

Background & objectives

- Acid sphingomyelinase deficiency disease (ASMD) is a rare, autosomal recessive, progressive disease, often with a fatal outcome. It is caused by a deficiency in acid sphingomyelinase associated with a mutation in the sphingomyelin phosphodiesterase 1 (*SMPD1*) gene [1, 2]. A study conducted in Portugal between 1982 and 2001 estimates a type A and type B ASMD prevalence of 0.60 per 100,000 births [3]. Historically, treatment for ASMD has been limited to symptom-based supportive care; however, a disease-modifying treatment - olipudase alfa enzyme replacement therapy was recently approved for non-CNS manifestations of ASMD in children and adults [2,4].
- The objective of this study was to describe the clinical practice and estimate the costs related to the treatment of ASMD, type B or A/B, in the Portuguese National Health Service.

Methods

- A panel with four experts (pediatrics and internal medicine), from four reference centers for lysosomal storage diseases, geographically distributed across north, center and south of the country, was conducted, during 2023, in order to characterize the Portuguese routine care, which includes follow-up and treatment of complications.
- Experts replied individually to a structured electronic questionnaire about their experience on ASMD treatment. Responses were collected and aggregated results were produced based on arithmetic averages, according to Portuguese methodological guidelines [5].
- Portuguese-specific management resource use related to ASMD was based on the expert panel and Portuguese Diagnosis-Related Group (DRGs) database. Episodes of interest were identified through the International Classification of Diseases, tenth Revision, Clinical Modification [6].
- The cost per class of ASMD complication (respiratory, splenic, hepatic, cardiovascular and hemorrhagic) was estimated as a weighted cost based on the events reported in Cox *et al.* (2018) [7]. Cox *et al.* (2018) is multinational retrospective study collected data on the burden of illness and healthcare resource use for 100 patients across the clinical spectrum of ASMD.
- Resources were valued according to publicly available national unit cost data - national legislation (Portaria nº 207/2017) and official national drug cost databases (Infomed).

Results

- The panel estimates that 6.1% of ASMD patients are hospitalized and 16.3% resort to emergency, per year.
- On average, patients go to 10.0 healthcare professionals’ visits, and do 10.1 laboratory tests and 6.9 exams, per year.
- Regarding medication, these patients use vitamin D (67.5%), flu vaccination (67.5%), antibiotics (61.3%), bronchodilators (35.8%), statins (28.8%), among others.
- Combining resource use and unit costs, we estimate a yearly follow-up cost of 923€ per ASMD patient, which can be broken down into costs with hospitalization, emergencies and medical visits, ambulatory procedures, and outpatient therapeutics (Figure 1).
- A total of 78 complications, grouped in five classes, were analyzed, and a mean cost per complication type was calculated: respiratory, splenic, hepatic, cardiovascular and hemorrhagic (Table 2).

Table 1. Resource use for the follow-up of patients with ASMD type A/B or B – average number per patient per year.

	Average number per patient per year
Hospitalizations	0.06
Emergency room visits without hospitalization	0.16
Medical visits	
Pediatrics/Internal Medicine	3.38
Other medical specialties	5.41
Nutrition	0.73
Psychology	0.50
Ambulatory procedures	
Blood count	2.88
General biochemical evaluation	2.88
Lipid profile	2.38
Thyroid function	1.16
Hormonal evaluation	0.75
Respiratory function tests	1.44
Electrocardiogram	1.00
Echocardiogram with Döppler study	0.75
Chest X-ray	1.13
High resolution chest CT scan	0.63
Hand and wrist X-ray	0.09
Upper abdominal ultrasound	1.00
MRI of the upper abdomen	0.25
Osteodensitometry	0.59
Growth hormone	0.13
Outpatient therapeutics	% of patients
Statins	28.8%
Vitamin D	67.5%
Flu vaccination	67.5%
Angiotensin-converting enzyme inhibitors	4.4%
Potassium-sparing diuretics	0.6%
Antibiotics	61.3%
Beta-adrenergic blockers	5.6%
Bronchodilators	35.8%
Oxygen therapy	10.0%

Figure 1. Average annual follow-up cost per patient.

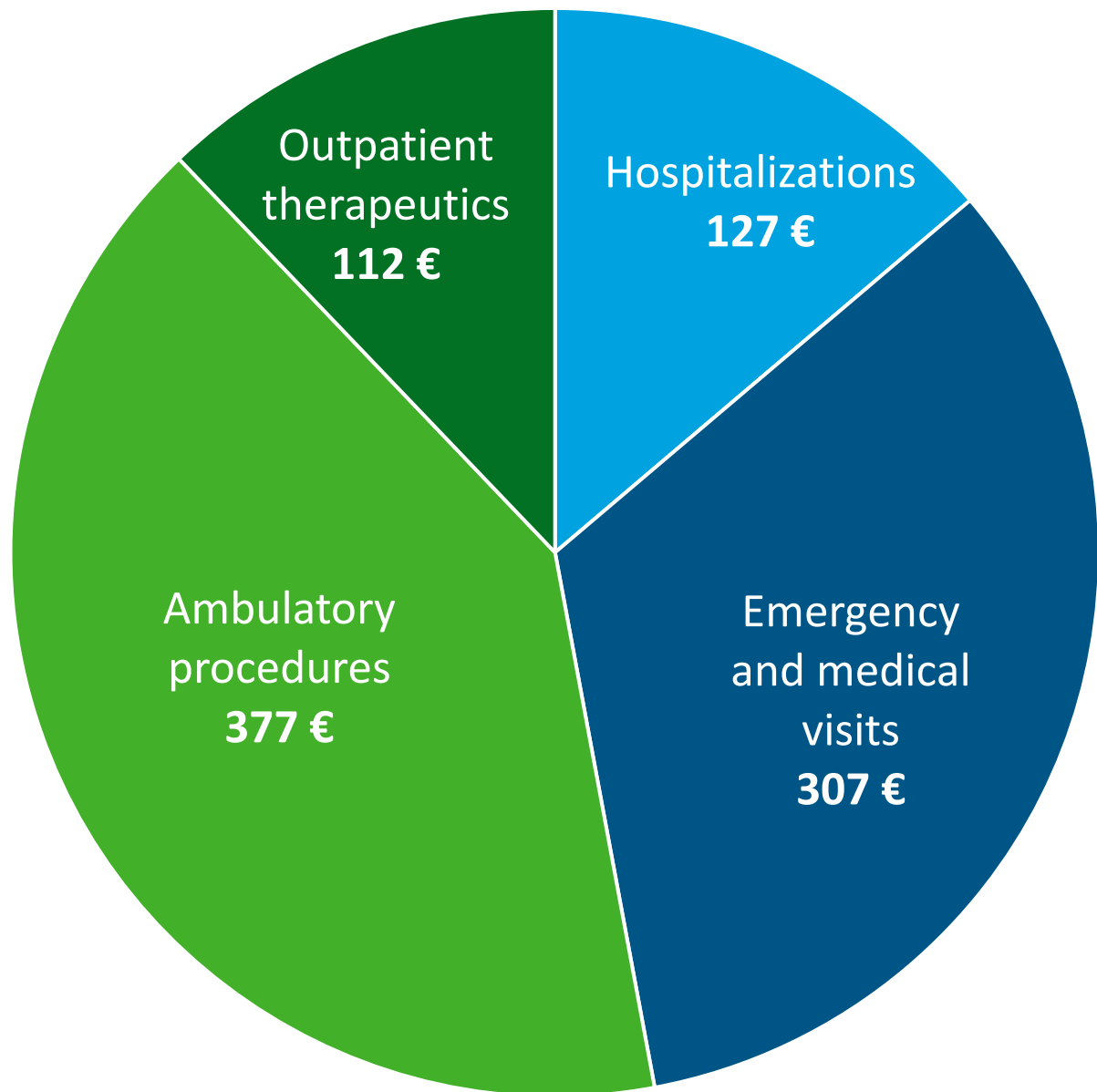


Table 2. Weighted cost per complication.

Complication	Complications with largest weighting	Total weighted cost (€)
Respiratory	Epistaxis	823 €
	Cough	
	Interstitial lung disease	
Splenic	Hepatosplenomegaly	1,786 €
	Hypersplenism	
	Splenic hematoma	
Hepatic	Hepatosplenomegaly	1,283 €
	Jaundice	
	Cholelithiasis	
Cardiovascular	Mitral valve insufficiency	3,668 €
	Aortic valve insufficiency	
	Sinus tachycardia	
	Tricuspid valve insufficiency	
Hemorrhagic	Presence of haematomas	124 €
	Gingival bleeding	
	Petechiae	

Conclusions

ASMD is a rare disease, therefore, data to characterize disease treatment is scarce. This study provides some insights on patient management, including disease complications, and estimates costs associated with ASMD in Portugal. The results show that, on average, the yearly follow-up for a patient with ASMD costs is 923 €. Additionally, the cost per complication type is 824 € (respiratory), 1,786 € (splenic), 1,283 € (hepatic), 3,668 € (cardiovascular) and 124 € (hemorrhagic).

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