Newborn screening for spinal muscular atrophy in Ukraine: from pilot project to national programme

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5q-Spinal muscular atrophy (SMA) is a progressive, autosomal recessive neuromuscular disease with an incidence of 1 in 14,848 births.[1] SMA is characterised by proximal muscle weakness and in severe and most frequent cases early death. Approximately 96% of SMA patients carry PCR-detectable homozygous deletions of exon 7 in the *SMN1* gene.[2,3] *SMN2*, which differs from *SMN1* by minor nucleotide base variations, provides limited functional compensation. Consequently, a higher *SMN2* copy number is associated with a milder disease phenotype.[4]

Three disease-modifying drugs, nusinersen, risdiplam, and onasemnogene abeparvovec, have been approved[3]; in Ukraine, nusinersen was approved and reimbursed in 2020, followed by risdiplam in 2022. Given the much better efficacy of all three drugs when delivered early after birth, newborn screening (NBS) for SMA was progressively implemented in numerous countries since 2018.[1,5,6]

Before the implementation of NBS, SMA in Ukraine was frequently diagnosed after significant neuromuscular deterioration, potentially limiting treatment efficacy. SMA prevalence has been estimated in 2021 between 200 and 300 cases suggesting underdiagnosis.[7]

In June 2021, the Ukrainian government initiated preparations to expand NBS from 4 disorders to 21, including SMA.[8] However, due to war-related delays, the nationwide programme—originally scheduled to launch in June 2022 —was postponed. Nonetheless, a pilot project in Kyiv and Lviv was launched in October 2022, followed by the full-scale nationwide programme in April 2023 across all non-occupied regions of Ukraine.

NBS was conducted through real time-PCR on dried blood spot specimens after parents had signed informed consent. All PCR-positive cases were referred to a central lab for confirmation using Multiplex ligation-dependent probe amplification. Identified patients were referred to a medical-genetic institution for management (Supplementary Method 1).

Between October 2022 and April 2024, 211,500 newborns were screened with a consent rate of 98%. 31 newborns were confirmed to have SMA, corresponding to an incidence of 1 in 6823 (95% CI 5046–10,528). The median age of blood sampling was 3 days (IQR 2–3 days), with confirmation of the result at a median of 26 days (IQR 19–32 days). The median turnaround time (from birth date to the first screening result) was 8 (IQR 7–10 days) (Supplementary Figure S2 and Supplementary Table S1).

18 patients were treated in Ukraine with risdiplam, three of whom later received onasemnogene abeparvovec abroad-as this drug is not currently available in Ukraine. Treatment was initiated at a median age of 52 days (IQR 38–75) (Supplementary Table S1).

Fig. 1 shows the outcome of the identified patients. One patient with a single *SMN2* copy presented with a severe phenotype and received palliative care. In patients for whom follow-up data (22 patients) are available, five patients with two *SMN2* copies received treatment at a median age of 49 days (IQR: 38–73 days). All achieved head control; one patient had not acquired

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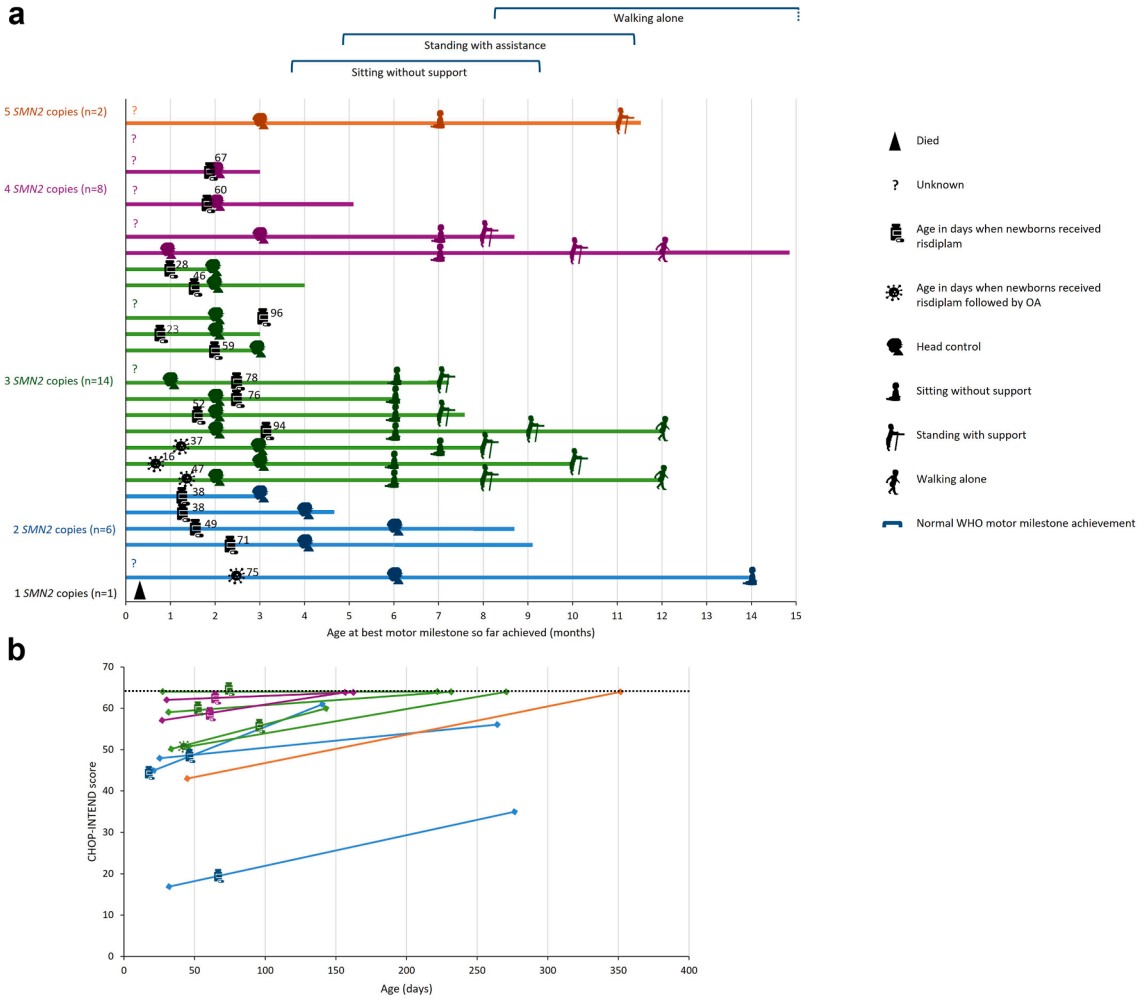

Fig. 1: **a. Motor milestone achievement and age at last follow-up in Spinal Muscular Atrophy (SMA) positive newborns identified through newborn screening (NBS).** The benchmark lines represent normal motor milestones. 1st and 99th centiles are used in reference to WHO motor milestones achievement. The 99th centile for walking alone is 17.6 months, which extends beyond the graph. **b. Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND) score at first and last visit for the 10 patients with follow-up.** The dashed line represents the ceiling effect at 64 points.

sitting position at 9 months (last follow-up) and one acquired sitting position at 14 months (Fig. 1a). Twelve patients with three *SMN2* copies received treatment at a median age of 50 days (IQR 33–77 days) and two with 4 copies received treatment at a median age of 64 days (IQR 60–67 days). Motor milestones of patients with >2 *SMN2* copies were reached within the expected time-frame (Fig. 1a). Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders scores are reported in Fig. 1b. Of the ten assessed patients, median improvement was 9 points (IQR 6–15 points), with six patients having reached the 64 points ceiling.

Early identification and treatment of affected newborns allowed for better survival rates and motor milestone acquisition compared to post-symptomatically treated patients in clinical trials or from real-world data.[1,3] The observed SMA incidence of 1 in 6823 aligns with that in other Eastern European countries[9] and is higher than global prevalence estimates of 1: 14,848.[1,10] No false-negative nor false-positive were observed however false-negative cases might not yet have been diagnosed or reported. The median turnaround time of 8 days aligns with other European programmes.[5] The high consent rate of 98%, despite an opt-in process for the consent, reflects strong public acceptance, surpassing the 87% consent rate reported for a German pilot project (2018–2021).[6]

While Ukraine's NBS programme is comparable to other European programmes in terms of accuracy, consent rate, and turn-around time, the war has

significantly impacted the NBS and access to treatment. The decentralisation of the health-care system created logistical challenges of timely and consistent collection and transport of samples partially compensated by the implementation of express delivery of samples. Regional infrastructure was improved by health-care professionals receiving training and support from international partners and a centralised coordination hub was established at the Kyiv Expert Centre for Newborn Screening to provide organisational and methodological support for the implementation and evaluation of the new system. The 52 days median age at treatment initiation is substantially higher than in other pilots,[1,5,6] primarily due to the mass displacement of families, especially in Eastern Ukraine, leading to logistical challenges in reaching parents and referring newborns to specialised hospitals.

Despite unprecedented challenges, the pilot SMA NBS programme in Ukraine successfully transitioned into a nationwide initiative and has demonstrated feasibility and acceptance in a war-affected country. Continued follow-up will provide long-term data on patient outcomes and the impact of delayed access to treatment. These insights will be invaluable for optimising NBS strategies in Ukraine and other countries facing similar circumstances.

Contributors

Natalia Olkhovych facilitated project administration, data analysis, accessed and verified the data, contributed to writing and is responsible for the submission of the manuscript with Laurent Servais. Nataliia Samonenko facilitated data curation, data interpretation, accessed and verified the data. Tetiana Shklyarskaya, Olena Grechanina, Mykola Veropotvelyan, Halyna Makukh, Oksana Barvinskaya, Nataliia Mytsyk were involved in data collection. Tetiana Ivanova was involved in data curation, access and verification of the data. Nataliia Gorovenko was involved in conceptualisation and reviewing. Serena Hill facilitated co-ordination of writing, data interpretation, access and verification of the data steered and reviewed by Professor Laurent Servais and Tamar Dangouloff.

Editor note

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Declaration of interests

All declarations of interest are reported with the past 36 months. Laurent Servais has been involved in personal consultancy, board attendance, grants and contracts. With the following companies: Biogen (Support to NBS academy and NBS in Belgium), Novartis (Support of educative event and NBS in Belgium and UK), Roche (Support of educative event and NBS in Belgium and UK), Biohaven (Support of ACE SMA UK), Scholar Rock (Support of ACE SMA UK) and Zentech (Support of educative event and NBS in Belgium). Tamara Dangouloff reports honoraria for lectures in relation to Biogen and Roche. Nataliia Olkhovych, Nataliia Samonenko and Tetiana Shkliarska report honoraria for lectures for Novartis and Roche whilst reporting support for attending a meeting with Roche. Nataliia Olkhovych is the Vice-president of All–Ukrainian Association of Specialists of Medical and Laboratory Genetics. Nataliia Samonenko is the Leader of the Rare Diseases Division at the Ukrainian Academy of Pediatric Specialties. Serena Hill, Olena Grechanina, Mykola Veropotvelyan, Halyna Makukh, Oksana Barvinska, Nataliia Mytsyk, Tetiana Ivanova and Nataliia Gorovenko have no interests to declare.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanepe.2025.101351.

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