LIVED EXPERIENCE: INSIGHTS INTO THYMIDINE KINASE 2 DEFICIENCY

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Introduction:

- Thymidine Kinase 2 deficiency (TK2d) is an ultra-rare inherited mitochondrial disorder. As of 2018, 107 unique cases had been reported in the literature, and worldwide prevalence was estimated at 1.64 (0.5, 3.1) cases per 1 million people.[1]
- Mutations to the TK2 gene can lead to the inability to recycle thymidine nucleotides meaning mitochondrial DNA cannot be repaired or replicated. As a result, mitochondrial function is greatly affected.[2]
- There is a spectrum of symptoms which depend on age of onset, which is generally linked to severity of disease, with earlier onset leading to worse outcomes, including premature death. Typically organs that require high energy production, such as the brain, heart, and skeletal muscles, are the most affected.[2]
- The treatment landscape for TK2d is currently evolving, with nucleoside treatments such as Doxecitine-doxribtimine currently being trialled in people with TK2d.

Aim: To gain insight into the lived experience of people with Thymidine Kinase 2 deficiency

Methods:

- A digital community-facing survey was conducted by the Lily Foundation and Metabolic Support UK, which ran between 08/07/2025 and 31/08/2025.
- Questions were designed based on the NICE patient organisation submission template and in-house TK2d knowledge.
- The survey was disseminated via social media, newsletters, and targeted outreach. Surveys were available in English, Italian and Spanish.
- Data were analysed using a mixed methods approach including both descriptive statistics and thematic content analysis.

Results:

- Fourteen responses were received and included people living with TK2d (n = 3), parents/carers of someone living with TK2d (n = 9) and bereaved parents/carers (n = 2).
- Respondents were from Costa Rica (n = 1), Ireland (n = 1), Italy (n = 1), Spain (n = 6), the UK (n = 4), and the USA (n = 1).
- The average patient age was 14 years (range: 4–50).

Family with a child with a mitochondrial disorder

Health status and daily living varied notably between treated and untreated respondents

- For those who have **experience with Doxecitine-doxribtimine 100% said their condition is stable or improving** (78% improving, 22% stable; n = 9)
- For those who do not currently receive Doxecitine-doxribtimine, 66% said their condition is deteriorating, and 33% said their condition is stable or improving (33% improving, 0% stable; n = 3)
- Some people said TK2d **affects many aspects of their lives**, describing profound limitations in mobility and independence.

"Physically, it does greatly limit me from performing everyday tasks, such as getting dressed, sitting on the toilet, or sitting in the shower chair. I need help from a third person to do this" – Person living with TK2d (person from Spain, currently not receiving Doxecitine-doxribtimine)

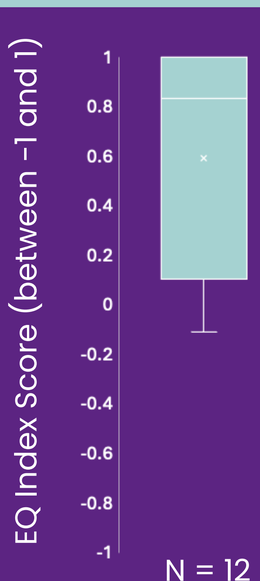
- Others said TK2d **affects daily life in some respects** but not every aspect.

"He can walk for less time than a child his age, and he struggles to climb stairs, even if he does. He tires more quickly than other children, and the heat is quite suffocating." – Person caring for someone living with TK2d (person from Spain, currently receiving Doxecitine-doxribtimine)

- Others said TK2d **affects daily life very little**, particularly when receiving nucleoside-based medication.

"He lives a life very much in keeping with his age, with some small, almost imperceptible limitations." – Person caring for someone living with TK2d (person from Spain, currently receiving Doxecitine-doxribtimine)

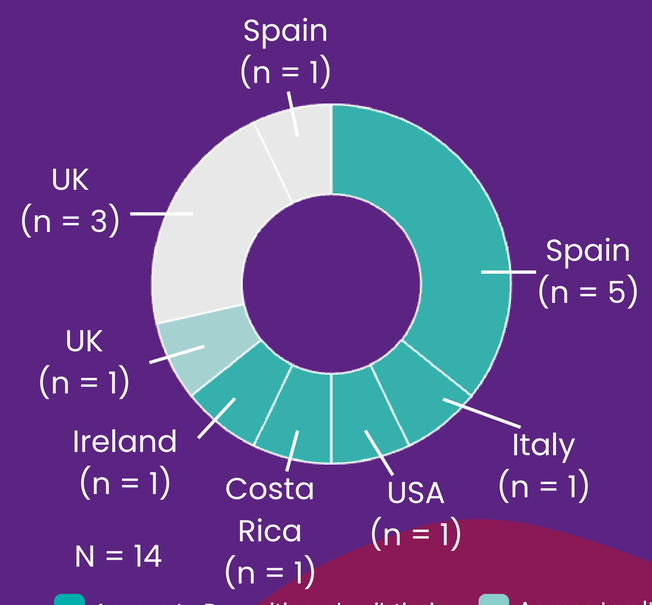
EQ-5D-3L data confirmed significantly reduced quality of life compared with general population norms



Average **EQ Index Score 0.59**
Range -0.108 to 1, Median: 0.8325

Many respondents felt that they or the person they cared for experienced some **problems with mobility, age-appropriate self-care and being able to undertake usual activities.**

Access to nucleoside-based therapy varied geographically: with those with access reporting stabilisation or improvement of symptoms



100% of respondents said that they would **recommend** Doxecitine-doxribtimine (N = 9)

100% of respondents said they saw **halting of the disease progression and reversal of symptoms** upon taking Doxecitine-doxribtimine (N = 9)

22% use the words **'living a normal life'** to describe their child upon taking Doxecitine-doxribtimine (N = 9)

Conclusions:

- This survey captures perspectives from a significant proportion of global TK2d population, offering valuable insights into life with this ultra-rare condition.
- The findings demonstrate substantial variation in quality of life, as well as potential inequities in access to nucleoside-based therapy.
- Coordinated care pathways, timely diagnosis, and equitable access to treatment are critical to improving outcomes for people with TK2d. Ongoing collaboration between clinicians, researchers, and patient organisations will be essential in addressing these unmet needs globally.

"He went from not even being able to hold his head up in November to starting to walk with the aid of a walker in December of the same year. Since then, he's continued to progress, leading a practically normal life.' – Person caring for someone with TK2d (Spain)

Acknowledgments:

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References:

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