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Management of neuromuscular diseases in Kazakhstan

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Joint Meeting
The Japan Muscle Society
The Japanese Society of Clinical Myology
COI Disclosure

Name of Lead Presenter: Altynshash Jaxybayeva

There are no companies, etc. in a relation of conflict of interest requiring disclosure in relation to the presentation.

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AOMC-JMS 2024 meets Kazakhstan

- **Kazakhstan** is a landlocked country mostly in Central Asia, with a part in Eastern Europe.
- Its capital is Astana, while the largest city and leading cultural and commercial hub is Almaty.
- Kazakhstan is the world's ninth-largest country by land area and the largest landlocked country. It has a population of 20 million and one of the lowest population densities in the world, at fewer than 6 people per square kilometre (16 people/sq mi).

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What has changed in the global practice of NMD management?

- **There are new treatments for some diseases like SMA,DMD some CMD** which until recently **was classified as incurable**

- The paradigm of perception and the management algorithms for these diseases have changed. There are opportunities **not only to alleviate disease symptoms,** but also make real attempts to **fully restore function**

- **The timeliness and accuracy of medical diagnostic procedures determine disease prognosis,** and affect the statistical parameters of infant and **child mortality and disability**

Orphan diseases in the Republic of Kazakhstan

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The disease is considered rare with a prevalence of 1 case per 10,000 people

The orphan list includes 62 groups of diseases, including a group of neuromuscular

152 names of orphan drugs are used for the treatment of orphan diseases

In the stricture of the incidence of orphan diseases in children, **diseases of the central and peripheral nervous system occupy a leading position** in the Republic of Kazakhstan is **7239 children.**

Neurological diseases occupy the **2nd place** in the structure of disability

The doubled or tripled increase in funding for medicines for the treatment of orphan diseases over the past 4 years does not cover all existing medical needs.

3 sources of financing for the purchase of orphan drugs:

- **Guaranteed amount of free medical care**
- **Regional local budget**
- **“Kazakhstan Khalkyna” public charity foundation**

Order of the Ministry of Health of the Republic of Kazakhstan dated October 20, 2020 on approval of the list of orphan diseases and medicines for their treatment

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Why is this important for Kazakhstan?

The birth rate in Kazakhstan in 2023 was 387,900 live births[1]

(for comparison, the rate was 403,500 live births in 2022)

- The incidence of SMA is 1 in **11,000 live births**
- The annual expected rate of patients with SMA in Kazakhstan based on the birth rate is approximately 45
- Currently, ~~**205 patients are diagnosed with SMA in Kazakhstan**~~

The expected total number of patients with SMA in Kazakhstan could be as many as 250

The incidence of DMD is **3600-6000 live births males.**

Currently **203 boys** are diagnosed with DMD in Kazakhstan

The expected total number of patients with DMD in Kazakhstan could be as many as **500 males**

Disease's burden for the patient, family, health care system, society

SMA, spinal muscular atrophy

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NMDs management practice in Kazakhstan

- A pathway for patients with NMDs (including SMA) was approved in June 2020
- An EAB has been operating since August 2020
- The protocols for SMA, DMD, CMD, PNP were approved in 2020
- The protocols have been updated since 2021
  (but the update has not yet been approved)
  - An algorithm for managing adult patients has been added, and drug therapy is being revised
  - Innovative treatments were added to the protocols including exon skipping and gene therapy

EAB, Expert Advisory Board; NMD, neuromuscular disorder; SMA, spinal muscular atrophy; UMC, University Medical Center.
Based on Dr Jaxybayeva's clinical experience.

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NMDs management practice in Kazakhstan

- MLPA is carried out free of charge within the framework of mandatory health insurance based on a referral from an outpatient clinic (there are two laboratories perform this analysis)

- The **Toll Free NMDs Diagnosis Hotline** has been operating since September 2021 up to August 2024

- Transportation of materials to the laboratory is free of charge, with grant support from the NGO Society of Pediatric Neurologists, Neurophysiologists, Psychiatrists and Psychotherapists,

MLPA, multiplex ligation-dependent probe amplification; NGO, non-governmental organization; SMA, spinal muscular atrophy,
Based on Dr Jaxybayeva's clinical experience

Algorithm for patients with NMDs

Diagnostic

Pediatrician/primary care GP

Symptoms in suspected NMD[1]

- Muscle weakness
- Fatigue
- Difficulty swallowing
- Gait disorders
- Lethargy
- Difficulty getting up from the floor or walking up stairs
- Low physical activity

Laboratory studies

- Complete blood count[2] and urinalysis
- Blood chemistry panel with the determination of:
  - ALT ↑; AST ↑ *

Neurologist at Clinical and Diagnostic Department level

2. Blood chemistry panel[2] with the determination of CK*; LDH*; lactate If necessary
3. Electromyogram/electroneuromyogram
4. Muscle ultrasound and MRI[2]
5. Brain, muscle MRI*
6. Molecular genetic testing[2] (MLPA* for SMA and DMD) is free of charge

Protocols for NMDs[2]

- Congenital/hereditary myopathies
- Congenital/hereditary neuropathies (neuropathies)
- SMA in children
- Progressive DMD/BMD

Competence centers

- NCJSC Medical University Astana (Astana): Coordinator
- UMC, National Research Center for Motherhood and Childhood (Astana)
- Multidisciplinary City Children's Hospital No. 1 (Astana)
- National Center for Children's Rehabilitation (Astana)
- City Children's Hospital No. 2 (Almaty)
- University Clinic "Aksay" (Almaty)
- Rehabilitation Center "Balbulak" (Almaty)

Approved protocols include[3]

Nusinersen for SMA (registered in Kazakhstan)
Risdiplam (not registered)
Onasemnogene abeparvovek (not registered)
Ataluren for DMD (registered in Kazakhstan)
Eteplirsen, casimersen and golodirsen for DMD (not registered in Kazakhstan)

Therapeutic

Expert Council at NCJSC Medical University Astana (Astana)

- When confirming the diagnosis, drug dosage is calculated, with the determination of the plan for their administration
- Based on the discharge record, current video recording, and child's body weight
- Organization of a video conference with specialists at the child's place of residence (hospital or primary health care organization)
- Monitoring of the child's movement and the effectiveness of therapy, including pathogenetic therapy (each 6 months)

The place of therapy is determined depending on the route of administration of the drug

Pathogenetic therapy

*Protocol No. 10 of the Expert Council at the Republican Center for Health Development dated June 26, 2020.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMD, Becker muscular dystrophy; CF, corporate fund; CPK, creatine phosphokinase; DMD, Duchenne muscular dystrophy; GP, general practitioner; LDH, lactate dehydrogenase; MRI, magnetic resonance imaging; NCJSC, non-commercial joint-stock company; RK, Republic of Kazakhstan

.1. McDonald CM. Phys Med Rehabil Clin N Am. 2012;23:495-563. 2. Barp A, et al. Diagnostics (Basel). 2021;11:701. 3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10041439/ 4. Gloss D, et al. Neurology. 2016;86:465-72.

Based on Dr Jaxybayeva's clinical experience

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Common NMDs[2]

- Congenital/hereditary myopathies
- Congenital/hereditary neuropathies (neuropathies)
- SMA in children
- Progressive DMD/BMD

When prescribing pathogenetic therapy, the parent/legal representative or guardian must

- **Be trained and have childcare skills including**
  - Feeding, breathing exercises with an Ambu bag, prevention of contractures
- **Follow all medical instructions strictly**
  - In the case of Duchenne muscular dystrophy, regular administration of corticosteroid therapy[4]

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Based on Dr Jaxybayeva's clinical experience.1. McDonald CM. Phys Med Rehabil Clin N Am. 2012;23:495-563. 2. Barp A, et al. Diagnostics (Basel). 2021;11:701. 3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10041439/ 4. Gloss D, et al. Neurology. 2016;86:465-72.

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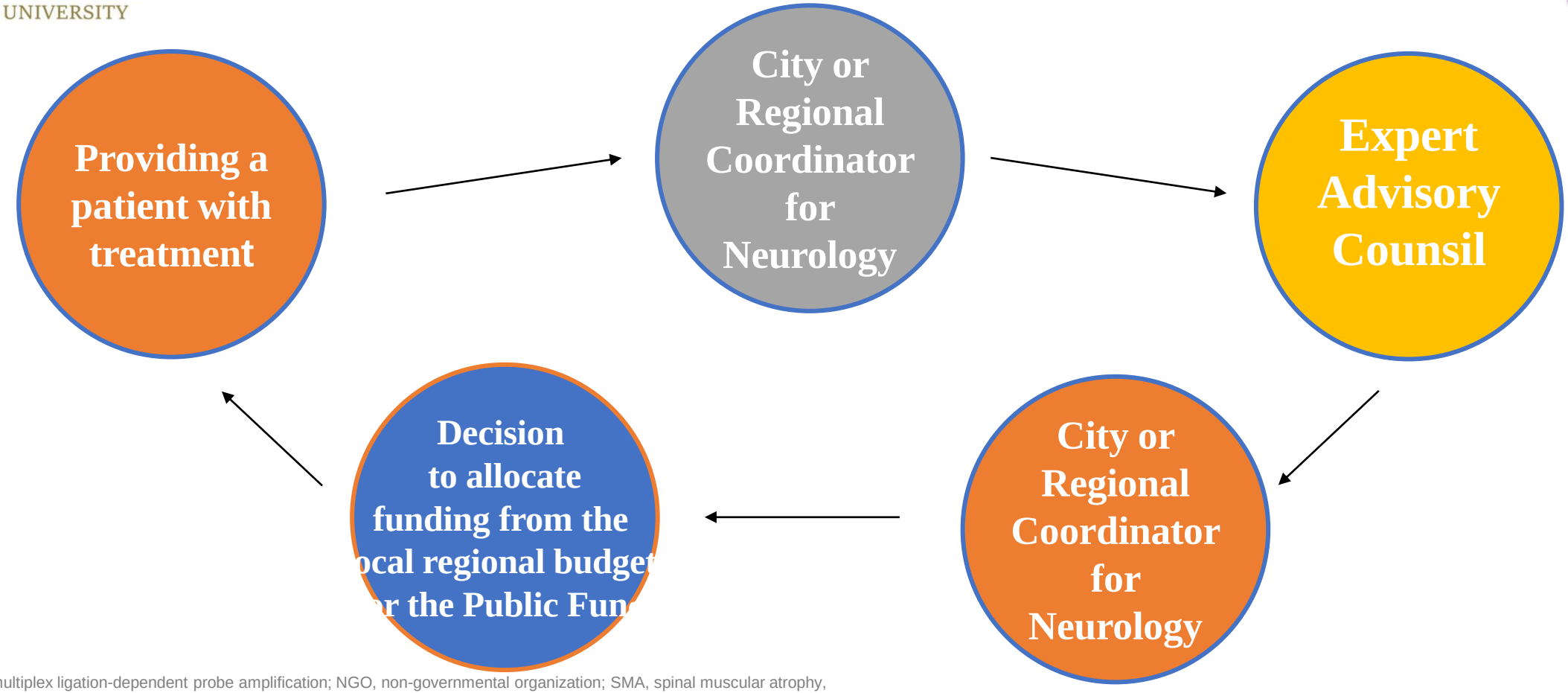
Organizational structure for making decisions about therapy



MLPA, multiplex ligation-dependent probe amplification; NGO, non-governmental organization; SMA, spinal muscular atrophy,

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What were already done and achieved during four years

Diagnosed **505 NMDs** among them

205 SMA (28 adults among them): **16** got gene replacement therapy (1 died, others improved)

70 is getting nusinersen; **48** is getting risdiplam

203 DMD: all patients on steroids as a basic treatment and additional **99** on exon skipping therapy and **29** on ataluren

ALL POSSBLE TREATMENT LINES IS AVAILABLE!

58 patients have others NMDs genetically proven

we also have a number of patients with high suspicious for NMDs but genetically negative

LIMITATION WITH DIAGNOSIS!

(muscle MRI, genetical testing and muscle biopsy, IGH)

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We believe in following factors to get success

Medical community	Patient/caregiver	Society/state
• Professionalism and high level of competence • Multidisciplinary approach	• Adherence to treatment (compliance) • Disease acceptance and responsibility	• Disease acceptance • Tolerance • Awareness of the value of life of each member of society

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What is stimulating us as a professionals for further development

- **? Rarity** of this pathology in the population
- **Heterogenity** and Leading to a change in **quality of life** and **limitation of a person's life expectancy**[1]
- **Highly specialized field** of medicine, requiring specific training and clinical experience
- Many medical specialists are not familiar with these conditions, which leads to an incorrect diagnosis and choice of treatment tactics, which in turn leads to a worsening of the patient's condition
- **Important! The status of many diseases often changes from "incurable" to "treatable"**
- **Correct, timely diagnosis is the key to successful care**

What we understood and finally create

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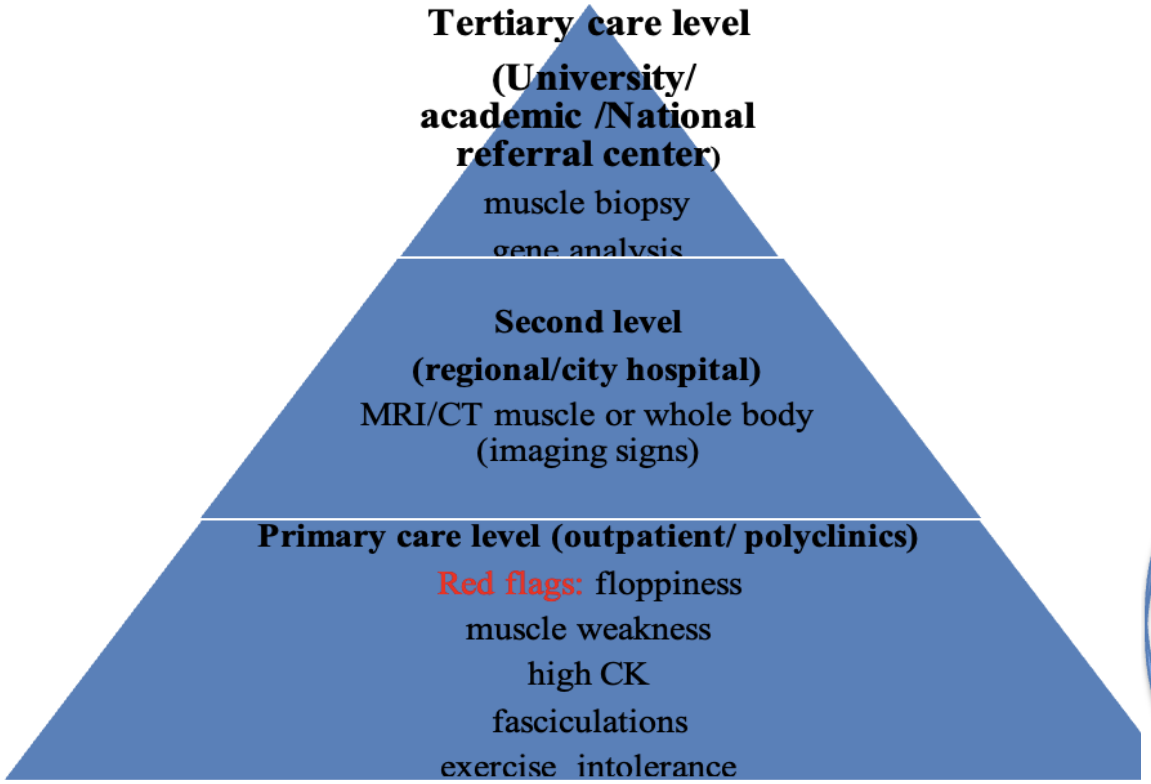
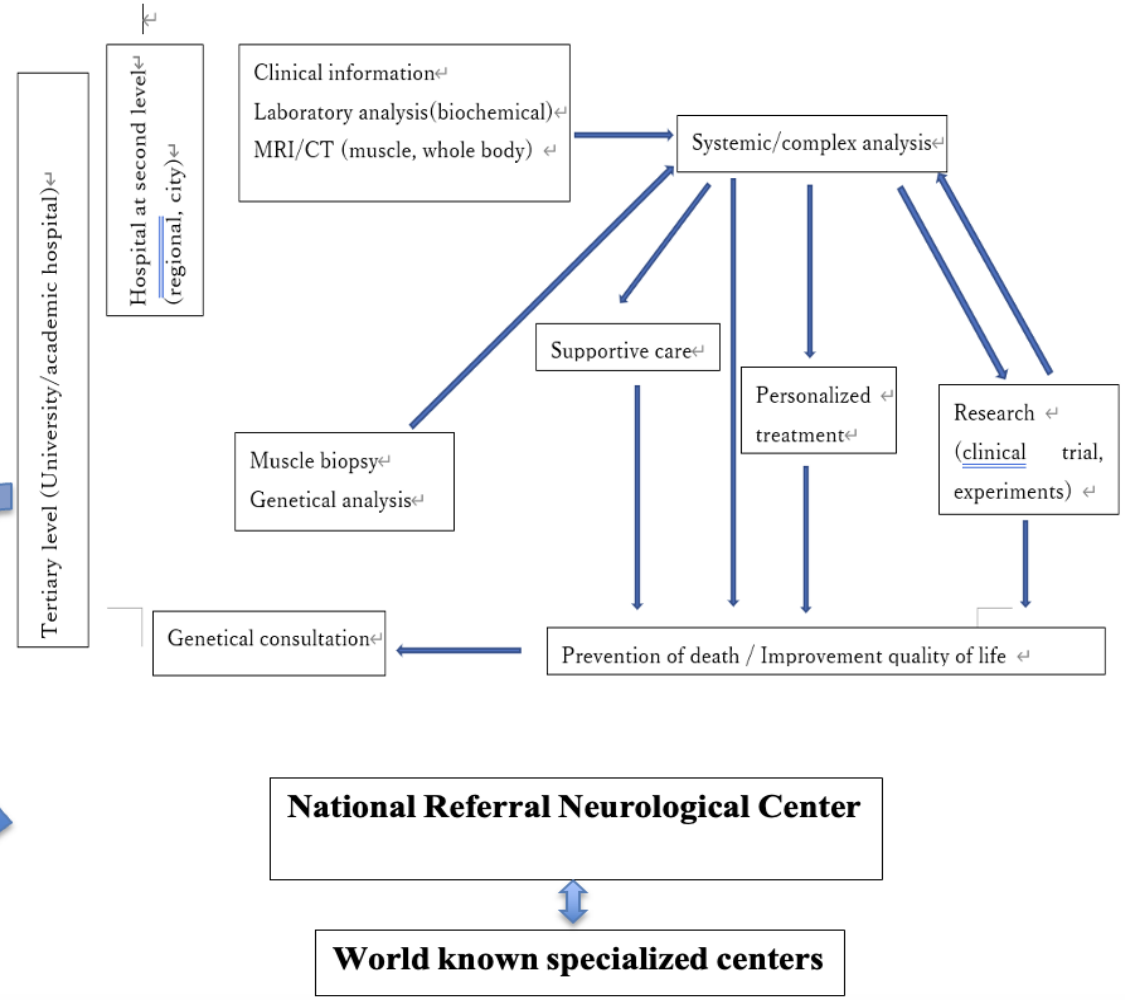
Diagnostical standard of care



Centralization of all facilities under an umbrella of the National referral center (University/academical hospital) will allow concentration of all resources (human, technical and financial) and developing a highly specialized sustainable diagnostical system for rare neurological/neuromuscular diseases and decrease a burden of these life-threatening condition on health care system.

Schematical picture of the management of neuromuscular diseases (and all other rare neurological diseases): Evidence based approach for decision making.



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We are open for any kind professional cooperation if the field of NMDs

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ARIGATO!
ご清聴ありがとうございました

Назар аударғаныңызға РАХМЕТ!

Thank you for you attention!

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