



# Direct cost analysis associated with the management of patients with metachromatic leukodystrophy (MLD) across nine European countries

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## BACKGROUND & OBJECTIVES

### Background:

- MLD is an ultra-rare and fatal inherited neurodegenerative disease, leading to a deficiency of the ARSA enzyme resulting in a build-up of toxic sulphatides. This leads to rapid motor and cognitive decline and premature death, particularly in early-onset MLD (late infantile and early juvenile). There are four forms of MLD based on the age of symptom onset:
  - late infantile (LI  $\leq$  30 months);
  - early juvenile (EJ >30 months to <7 years),
  - late juvenile (LJ  $\geq$  7 to 16 years),
  - and finally adult ( $\geq$  17 years).

- The Gross Motor Function Classification-MLD (GMFC-MLD) is a validated measure of motor dysfunction in MLD, which represents all clinically relevant stages from normal (GMFC-MLD 0) to loss of all gross motor function (GMFC-MLD 6)<sup>1</sup>, the levels of which are shown in Table 1.

**Table 1: The seven different levels of gross motor function classification in MLD**

|         |                                                                                                                                                 |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------|
| Level 0 | Walking without support with quality of performance normal for age                                                                              |
| Level 1 | Walking without support but with reduced quality of performance, i.e. instability when standing or walking                                      |
| Level 2 | Walking with support. Walking without support not possible (fewer than five steps)                                                              |
| Level 3 | Sitting without support <b>and</b> locomotion such as crawling or rolling. Walking with or without support not possible                         |
| Level 4 | (a)Sitting without support but no locomotion or<br>(b)Sitting without support possible not possible, but locomotion such as crawling or rolling |
| Level 5 | No locomotion nor sitting without support, but head control is possible                                                                         |
| Level 6 | Loss of any locomotion as well as loss of any head and trunk control                                                                            |

- By using the GMFC-MLD classification as the framework to model disease progression and define health states, the healthcare costs necessary to manage all the symptoms of early- onset MLD through different stages of the disease can be calculated.
- This contributes to an extremely high caregiving burden, but also has a significant impact on healthcare resource use.

### Objective:

The aim of this study was to determine and compare the average cost of care by GMFC-MLD health state across nine European countries.

## METHODS

### Healthcare Resource Use (HCRU) across the countries:

- In the first instance, Delphi panel methodology was employed using a bottom-up approach to determine the total healthcare resource use (HCRU) by GMFC-MLD health state based on the experience of six clinical experts in the UK.
- Individuals were selected to best represent the range of healthcare professionals known to treat MLD and included paediatric haematologists, consultants in paediatric inherited metabolic diseases, and clinical neuropsychologists.
- Each clinical expert took part in an individual, Excel-based worksheet, which quantified specific HCRU values. Clinical experts were asked to provide information on the frequency and proportion of HCRU for MLD patients in each GMFC-MLD stage. Weighted means of proportions of patients using specific resources, as well as frequency and, where relevant, duration of each type of resource used were calculated.
- Subsequent to the Delphi panel, clinical experts in the management of MLD from each of the other European countries then reviewed the UK HCRU and amended or corroborated the results based on the MLD care pathway in their respective countries.

### Country costs:

- The unit costs for each item of healthcare were derived using a variety of sources including national databases and official tariffs specific to each country e.g., Nederlandse Zorgautoriteit in the Netherlands or Laeger.dk Takstkort in Denmark.
- HCRU costs were calculated on a monthly basis to take in to account the rapid progression of the disease through stages GMFC-MLD 2 through 5.<sup>3</sup>
- In order to allow comparison across the different European countries, local currency unit (LCU) was converted to USD using purchasing power parities (PPP) ratios derived from OECD 2021 data.<sup>4</sup>

## RESULTS

- Clinical experts from each of the European countries confirmed that the pathway of care does not significantly differ between countries, and as such healthcare consumption was very similar. Consequently, any difference in cost of care between countries is driven by local pricing and reimbursement context, e.g., some of the cost categories listed below are reimbursed differently between the countries.
- HCRU categories for the management of MLD included: 1) Drugs - for example to manage seizures, pain and spasticity, 2) Medical tests – for example to assess vision and hearing ability; 3) Medical visits - for example physiotherapy to relieve spasticity 4) Hospitalisations, 5) GP & Emergency, 6) Healthcare equipment – for example enteral feeding pump, wheelchair and adaptable bed, 7) Respite care and 8) Social services – for example enteral nutrition and community nurse/caregiver time.
- In the early stages of the disease (GMFC-MLD 1 to 2) most of the costs were attributable to medical tests and medical visits; whereas in the latter stages of the disease (GMFC-MLD 5 and 6), the greatest costs were due to hospitalizations and the need for round the clock care necessitating the cost of a daily nurse/caregiver.

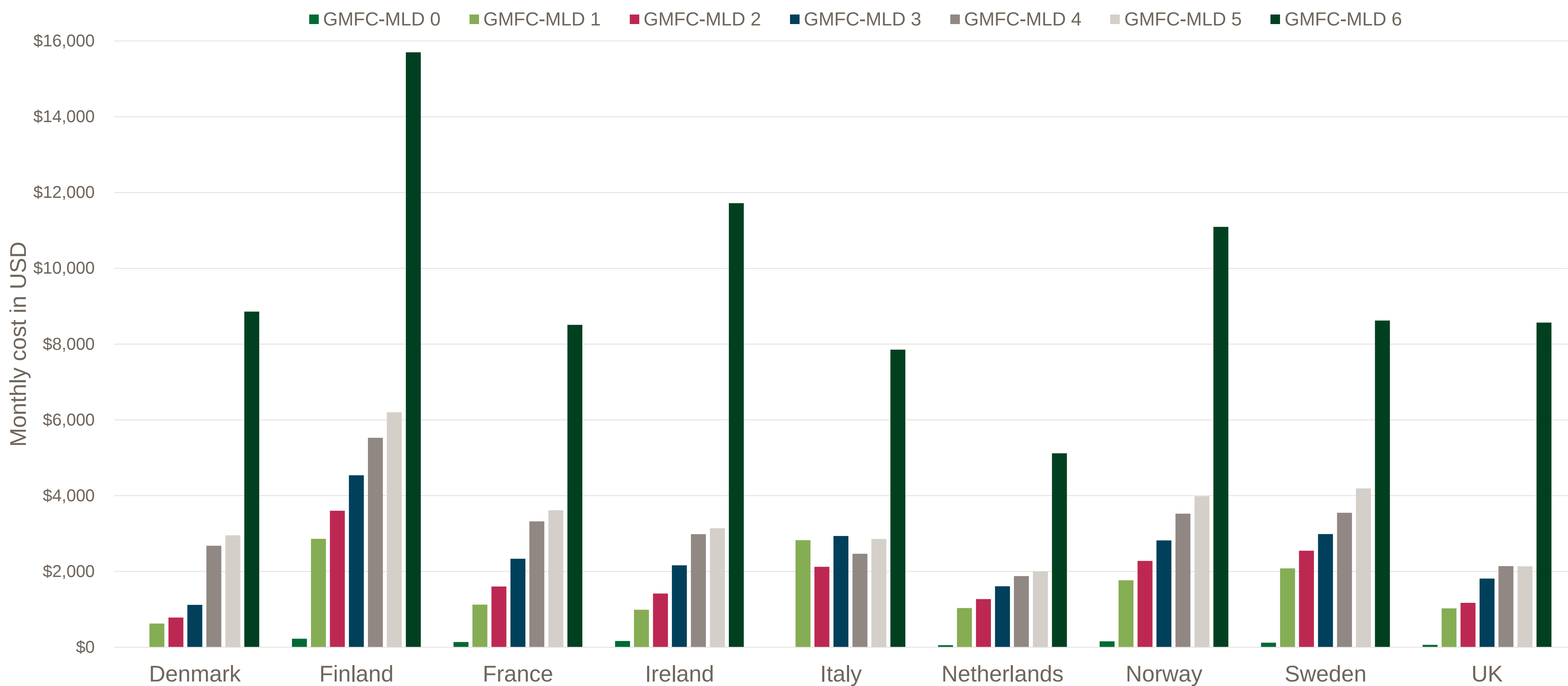
**Table 2. Healthcare Resource Use Across Countries in LCU and USD**

| Country     | GMFC 0 LCU (USD) | GMFC 1 LCU (USD) | GMFC 2 LCU (USD) | GMFC 3 LCU (USD) | GMFC 4 LCU (USD) | GMFC 5 LCU (USD) | GMFC 6* LCU (USD) |
|-------------|------------------|------------------|------------------|------------------|------------------|------------------|-------------------|
| Denmark     | 0 (0)            | 4,114 (624)      | 5,158 (782)      | 7,378 (1,119)    | 17,668 (2,679)   | 19,479 (2,954)   | 58,395 (8,856)    |
| Finland     | 190 (222)        | 2,446 (2,862)    | 3,079 (3,602)    | 3,878 (4,538)    | 4,723 (5,526)    | 5,300 (6,201)    | 13,419 (15,701)   |
| France      | 108 (138)        | 882 (1,124)      | 1,256 (1,602)    | 1,830 (2,334)    | 2,604 (3,320)    | 2,834 (3,613)    | 6,671 (8,506)     |
| Ireland     | 136 (165)        | 815 (988)        | 1,167 (1,416)    | 1,782 (2,162)    | 2,460 (2,984)    | 2,588 (3,139)    | 9,659 (11,717)    |
| Italy       | 0 (0)            | 2,098 (2,824)    | 1,576 (2,121)    | 2,180 (2,934)    | 1,833 (2,467)    | 2,123 (2,858)    | 5,834 (7,853)     |
| Netherlands | 44 (54)          | 841 (1,269)      | 1,032 (1,269)    | 1,306 (1,607)    | 1,525 (1,876)    | 1,625 (1,999)    | 4,161 (5,117)     |
| Norway      | 1,507 (156)      | 17,098 (1,767)   | 22,032 (2,277)   | 27,267 (2,818)   | 34,103 (3,525)   | 38,562 (3,986)   | 107,339 (11,094)  |
| Sweden      | 1,040 (119)      | 18,111 (2,080)   | 22,166 (2,545)   | 26,000 (2,985)   | 30,899 (3,548)   | 36,506 (4,192)   | 75,092 (8,622)    |
| UK          | 49 (64)          | 785 (1,026)      | 897 (1,173)      | 1,385 (1,810)    | 1,636 (2,139)    | 1,632 (2,133)    | 6,554 (8,566)     |

\* GMFC 6 costs are a blended cost comprising 90% care at home and 10% care at hospital based on clinical expert opinion.

- Figure 1 presents the monthly costs by GMFC-MLD health state in USD across nine European countries. The average monthly medical costs across all countries for each GMFC-MLD health state from 0 through to 6 were \$102, \$1,592, \$1,865, \$2,478, \$3,118, \$3,453, and \$9,559, respectively. The minimum and maximum monthly medical costs were observed in the Netherlands and Finland, respectively.

**Figure 1: Monthly costs associated with the management of MLD by GMFC-MLD health state in nine European countries (LCU have been converted to USD using PPP)**



## CONCLUSION

- Monthly medical costs increase with disease severity in the majority of countries. Given the rapid initial progression of the disease,<sup>2,3</sup> early onset MLD patients potentially spend years in the latter stages of the disease (GMFC-MLD 5 and 6), which are associated with the highest costs.
- In the absence of claims data analysis, using Delphi panel data with the relevant clinical expert input and a bottom-up micro-costing approach could provide a useful approximation of the cost of care for MLD in the appropriate country of interest.

### References

1. Kehrer et al. 2011. Development and reliability of a classification system for gross motor function in children with MLD. *Dev Med Child Neurol*; 53(2):156–60  
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4. OECD purchasing power parities ratio 2021 data. <https://data.oecd.org/conversion/purchasing-power-parities-ppp.htm>. Accessed April 2023.