillance form, Consensus Statement (USA))			

Beyond oncological risks, neurocognitive impairments represent a major source of morbidity. Many patients present with learning difficulties, attention deficit and hyperactivity disorder (ADHD), autism spectrum disorders, executive dysfunction, anxiety, and depression, which substantially affect quality of life and social integration [1, 7, 8, 10, 14, 18, 23].

Additional complications include vasculopathy, Moyamoya disease, skeletal deformities such as pseudarthrosis and sphenoid wing dysplasia, scoliosis, and reduced bone mineral density [2, 4, 12, 16, 19]. Collectively, these findings highlight the necessity of dynamic surveillance involving multidisciplinary teams [27, 29].

The infrastructure of the proposed model incorporates multiple layers designed to strengthen continuity of care. At the national level, the establishment of a Coordination Center is proposed, which will provide methodological leadership, maintain the national registry, and organize multidisciplinary consultations, including telemedicine services. This center would also lead professional training, guideline development, and integration with international networks.

Regional centers, located in multi-profile provincial hospitals, are intended to manage patients with low- to moderate-risk profiles, conduct regular assessments, and collaborate with the national center for complex clinical cases. These centers also serve as transitional hubs, preparing pediatric patients for transfer to adult services, managing digital patient passports, and coordinating support of patients.

A digital transitional care passport is proposed as a central tool to ensure continuity. This electronic document consolidates diagnostic history, imaging, genetic results, care coordinators' notes, and follow-up schedules, and facilitates communication across healthcare levels. Additional components of the model include structured physician training programs, integration of psychosocial services, and partnerships with patient advocacy organizations.

The age-related structure of the transitional period in NF1 involves the sequential implementation of four key stages aimed at ensuring continuity of care and supporting patients in their adaptation to the adult healthcare system.

The first stage – Early Preparation (12–14 years) – includes an initial discussion with the patient and their family, as well as education about the disease and forthcoming changes in healthcare organization.

During the Active Preparation stage (14–17 years), a transition coordinator is appointed, and a systematic assessment of the patient's self-management skills and engagement in their own care is conducted.

The third stage – Transfer (18–19 years) – is characterized by joint visits with pediatric and adult specialists and the handover of the full medical record, which facilitates the establishment of a stable relationship with the adult care provider.

The final stage – Post-Transition Follow-up (20–25 years) – focuses on the patient's adaptation within the adult care system, monitoring of treatment adherence, and timely identification of risk factors associated with NF1.

In addition to age-based staging, the model introduces a three-tiered risk stratification system to guide the intensity of follow-up and level of care required.

Patients classified as Low Risk, characterized by exclusively cutaneous manifestations, can be safely followed at the regional level.

The Moderate Risk group includes patients with stable PNF, cognitive impairment, or hypertension. For these individuals, referral to a specialized regional center is recommended, along with periodic neuroimaging every 1–2 years and multidisciplinary follow-up involving neurologists, dermatologists, oncologists, psychologists, and other specialists [17].

Conclusion

This review emphasizes the importance of structured transitional care in Neurofibromatosis Type 1, highlighting early preparation, risk-based management, and multidisciplinary support as essential elements.

For Kazakhstan, the proposed stratified model offers a practical framework to improve continuity of care.

The model has the potential to enhance early detection of complications, ensure smoother transfer from pediatric to adult services. Implemented within the framework of the national rare disease strategy, it could serve as a pilot initiative to strengthen patient outcomes and quality of life.

Gratitude, conflict of interest

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