Humanistic and Economic Burden of Metachromatic Leukodystrophy on Patients, Caregivers, and Healthcare Systems

Findings from a Targeted Literature Review

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1 BACKGROUND

- **Metachromatic leukodystrophy (MLD)** is a rare, inherited lysosomal storage disorder characterised by progressive demyelination and rapid neurological deterioration.[1] MLD has three age-based subtypes: late-infantile (≤2.5 years), juvenile (2.5 – <16 years), and adult (≥16 years).[1]
- Patients progressively lose **motor, cognitive, communication and functional abilities**, ultimately resulting in severe disability and premature mortality.[2] The progressive, disabling course of MLD imposes substantial emotional, physical, social, and financial burden on families and caregivers, affecting health-related quality of life (**HRQoL), education, caregiver well-being, employment, healthcare resource use (HCRU), costs, and productivity.**[2]

GAP: Evidence describing the humanistic and economic burden on patient, caregivers and healthcare system of MLD remains fragmented

2 OBJECTIVES

We aimed to evaluate and synthesize the **humanistic and economic burden** of MLD on patients, caregivers, families and healthcare systems.

PATIENTS & CAREGIVERS

Quality of life (QoL), productivity and work impairment

HEALTH SYSTEMS

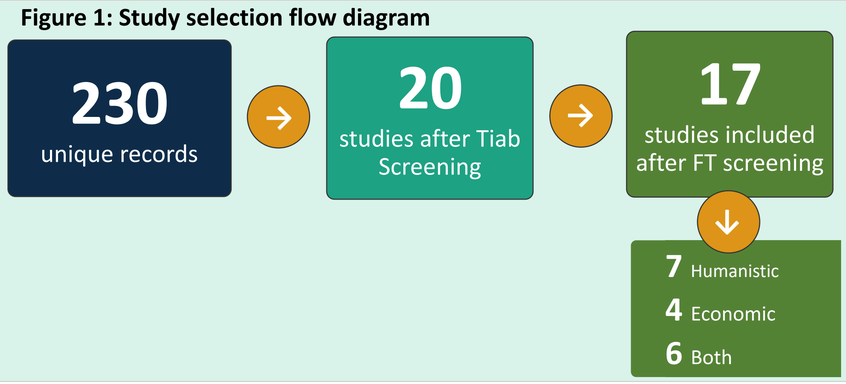
HCRU and costs

Purpose: To bring fragmented quantitative and qualitative evidence together to characterise the burden of MLD.

3 METHODS

- **Design**: Targeted literature review (TLR) of PubMed, Embase® and Google Scholar, January 2012 - April 2026 was conducted as shown in **figure 1**.
- **Eligibility:** Quantitative or qualitative evidence on the humanistic or economic burden of MLD in patients or caregivers.
- **Outcomes:** HRQoL, education and social participation, emotional burden, employment and productivity, diagnostic experience, HCRU, direct and out-of-pocket costs.
- **Synthesis:** Studies classified as humanistic, economic or both; location, population, severity and outcomes synthesized descriptively.

Figure 1: Study selection flow diagram



4 RESULTS

~10-14
months of diagnostic delay in children (2 studies)[3,10]

0.71 to -0.62
of utility values as disease progressed in patients (3 studies)[6,8,9]

48-80%
of caregivers reported anxiety, depression or emotional burden (7 studies)[5-7,10-13]

77-90%
of caregivers reduced or stopped work (6 studies)[4,5,7,10,13,14]

80%
of caregivers reported reduced social engagement (5 studies)[4-6,10,13]

- **Evidence base:** Out of 17 included studies, most were from **Europe (n=8),** followed by multi-country (n=4), North America (n=2) and Asia (n=1); two did not report a region.
- **Patients:** Reduced educational participation (5 studies)[3-7] Neurological and functional decline was reflected by difficulties with talking, walking, and eating; utility values fell in advanced disease (3 studies) (**Table 1**).[6,8,9]
- **Diagnosis:** Delays were attributed to limited recognition of early, nonspecific symptoms (e.g., clumsiness, frequent falls) and late acknowledgement of parental concerns.
- **Caregivers' QoL:** Quality of life declined with disease progression (free walking → limited locomotion → loss of locomotion) and increasing care needs (6 studies).[6,11,13-16]
- **Caregivers' Economic burden:** Driven by substantial out-of-pocket expenses (2 studies)[4,13] and Productivity losses resulting from reduced work participation or workforce departure (6 studies).[2,3,5,8,11,12]
- **Overall costs across the healthcare system:** Costs increased across disease stages as care became more intensive and complex (5 studies),[4,13,17-19] driven by hospitalisations, specialist consultations, home nursing, assistive devices, rehabilitation and long-term supportive care as shown in **figure 2.**

Table 1: Burden domains across included studies

Stakeholder	Findings
Patients	Reduced educational participation[3-7]
	Lower utility values in advanced disease[6,8,9] **(0.71 to -0.62)**
Caregivers	Quality of life reduced with progression[6,11,13-16]
	Substantial out-of-pocket (OOP) expenses[4,13] **€150 - 100,000 per family[4] and 47.8% incurred OOP costs for nursing assistance[13]**
	Productivity losses[2,3,5,8,11,12] **53.5% - 90% of caregivers reported reduced productivity, averaging 3.6 missed workdays in 4 weeks**

Burden spans every stakeholder; caregiver quality of life and productivity losses has the broadest evidence (6 studies).

Figure 2: Monthly medical costs by severity (from a multinational European study)



Severity scale used: GMFC-MLD

5 DISCUSSION & CONCLUSION

- MLD places a substantial and progressive burden on patients, caregivers, families, and healthcare systems, with impacts extending across clinical, psychosocial, and economic domains.
- As the disease advances, patient dependence increases, HRQoL declines, caregiver burden intensifies, and healthcare resource utilization and costs rise.
- The impact extends beyond caregiving, affecting emotional well-being, family relationships, employment, and daily functioning.[5]
- Diagnostic delays of approximately 10-14 months highlight the need for greater awareness and earlier recognition of symptoms.
- Earlier diagnosis and timely intervention may help reduce avoidable delays and mitigate the long-term humanistic and economic burden of MLD.

> **MLD's burden escalates with progression: 77-90% of caregivers reduce or stop work and monthly medical costs rise from US $102 to US $9,559. Earlier diagnosis may help in reducing the burden.**

REFERENCES

1. Van Rappard DF, et al. Best Pract Res Clin Endocrinol Metab. 2015;29(2):261–73.
2. Kehrer et al. Neurology. 2021;96(2), e255-e266.
3. Eichler F, et al. Orphanet Journal of Rare Diseases. 2022; **17**(1): 370.
4. Kehrer C, et al. Orphanet J Rare Dis. 2025; **20**(1): 242.
5. Koto Y, et al. Mol Genet Metab Rep. 2024; **38**: 101059.
6. Pang F, et al. Molecular Genetics and Metabolism. 2021; **132**(2): S81.
7. Thomas S, et al. Orphanet Journal of Rare Diseases. 2024; **19**(1): 87.
8. Bean K, et al. Val Health. 2022; **25**(7): S344.
9. Lo SH, et al. Val Health. 2023; **26**(6): S345.
10. Yazbeck E, et al. Archives de Pédiatrie. 2026; **33**(3):105483.
11. Gavazzi F, et al. *Journal of Child Neurology.* 2025; **40**(10): 852-61.
12. Pang F, et al. *Molecular Genetics and Metabolism.* 2022; **135**(2): S93.
13. Sevin C, et al. Orphanet J Rare Dis. 2022. **17**(1): 329.
14. Ammann-Schnell L, et al. *Orphanet Journal of Rare Diseases.* 2021; **16**(1): 211.
15. Bean K, et al. International Journal of Neonatal Screening. 2024.
16. Pang F, et al. *Molecular Genetics and Metabolism.* 2021; **132**(2): S81-S2.
17. Bean K, et al. *Val Health.* 2023; **26**(6): S134.
18. Bean K, et al. *Val Health.* 2023; **26**(12): S157-S8.
19. Mohajer A, et al. Val Health. 2023; 26(12): S515.

Abbreviations:

HRQoL: Health-related quality of life
HCRU: Healthcare resource utilisation.
FT: Full-text
GMFC-MLD: Gross Motor Function Classification in Metachromatic Leukodystrophy
OOP: Out-of-pocket
QoL: Quality of life
TLR: Targeted Literature Review
Tiab: Title-abstract

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