UNIVERSITATEA DE MEDICINĂ ȘI FARMACIE
„CAROL DAVILA“ DIN BUCUREȘTI

Str. Dionisie Lupu 37, sector 2, București, 020021, România, www.umfcd.ro, email: rectorat@umfcd.ro

"CAROL DAVILA" UNIVERSITY OF MEDICINE AND PHARMACY, BUCHAREST

DOCTORAL SCHOOL

FIELD: MEDICINE

PhD Thesis

PhD Supervisor

PROFESSOR EMILIA SEVERIN, PHD

PhD Candidate

HALIP m. LUPU MARIA, MD

2025

"Carol Davila" University of Medicine and Pharmacy, Bucharest

37 Dionisie Lupu Street, Sector 2, 020021, Bucharest,

Romania Tax Identification Number: 4192910

IBAN: RO57TREZ70220F330500XXXX, Bank: Treasury, Sector 2

+40.21 318.0719; +40.21 318.0721; +40.21 318.0722

www.umfcd.ro

UNIVERSITATEA DE MEDICINĂ ȘI FARMACIE
„CAROL DAVILA“ DIN BUCUREȘTI

Str. Dionisie Lupu 37, sector 2, București, 020021, România, www.umfcd.ro, email: rectorat@umfcd.ro

"CAROL DAVILA" UNIVERSITY OF MEDICINE AND PHARMACY, BUCHAREST

DOCTORAL SCHOOL

FIELD: MEDICINE

MUSCULAR DYSTROPHY:

BETWEEN SCIENTIFIC PROGRESS AND CLINICAL REALITIES

PhD Supervisor

PROFESSOR EMILIA SEVERIN, PHD

PhD Candidate

HALIP m. LUPU MARIA, MD

2025

TABLE OF CONTENTS

FUNDAMENTAL RESEARCH PROBLEM

Duchenne (DMD) and Becker (BMD) muscular dystrophies are rare genetic neuromuscular disorders characterized by severe motor impairment and multisystem involvement, with a progressive course. The implementation of modern standards of care has led, over the past decades, to a significant increase in life expectancy and an improvement in the quality of life of these patients [1–3].

However, this increased survival has revealed previously underrecognized aspects of the disease, such as neuropsychiatric and cognitive comorbidities, the challenges related to transition to adult care, and the presence of atypical clinical forms. In Romania, the systematic documentation and integration of these aspects into clinical practice are still under development. The lack of functional national registries, difficulties in interspecialty coordination, and the absence of well-defined medical transition pathways represent major challenges that require the development of applicable and sustainable strategies [4].

At the same time, advances in molecular therapies and the growing focus on personalized medicine demand a deeper understanding of the relationship between genetic profile and phenotypic variability. Genotype–phenotype correlations are becoming essential both for anticipating prognosis and for tailoring therapeutic interventions to the individual characteristics of each patient [5,6].

The fundamental research problem lies in the need for an integrated approach that correlates genetic, clinical, and functional data, adapted to the specific context of DMD and BMD patients in Romania, and that supports the development of predictive and sustainable care models.

Research hypothesis

Based on the premise that Duchenne and Becker muscular dystrophies are multisystem disorders with significant phenotypic variability, the research hypothesis is that integrating genetic, clinical, and functional data enables the identification of meaningful genotype–phenotype correlations, with direct implications for diagnosis, prognosis, and therapeutic decision-making. Furthermore, the systematic assessment of neuropsychiatric comorbidities and the medical transition process may support the development of adapted, sustainable models of care aligned with the principles of personalized medicine.

The aim of the studies conducted within this thesis is to analyze scientific progress in the field of muscular dystrophies, to investigate the relationship between genetic profile and the variability of clinical manifestations in patients, and to explore ways of integrating this knowledge into clinical practice in order to improve patients' quality of life.

Research objectives

1. Comprehensive evaluation of the phenotypic profile in patients with DMD and BMD, through the characterization of both motor and non-motor involvement, including associated comorbidities.
2. Analysis of genotype–phenotype correlations, with a focus on the type and location of the genetic variant and the expression of dystrophin isoforms, in relation to clinical severity and the risk of neuropsychiatric comorbidities.
3. Characterization of the spectrum of neuropsychiatric comorbidities by identifying the frequency and typology of affective, behavioral, and neurodevelopmental disorders.
4. Assessment of the actual pathways of medical transition from pediatric to adult care and identification of systemic obstacles influencing this process.
5. Presentation of representative clinical cases illustrating the variability of clinical phenotypes and the complexity of multidisciplinary management, including atypical phenotypes (e.g. DMD in females, early-onset severe forms).
6. Formulation of clinical and organizational intervention proposals, based on the obtained results, to support the development of predictive, integrated, and personalized care models for DMD and BMD in Romania.

Research methodology

The studies included in this research were conducted within the Department of Pediatric Neurology at "Dr. Victor Gomoiu" Clinical Children's Hospital in Bucharest, a tertiary reference center for rare diseases, an academic affiliate, and an accredited DMD Center by the World Duchenne Organization. The center's activity involves the evaluation, diagnosis, and multidisciplinary follow-up of patients with Duchenne and Becker muscular dystrophies.

The research had a composite structure, including both retrospective and prospective observational studies, carried out on distinct patient cohorts selected according to specific objectives: characterization of clinical phenotypes, analysis of genotype–phenotype correlations, evaluation of neuropsychiatric comorbidities, and assessment of medical transition pathways.

Collected data included genetic parameters (variant type and location, affected dystrophin isoforms, diagnostic method), clinical aspects (motor, cardiac, respiratory, orthopedic, endocrine, digestive), functional status, and neuropsychiatric features (assessed using CBCL, SNAP-IV, and ASD screening tools). The degree of autonomy and transition readiness was evaluated using the Transition Readiness Assessment Questionnaire (TRAQ).

The methodology also involved a detailed analysis of three representative clinical cases selected to illustrate the phenotypic variability and the complexity of multidisciplinary care.

Data were centralized in an anonymized database and analyzed statistically using descriptive methods and, where applicable, correlation analyses between genetic profiles and clinical characteristics. All studies were conducted in accordance with ethical standards and informed consent regulations, following current legal requirements.

CHAPTER SUMMARY

Current state of knowledge

The general part of the thesis is structured into three chapters that synthesize current knowledge on Duchenne and Becker muscular dystrophies, with emphasis on genetic foundations, multisystemic manifestations, and therapeutic perspectives.

Chapter 1 presents the genetic and clinical characteristics of DMD and BMD, with a focus on the types of variants identified in the DMD gene, the role of dystrophin in skeletal muscle and other tissues, and the implications of Dp427, Dp140, and Dp71 isoform expression in phenotypic variability. Diagnostic criteria and the natural history of disease progression are also addressed [7,8].

Chapter 2 is dedicated to multisystem involvement and associated comorbidities: cardiac, respiratory, endocrine, orthopedic, and neuropsychiatric, and to how these affect quality of life and prognosis. The chapter concludes with a discussion on the transition from pediatric to adult care, summarizing international recommendations and current challenges in Romanian clinical practice [2,9].

Chapter 3 briefly outlines current directions in therapeutic research, including gene therapy, exon skipping, stop codon read-through, and other innovative treatments under clinical investigation [10–19].

Chapter 4 formulates the working hypothesis and general objectives of the research, as previously presented in earlier sections of the abstract.

The special part of the thesis is structured into five chapters and represents the original contribution of the PhD candidate. It includes four distinct clinical observational studies (chapters 5–8) and one chapter dedicated to the presentation of three representative clinical cases (chapter 9). The studies address major topics that are insufficiently documented in both national and international literature, and are based on data collected in clinical practice and the use of internationally validated tools.

Capitolul 5 – Anxietatea și depresia în DMD și DMB: influența genotipului, a progresiei bolii și a suportului psihosocial în context postpandemic

Capitolul investighează incidența simptomelor de anxietate și depresie în rândul pacienților cu DMD și DMB, analizând posibilele corelații cu stadiul bolii, profilul genetic și

nivelul de suport familial și psihologic. Studiul a inclus pacienți evaluați într-un context postpandemic, utilizând chestionare validate și observații clinice integrate în evaluarea psihologică standard. Rezultatele sugerează o prevalență crescută a simptomelor afective, cu severitate mai mare în rândul pacienților cu afectare motorie avansată, izolare socială accentuată și expresie absentă a izoformelor cerebrale Dp140 și Dp71 [8,20–24]. Discuțiile pun în evidență importanța unui screening sistematic al tulburărilor afective și integrarea suportului psihologic în echipa multidisciplinară. Capitolul se încheie cu propuneri de bune practici privind monitorizarea simptomelor psihiatrice și susținerea psihoemoțională a pacienților și familiilor acestora [20,21,24–27].

Chapter 5 – Anxiety and depression in DMD and BMD: the influence of genotype, disease progression, and psychosocial support in the post-pandemic context

This chapter investigates the incidence of anxiety and depression symptoms among patients with DMD and BMD, analyzing potential correlations with disease stage, genetic profile, and the level of familial and psychological support. The study included patients evaluated in a post-pandemic context, using validated questionnaires and clinical observations integrated into the standard psychological assessment. The results suggest a high prevalence of affective symptoms, with greater severity among patients with advanced motor impairment, marked social isolation, and absent expression of the cerebral isoforms Dp140 and Dp71 [8,20–24]. The discussion highlights the importance of systematic screening for affective disorders and the integration of psychological support within the multidisciplinary team. The chapter concludes with recommendations for best practices in monitoring psychiatric symptoms and providing psycho-emotional support to patients and their families [20,21,24–27].

Chapter 7 – Autism spectrum disorder associated with Duchenne and Becker muscular dystrophies: an observational study and the relevance of cerebral isoform expression

This chapter investigates the association between autism spectrum disorder (ASD) and DMD/BMD, based on the hypothesis that the absence of cerebral dystrophin isoforms plays a pathogenic role. All patients included in the study underwent psychological and psychiatric evaluation, and in cases where features suggestive of ASD were observed, specific screening and diagnostic tools were applied. The results indicated a higher prevalence of autistic traits among patients lacking the Dp140 and Dp71 isoforms, supporting the hypothesis of their involvement in neurodevelopment. The study highlights the importance of careful monitoring

of ASD-related symptoms in DMD and BMD and the need to include genetic profiling in neurodevelopmental assessment algorithms [32,33].

Chapter 8 – Transition from pediatric to adult care in muscular dystrophy: challenges, specific needs, and proposed solutions

This chapter examines the medical transition process in patients with muscular dystrophy, aiming to identify encountered difficulties, the level of transition readiness, and possible solutions applicable to the Romanian context. The study included adolescents and young adults with DMD and BMD, who were assessed in terms of transition through a retrospective analysis of their medical history and by applying the standardized Transition Readiness Assessment Questionnaire (TRAQ) [1,2,26,34]. The results revealed a low level of autonomy and a lack of continuity in care after leaving pediatric services, mainly due to the absence of institutionalized transition pathways. The discussion highlights the need to develop a formal transition model that includes the gradual preparation of both the patient and their family, interinstitutional collaboration, and the empowerment of young individuals in managing their condition. The chapter proposes concrete elements for structuring such a model, tailored to the realities of the Romanian healthcare system.

Chapter 9 – Clinically relevant cases illustrating the studied pathology

This chapter presents three clinical cases selected to illustrate the variability in disease progression and the complexity of care in Duchenne muscular dystrophy. The first case describes a patient with DMD who developed severe respiratory complications and experienced an unfavorable outcome despite supportive interventions, highlighting the challenges of advanced respiratory management [35]. The second case follows a DMD patient with early-onset dilated cardiomyopathy during childhood, emphasizing the importance of early cardiac monitoring and proactive therapeutic intervention [36]. The third case presents a severe DMD phenotype in a female patient, a genetically and histopathologically confirmed ultra-rare case, illustrating the diagnostic and prognostic implications of such an atypical presentation [37,38].

Conclusions

The conducted research highlighted the importance of a multidimensional approach in the evaluation and management of patients with DMD and BMD. The analysis of neuropsychiatric comorbidities revealed a significant prevalence of anxiety and depression

symptoms, correlated with disease severity, social support level, and genetic profile, emphasizing the need to integrate psychological assessment into the standard care protocol. The study on cognitive profiles confirmed the association between intellectual disability and the absence of cerebral dystrophin isoforms Dp140 and Dp71, underlining the importance of early neurocognitive evaluation. Data regarding ASD showed an increased prevalence of autistic traits in genetic forms with impaired cerebral isoform expression, supporting the inclusion of specific screening in routine assessments.

The analysis of the transition from pediatric to adult care revealed major challenges in preparing adolescents and their families for this stage, as well as the lack of functional transition pathways in Romania. The findings support the need to develop a formal, gradual, and personalized transition model.

The clinical case studies illustrated critical aspects of disease progression in DMD, including severe respiratory complications, early-onset cardiomyopathy, and rare phenotypes in female patients, reinforcing the need for proactive monitoring and continuous adaptation of care.

Overall, the research underscores the essential role of correlating genetic, clinical, and psychosocial data in enabling predictive and personalized medicine in Duchenne and Becker muscular dystrophies.

Personal contributions

1. Conducting a systematic analysis of anxiety and depression symptoms in patients with DMD and BMD, in correlation with genetic profile, disease stage, and post-pandemic psychosocial context, identifying specific risk factors and proposing the integration of affective screening into routine assessments.
2. Characterizing the intellectual profile of patients with DMD and BMD and demonstrating the correlation between the absence of cerebral isoforms Dp140/Dp71 and cognitive impairment, supporting the importance of early neurocognitive evaluation.
3. Investigating the frequency of ASD in patients with DMD and BMD and correlating it with cerebral isoform expression.
4. Evaluating transition readiness from pediatric to adult care in patients with DMD and BMD by applying the TRAQ questionnaire and identifying major systemic barriers in the current care model.

5. Proposing concrete directions for the development of a formal transition model in Romania, tailored to the needs of young people with muscular dystrophy.
6. Presenting three representative clinical cases illustrating rare or severe aspects of disease progression: fatal respiratory complications, early-onset dilated cardiomyopathy, and a severe DMD phenotype in a female patient.

Contributing to the documentation of clinical, psychosocial, and organizational realities of patients with DMD and BMD in Romania, providing a foundation for future research, intervention programs, and health policy development in the field of neuromuscular disorders.

Bibliography

1. Lupu M, Marcu M-A, Epure DA, Vladacenco OA, Severin EM, Teleanu RI. Lost in Transition: Challenges in the Journey from Pediatric to Adult Care for a Romanian DMD Patient. Healthcare. 2025;13:830.

2. Lupu M, Ioghen M, Perjoc R-Ștefan, Scarlat A-M, Vladâcenco OA, Roza E, et al. The Importance of Implementing a Transition Strategy for Patients with Muscular Dystrophy: From Child to Adult—Insights from a Tertiary Centre for Rare Neurological Diseases. Children. 2023;10:959.

3. Birnkrant DJ, Bushby K, Bann CM, Apkon SD, Blackwell A, Brumbaugh D, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. Lancet Neurol. 2018;17:251–67.

4. Ministerul Sănătății. Programul național pentru boli rare. 2024.

5. Doorenweerd N. Combining genetics, neuropsychology and neuroimaging to improve understanding of brain involvement in Duchenne muscular dystrophy - a narrative review. Neuromuscular Disorders. 2020;30:437–42.

6. Mercuri E, Bönnemann CG, Muntoni F. Muscular dystrophies. The Lancet. 2019;394:2025–38.

7. Pascual-Morena C, Cavero-Redondo I, Martínez-Vizcaíno V, Sequí-Domínguez I, Fernández-Bravo-Rodrigo J, Jiménez-López E. Dystrophin Genotype and Risk of Neuropsychiatric Disorders in Dystrophinopathies: A Systematic Review and Meta-Analysis. J Neuromuscul Dis. 2023;10:159–72.

8. Naidoo M, Anthony K. Dystrophin Dp71 and the Neuropathophysiology of Duchenne Muscular Dystrophy. Mol Neurobiol. 2020;57:1748–67.

9. Teleanu Raluca Ioana, Epure Diana Ana-Maria, Vladâcenco Oana Aurelia, Lupu Maria. Esențialul în neurologia pediatrică. 1st ed. Bucharest: . Editura Universitară „Carol Davila" Bucureşti a Universităţii de Medicină şi Farmacie „Carol Davila" ; 2022.

10. Duan D. Micro-Dystrophin Gene Therapy Goes Systemic in Duchenne Muscular Dystrophy Patients. Hum Gene Ther. 2018;29:733–6.

11. Hart CC, Lee Y il, Xie J, Gao G, Lin BL, Hammers DW, et al. Potential limitations of microdystrophin gene therapy for Duchenne muscular dystrophy. JCI Insight. 2024;9.

12. Goyenvalle A, Griffith G, Babbs A, Andaloussi S El, Ezzat K, Avril A, et al. Functional correction in mouse models of muscular dystrophy using exon-skipping tricyclo-DNA oligomers. Nat Med. 2015;21:270–5.

13. Leckie J, Zia A, Yokota T. An Updated Analysis of Exon-Skipping Applicability for Duchenne Muscular Dystrophy Using the UMD-DMD Database. Genes (Basel). 2024;15:1489.

14. Anwar S, He M, Lim KRQ, Maruyama R, Yokota T. A Genotype-Phenotype Correlation Study of Exon Skip-Equivalent In-Frame Deletions and Exon Skip-Amenable Out-of-Frame Deletions across the DMD Gene to Simulate the Effects of Exon-Skipping Therapies: A Meta-Analysis. J Pers Med. 2021;11:46.

15. Mercuri E, Osorio AN, Muntoni F, Buccella F, Desguerre I, Kirschner J, et al. Safety and effectiveness of ataluren in patients with nonsense mutation DMD in the STRIDE Registry compared with the CINRG Duchenne Natural History Study (2015–2022): 2022 interim analysis. J Neurol. 2023;270:3896–913.

16. Siemionow M, Cwykiel J, Heydemann A, Garcia-Martinez J, Siemionow K, Szilagyi E. Creation of Dystrophin Expressing Chimeric Cells of Myoblast Origin as a Novel Stem Cell Based Therapy for Duchenne Muscular Dystrophy. Stem Cell Rev Rep. 2018;14:189–99.

17. Dumont NA, Rudnicki MA. Targeting muscle stem cell intrinsic defects to treat Duchenne muscular dystrophy. NPJ Regen Med. 2016;1:16006.

18. Park SE, Jeong J Bin, Oh SJ, Kim SJ, Kim H, Choi A, et al. Wharton's Jelly-Derived Mesenchymal Stem Cells Reduce Fibrosis in a Mouse Model of Duchenne Muscular Dystrophy by Upregulating microRNA 499. Biomedicines. 2021;9:1089.

19. Akat A, Karaöz E. Cell Therapy Strategies on Duchenne Muscular Dystrophy: A Systematic Review of Clinical Applications. Stem Cell Rev Rep. 2024;20:138–58.

20. özer Ü. Psychiatric comorbidities in cases with Duchenne muscular dystrophy: Case series. Dusunen Adam: The Journal of Psychiatry and Neurological Sciences. 2019;

21. Gocheva V, Schmidt S, Orsini A-L, Hafner P, Schaedelin S, Weber P, et al. Psychosocial adjustment and parental stress in Duchenne Muscular Dystrophy. European Journal of Paediatric Neurology. 2019;23:832–41.

22. Colvin MK, Poysky J, Kinnett K, Damiani M, Gibbons M, Hoskin J, et al. Psychosocial Management of the Patient With Duchenne Muscular Dystrophy. Pediatrics. 2018;142:S99–109.

23. Bushby K, Finkel R, Birnkrant DJ, Case LE, Clemens PR, Cripe L, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. Lancet Neurol. 2010;9:77–93.

24. O'Dowd DN, Bostock EL, Smith D, Morse CI, Orme P, Payton CJ. Psychological parameters impact health-related quality of life in mental and physical domains in adults with muscular dystrophy. Neuromuscular Disorders. 2021;31:328–35.

25. Colvin MK, Poysky J, Kinnett K, Damiani M, Gibbons M, Hoskin J, et al. Psychosocial Management of the Patient With Duchenne Muscular Dystrophy [Internet]. Pediatrics. 2018. Available from: http://publications.aap.org/pediatrics/article-pdf/142/Supplement_2/S99/904208/peds_201803331.pdf

26. Birnkrant DJ, Bushby K, Bann CM, Apkon SD, Blackwell A, Colvin MK, et al. Diagnosis and management of Duchenne muscular dystrophy, part 3: primary care, emergency management, psychosocial care, and transitions of care across the lifespan. Lancet Neurol. Lancet Publishing Group; 2018. p. 445–55.

27. Lee HE, Cho J. Social Media Use and Well-Being in People with Physical Disabilities: Influence of SNS and Online Community Uses on Social Support, Depression, and Psychological Disposition. Health Commun. 2019;34:1043–52.

28. Jurj-Tudoran Maria, Lupu Maria, Tudosie Victorița, Teleanu Raluca Ioana, Severin Emilia Maria. Exploring intellectual deficits in Duchenne and Becker muscular dystrophies. Revista de Neurologie şi Psihiatrie a Copilului şi Adolescentului din România. 2024;30:17–27.

29. Koo J, Park S, Sung S-E, Lee J, Kim DS, Lee J, et al. Altered Gene Expression Profiles in Neural Stem Cells Derived from Duchenne Muscular Dystrophy Patients with Intellectual Disability. Exp Neurobiol. 2021;30:263–74.

30. Geuens S, Goemans N, Lemiere J, Doorenweerd N, De Waele L. Duchenne Muscular Dystrophy-Associated Neurobehavioral Difficulties: Insights from Clinical Practice. J Neuromuscul Dis. 2024;11:791–9.

31. Darmahkasih AJ, Rybalsky I, Tian C, Shellenbarger KC, Horn PS, Lambert JT, et al. Neurodevelopmental, behavioral, and emotional symptoms common in Duchenne muscular dystrophy. Muscle Nerve. 2020;61:466–74.

32. Thangarajh M, McDermott MP, Guglieri M, Griggs RC. Association between neurodevelopmental impairments and motor function in Duchenne muscular dystrophy. Ann Clin Transl Neurol. 2023;10:2285–96.

33. Simone M, Margari L, Pompamea F, De Giacomo A, Gabellone A, Marzulli L, et al. Autism Spectrum Disorder and Duchenne Muscular Dystrophy: A Clinical Case on the Potential Role of the Dystrophin in Autism Neurobiology. J Clin Med. 2021;10:4370.

34. Wood DL, Sawicki GS, Miller MD, Smotherman C, Lukens-Bull K, Livingood WC, et al. The Transition Readiness Assessment Questionnaire (TRAQ): Its factor structure, reliability, and validity. Acad Pediatr. 2014;14:415–22.

35. Voicu A-C, Lupu M*, Scarlat AM, Chindriș S, Vasile D, Ioana TR, et al. Respiratory pathology in a patient with muscular dystrophy. Pneumologia. 2022;71:81–8.

36. Lupu M, Mihaela Pintilie I, Ioana Teleanu R, Marin G-G, Aurelia Vla- O, Maria Severin E. Early cardiac dysfunction in Duchenne muscular dystrophy: a case report and literature update. Int J Mol Sci [Internet]. 2025; Available from: https://doi.org/10.3390/xxxxx

37. CRUZEIRO MM, VALE TC, MARRONE CD. Symptomatic female carriers of mutations in the Duchenne muscular dystrophy gene. Arq Neuropsiquiatr. 2020;78:598–9.

38. Quak ZX, Tan SML, Tan KB, Lin W, Chai P, Ng KWP. A manifesting female carrier of Duchenne muscular dystrophy: importance of genetics for the dystrophinopathies. Singapore Med J. 2023;64:81–7.

List of scientific publications

BOOKS – CO-AUTHOR

Essentials of pediatric neurology, Carol Davila University Press, Bucharest, 2022 – edited by Raluca Ioana Teleanu, ISBN: 978-606-011-221-1 (Chapter 1).

FULL-LENGTH ARTICLES PUBLISHED IN ISI-INDEXED, PUBMED-LISTED, OR OTHER BDI/CNCSIS-RECOGNIZED JOURNALS

A. ISI:

1. **Lupu, M.**; Pintilie, I.M.; Teleanu, R.I.; Marin, G.G.; Vladâcenco, O.A.; Severin, E.M. Early Cardiac Dysfunction in Duchenne Muscular Dystrophy: A Case Report and Literature Update. Int. J. Mol. Sci. 2025, 26(4), 1685. https://doi.org/10.3390/ijms26041685, IF 4.9, https://www.mdpi.com/1422-0067/26/4/1685 (capitolul 9, pag. 108-119)
2. **Lupu, M.**; Ioghen, M.; Perjoc, R.Ș.; Scarlat, A.M.; Vladâcenco, O.A.; Roza, E.; Epure, D.A.-M.; Teleanu, R.I.; Severin E.M. The Importance of Implementing a Transition Strategy for Patients with Muscular Dystrophy: From Child to Adult—Insights from a Tertiary Centre for Rare Neurological Diseases. Children 2023, 10, 959. https://doi.org/10.3390/children10060959, IF 2.4, https://www.mdpi.com/2227-9067/10/6/959 (capitolul 8, pag. 84-97)
3. **Lupu, M**, Marcu MA, Epure DA, Vladacenco OA, Severin EM, Teleanu RI. Lost in Transition: Challenges in the Journey from Pediatric to Adult Care for a Romanian DMD Patient. Healthcare. 2025 Apr 5;13(7):830. 10.3390/healthcare13070830, IF 2.9, https://www.mdpi.com/2227-9032/13/7/830 (capitolul 8, pag. 84, 85, 88, 90, 91, 94-97)

B. PUBMED/ BDI:

4. Tudoran, M.; **Lupu, M.***; Tudosie, V.; Lupulescu, A.E.; Perjoc, R.S.; Vladâcenco, O.A.; Roza, E.; Epure, D.A.; Teleanu, R.I.; Severin, E.M. Explorarea deficitelor intelectuale în distrofia musculară Duchenne și Becker. Revista de Neurologie şi Psihiatrie a Copilului şi Adolescentului din România, 2024, 30(3), 15–27. ISSN: 2068-8040, https://snpcar.ro/en/numarul-3-vol-30-2024/ (capitolul 6, pag. 67-75)
5. **Lupu, M.**; Voicu, A.C.; Scarlat, A.M.; Chindriș, S.; Vasile, D.; Teleanu, R.I.;

Severin, M.E. Respiratory pathology in a patient with muscular dystrophy. Pneumologia - Journal of Romanian Society of Pulmonology, Oct 17, 2023, pp. 81–88, https://sciendo.com/article/10.2478/pneum-2023-0025 (capitolul 9, pagina 98-107)

6. Petrov, E.C.; Epure, D.A.; Vladâcenco, O.A.; Vasile, D.D.; **Lupu, M.**; Roza, E.; Teleanu, R.I. LGI1 and CASPR2-related Morvan syndrome - diagnostic challenges in a pediatric case. Romanian Journal of Pediatrics, 2023, 72(2), 86–89. ISSN: 1454-0398. doi:10.37897/RJP.2023.2.5, https://rjp.com.ro/articles/2023.2/RJP_2023_2_Art-05.pdf

---

ABSTRACTS OF PAPERS PRESENTED AT INTERNATIONAL CONFERENCES, PUBLISHED IN ISI-INDEXED JOURNALS

7. Ioghen, M.R.; Epure, D.; Vladâcenco, O.; Roza, E.; Vasile, D.; **Lupu, M.**; Teleanu, R.I. Sturge-Weber syndrome without port-wine stain, a case report. EAN Congress 2022, European Journal of Neurology, 2022, 29(Suppl. 1), 845. ISSN: 1468-1331. IF: 6.089.

OTHER SCIENTIFIC WORKS AND CONTRIBUTIONS

Papers presented and published in the proceedings of national and international scientific events with ISBN and ISSN:

8. **Lupu, M.**; Perjoc, R.S.; Vladâcenco, O.A.; Roza, E.; Ioghen, M.; Epure, D.A.; Teleanu, R.I.; Severin, E.M. The importance of implementing a transition strategy for patients with muscular dystrophy: from child to adult – insights from a tertiary centre for rare neurological diseases. 15th EPNS Congress, 20-24 June 2023, Prague, Czech Republic (poster EPNS23-2292), Abstract Book – p. 610.
9. **Lupu, M.**; Vladâcenco, O.A.; Roza, E.; Epure, D.A.; Vasile, D.; Teleanu, R.I. The fingerprint of traumatic brain injury on d-2-alpha hydroxyglutaric aciduria delayed diagnosis. 14th Congress of the European Pediatric Neurology Society, Glasgow 2022, p. 373, ISBN: 978-3-00-072065-9.
10. Teleanu, R.I.; Vladâcenco, O.A.; **Lupu, M.**; Epure, D.A.; Roza, E. Abordarea multidisciplinară modernă a amiotrofiei spinale la copil – aspect practice. Congresul Internațional de Pediatrie din Republica Moldova, ediția a VIII-a, „Pediatria – Specialitate Multidisciplinară”, 6-8 iunie 2024, Chișinău, Moldova, p. 146, ISBN:

978-9975-58-308-4.

11. Perjoc, R.Ș.; Roza, E.; Vladâcenco, O.A.; **Lupu, M.**; Duchi, L.; Mărgărita, M.; Teleanu, R.I. Epilepsie și dieta ketogenică: un bilanț al beneficiilor și provocărilor. Congresul Internațional de Pediatrie din Republica Moldova, ediția a VIII-a, „Pediatria – Specialitate Multidisciplinară", 6-8 iunie 2024, Chișinău, Moldova, p. 147, ISBN: 978-9975-58-308-4.

Original contributions not included in abstract volumes

12. **Lupu, M**. Tulburările de somn la copil. Cercul de Neurologie și Neurologie Pediatrică UMFCD, 20 martie 2025, București, România.
13. **Lupu, M.**, Vladâcenco, O.A., Teleanu, R.I. Beyond the obvious – progressive involuntary movements. EPNS Ferrara Training Courses, 19 februarie 2025, Ferrara, Italia.
14. Teleanu, R.I.; Roza, E.; Vladâcenco, O.A.; Perjoc, R.; **Lupu, M.**; Marcu, M.A. Centrul de expertiză pentru boli rare în domeniul neurologiei pediatrice: puntea dintre rar și posibil. Spitalul Clinic de Copii Dr. V. Gomoiu / UMFCD, Conferința Națională Ziua Bolilor Rare, 28 februarie 2025, București, România.
15. **Lupu, M**.; Marcu, M.; Vladâcenco, O.; Damaschin, A.; Teleanu, R. Lost in transition: călătoria pacienților cu distrofie musculară de la pediatrie la medicina dedicată adulților. Simpozion, Ediția a XVII-a, 25 februarie 2025, București, România.
16. **Lupu, M**.; Teleanu, R.I. Severe motor neuropathy and craniofacial dysmorphism in a plurimalformative syndrome: initial evaluation in a pediatric neurology clinic. Workshop despre Boli Neuromusculare, 28-29 noiembrie 2024, București, România.
17. Perjoc, R.S.; Roza, E.; Vladâcenco, O.A.; Tudosie, V.; **Lupu, M.**; Marcu, M.; Teleanu, R.I. Implicațiile bolilor rare asupra vieții de familie. Conferința Europlan, 11-13 octombrie 2024, București, România.
18. **Lupu, M.**; Roza, E.; Teleanu, R.I. When the night brings the storm: descifrarea manifestărilor hipnice. Conferința de Somnologie Pediatrică cu participare internațională, 25 mai 2024, București, România.
19. **Lupu, M.**; Teleanu, R.I. Snooze or seize: abordarea pacientului cu manifestări hipnice. Conferința Națională AREPMF, ediția a IX-a, 7-10 martie 2024, Poiana Brașov, România.

20. Vladâcenco, O.A.; Roza, E.; **Lupu, M.**; Perjoc, R.Ș.; Teleanu, R.I. Bolile neurologice inflamatorii – cum stabilim diagnosticul corect? Care sunt provocările terapeutice? Congresul Internațional de Pediatrie din Republica Moldova, ediția a VIII-a, „Pediatria – Specialitate Multidisciplinară", 6-8 iunie 2024, Chișinău, Moldova, p. 148, ISBN: 978-9975-58-308-4.
21. Voicu, A.C.; Andrieș, M.; Bujan, A.B.; **Lupu, M.**; Epure, D.A.; Vasile, D.; Teleanu, R.I. Patologia respiratorie la pacientul cu distrofie musculară. Poster, Al 27-lea Congres Național al Societății Române de Pneumologie, 2022, Sinaia, România.
22. Roza, E.; **Lupu, M.**; Vladâcenco, O.A.; Vasile, D.D.; Epure, D.A.; Neacșu, R.; Teleanu, R.I. Encefalita autoimună: Patologie de graniță în context pandemic. Conferința Națională de Sănătate Mintală a Copilului și Adolescentului, ediția a XVII-a, 2022.
23. Perjoc, R.; **Lupu, M.**; Vladâcenco, O.; Teleanu, R.I. Importanța implementării unei strategii de tranziție a pacientului cu boală cronică neurologică: de la copil la adult. Congresul Asociației Române pentru Educație Pediatrică în Medicina de Familie, București, 24-27 aprilie 2022.
24. Perjoc, R.S.; Roza, E.; Vladâcenco, O.A.; Tudosie, V.; **Lupu, M.**; Marcu, M.; Teleanu, R.I. Implicațiile bolilor rare asupra vieții de familie. Conferința Europlan, 11-13 octombrie 2024, București, România.
25. Teleanu, R.I.; Vladâcenco, O.A.; **Lupu, M.**; Epure, D.A.; Roza, E. Manifestările paroxistice non-epileptice la copil și sugar – o provocare universală. A 46-a Conferință Națională de Neurologie, Psihiatrie și Profesiuni Asociate Copii și Adolescenți din România, 25-28 septembrie 2024, Craiova, România.
26. Roza, E.; Vladâcenco, O.A.; **Lupu, M.**; Perjoc, R.S.; Epure, D.A.; Teleanu, R.I. Deslușind epilepsiile genetice generalizate – tranziționând de la copil la tânăr adult. A 46-a Conferință Națională de Neurologie, Psihiatrie și Profesiuni Asociate Copii și Adolescenți din România, 25-28 septembrie 2024, Craiova, România.
27. Ciuban, F.; Vladâcenco, O.; Epure, D.A.; **Lupu, M.**; Teleanu, R.I. Abordarea distrofiei musculare Duchenne: soluții și sprijin dincolo de spital. A 46-a Conferință Națională de Neurologie, Psihiatrie și Profesiuni Asociate Copii și Adolescenți din România, 25-28 septembrie 2024, Craiova, România.
28. Tudosie, V.; **Lupu, M.**; Vladâcenco, O.; Roza, E.; Teleanu, R.I. Evaluarea comorbidităților neurologice în TSA. A 46-a Conferință Națională de Neurologie,

Psihiatrie și Profesiuni Asociate Copii și Adolescenți din România, 25-28 septembrie 2024, Craiova, România.

29. Perjoc, R.S.; Roza, E.; Epure, D.A.; Vladâcenco, O.A.; **Lupu, M.**; Teleanu, R.I. Spectrul sclerozei tuberoase în populația pediatrică. A 46-a Conferință Națională de Neurologie, Psihiatrie și Profesiuni Asociate Copii și Adolescenți din România, 25-28 septembrie 2024, Craiova, România.
30. Perjoc, R.S.; Epure, D.A.; Vladâcenco, O.A.; **Lupu, M.**; Teleanu, R.I. Hint-uri în diagnosticul polineuropatiilor. A 46-a Conferință Națională de Neurologie, Psihiatrie și Profesiuni Asociate Copii și Adolescenți din România, 25-28 septembrie 2024, Craiova, România.
31. Marcu, M.; **Lupu, M.**; Vladâcenco, O.A.; Tudosie, V.; Perjoc, R.S.; Roza, E.; Epure, D.A.; Teleanu, R.I. Explorând provocările intelectuale în distrofiile musculare Duchenne și Becker. A 46-a Conferință Națională de Neurologie, Psihiatrie și Profesiuni Asociate Copii și Adolescenți din România, 25-28 septembrie 2024, Craiova, România.
32. Pintilie, I.M.; Vladâcenco, O.A.; Tudosie, V.; **Lupu, M.**; Perjoc, R.S.; Roza, E.; Epure, D.A.; Teleanu, R.I. "Levetiracetam-rage": de la tratament la comportament – o serie de cazuri. A 46-a Conferință Națională de Neurologie, Psihiatrie și Profesiuni Asociate Copii și Adolescenți din România, 25-28 septembrie 2024, Craiova, România.
33. Epure, D.A.; Vladâcenco, O.A.; **Lupu, M.**; Marcu, M.; Teleanu, R.I. Managementul amiotrofiei spinale, de la teorie la practică – experiența unui centru terțiar. A 46-a Conferință Națională de Neurologie, Psihiatrie și Profesiuni Asociate Copii și Adolescenți din România, 25-28 septembrie 2024, Craiova, România.
34. **Lupu, M.**; Roza, E.; Teleanu, R.I. When the night brings the storm: descifrarea manifestărilor hipnice. Conferința de Somnologie Pediatrică cu participare internațională, 25 mai 2024, București, România.
35. Teleanu, R.I.; Vladâcenco, O.A.; Epure, D.A.; **Lupu, M.**; Perjoc, R.S.; Roza, E. Când boala rară își găsește o soluție terapeutică – experiența CExBR Neurologie Pediatrică, Spitalul Clinic de Copii Dr. V. Gomoiu. Conferința Ziua Bolilor Rare, 29 februarie – 1 martie 2024, Palatul Parlamentului, București, România.
36. Vladâcenco, O.A.; Roza, E.; Epure, D.A.; **Lupu, M.**; Perjoc, R.S.; Teleanu, R.I. Cum aplicăm conceptul de "one stop shop" în îngrijirea pacientului cu acondroplazie – experiența CExBR Neurologie Pediatrică, Spitalul Clinic de Copii

Dr. Victor Gomoiu. Conferința Ziua Bolilor Rare, 29 februarie – 1 martie 2024, Palatul Parlamentului, București, România.

37. Perjoc, R.S.; Roza, E.; **Lupu, M.**; Vladâcenco, O.A.; Teleanu, R.I. Provocări în managementul neurofibromatozei de tip 1. Simpozionul „Provocări actuale în diagnosticul bolilor rare: puzzle-ul abordării multidisciplinare", ediția a XVI-a, 27 februarie 2024, București, România.
38. Roza, E.; Vladâcenco, O.A.; **Lupu, M.**; Teleanu, R.I. Experiența Centrului de expertiză în boli rare în neurologia pediatrică, Spitalul Clinic de Copii „Dr. Victor Gomoiu". Simpozionul „Provocări actuale în diagnosticul bolilor rare: puzzle-ul abordării multidisciplinare", ediția a XVI-a, 27 februarie 2024, București, România.
39. Roza, E.; Vladâcenco, O.A.; Perjoc, R.S.; **Lupu, M.**; Epure, D.A.; Teleanu, R.I. Capcane de diagnostic în epilepsia sugarului. A XXXI-a Conferință SRIE, 23-25 noiembrie 2023, București, România.
40. Roza, E.; Vladâcenco, O.A.; Perjoc, R.S.; **Lupu, M.**; Epure, D.A.; Teleanu, R.I. Encefalopatii epileptice la copil – de la fenotip la genotip. A XXXI-a Conferință SRIE, 23-25 noiembrie 2023, București, România.
41. **Lupu, M.**; Perjoc, R.S.; Vladâcenco, O.A.; Roza, E.; Teleanu, R.I. Explorarea epilepsiilor asociate malformațiilor cerebrale. A XXXI-a Conferință SRIE, 23-25 noiembrie 2023, București, România.
42. Vladâcenco, O.A.; Roza, E.; Perjoc, R.S.; **Lupu, M.**; Epure, D.A.; Teleanu, R.I. Asociere rară de boli neuroinflamatorii – la ce (nu) ne așteptăm după FIRES. A XXXI-a Conferință SRIE, 23-25 noiembrie 2023, București, România.
43. Oprean, A.; Rotaru, F.; Perjoc, R.S.; **Lupu, M.**; Vladâcenco, O.A.; Roza, E.; Teleanu, R.I. Caz rar de encefalopatie epileptică cu debut precoce. A XXXI-a Conferință SRIE, 23-25 noiembrie 2023, București, România.
44. Rotaru, F.; Oprean, A.; Perjoc, R.S.; **Lupu, M.**; Vladâcenco, O.A.; Roza, E.; Teleanu, R.I. Neurodegenerarea și epilepsia – când rar devine ultra rar. A XXXI-a Conferință SRIE, 23-25 noiembrie 2023, București, România.
45. Teleanu, R.I.; Roza, E.; Vladâcenco, O.A.; Epure, D.; Perjoc, R.S.; **Lupu, M.**; Pâslaru, A. Centrul de expertiză în boli rare neurologice – Spitalul Clinic de Copii Dr. V. Gomoiu București, provocări și oportunități. Conferința Europlan și Întâlnire Intersectorială Privind Bolile Rare, 16-18 noiembrie 2023, Zalău, România.
46. **Lupu, M.** Neurochildren – a European Medical Students' Association Bucharest event. Medical Students' Society, București, august 2022.

47. **Lupu, M.** Pediatric Neurology – Case Presentations. Medical Education Days (ZEM), Medical Students' Society, București, online, martie 2022.
48. **Lupu, M.** What It Means to Be a Pediatric Neurologist, Case Series. Club SavaMed (The Medical Club of "Sfântul Sava" National College), București, decembrie 2022.
49. Epure, D.; **Lupu, M.**; Vladâcenco, O.; Vasile, D.; Teleanu, R.I. Tranziția copilului cu Distrofie Musculară Duchenne către vârsta adultă – perspectiva neurologului pediatru. A 13-a Conferință Națională ASNER, octombrie 2022, București, România.
50. Vasile, D.; **Lupu, M.**; Epure, D.A.; Vladâcenco, O.; Roza, E.; Teleanu, R.I. Early onset Dilatative Cardiomyopathy in a patient with Duchenne Muscular Dystrophy. Poster, Global Scientific Exchange Meeting, 2020, București, România.
51. Epure, D.; Lungu, A.; **Lupu, M.**; Lupescu, I.; Teleanu, R.I.; Gener, I. Afecțiuni renale în bolile neurocutanate – linii moderne de terapie. A II-a Ediție a Conferinței Naționale de Boli Renourinare cu tema „Actualități și Interdisciplinaritate în Boala Cronică de Rinichi la copil", 25-27 octombrie 2018, București, România.
52. Epure, D.; Roza, E.; **Lupu, M.**; Teleanu, R.I. Sindromul Morvan – provocare de diagnostic la copil. Conferința Imunopedia, 21-24 noiembrie 2018, București, România.