BURDEN OF DISEASE IN HEREDITARY TRANSTHYRETIN AMYLOIDOSIS WITH POLYNEUROPATHY IN SPAIN

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INTRODUCTION

- Hereditary transthyretin amyloidosis with polyneuropathy (ATTRv-PN) is a progressive, debilitating, systemic and life-threatening disease.[1]
- Patients suffer from debilitating symptoms such as paresthesia, neuropathic pain, dysautonomia, progressive weakness, and functional loss, which severely affect their quality of life and autonomy.[2,3]
- Diagnosis is often delayed by 3-4 years due to phenotypic variability, sporadic onset, and low clinical suspicion.[1] This delay negatively affects prognosis and reduces treatment effectiveness.[2]

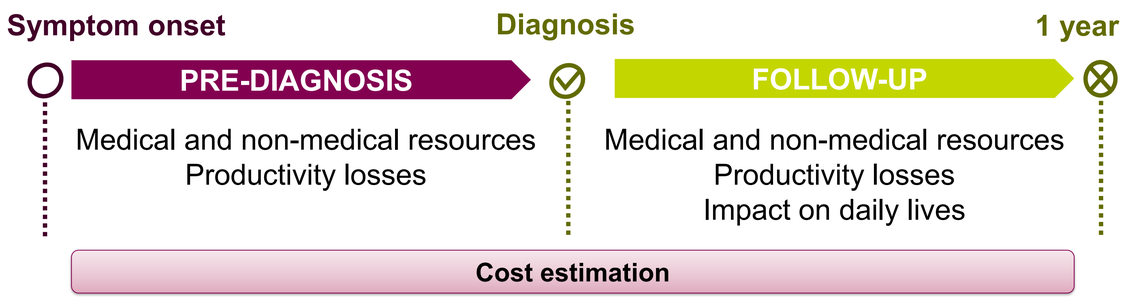
OBJECTIVE

- To estimate direct, indirect, and intangible costs of ATTRv-PN in Spain from societal, National Healthcare System (NHS), patient, and caregiver perspectives.

METHODS

- A prevalence Excel-based model was developed to estimate direct, indirect and intangible costs associated with pre-diagnosis (from symptom onset to diagnosis) and follow-up (one year) of ATTRv-PN (Figure 1).

Figure 1: Model design



- Model inputs were derived from published literature, a market research survey of Spanish patients and caregivers, and were validated by experts.
- The **prevalent population** was estimated from the Spanish adult population, using prevalence data weighted according to endemic and non-endemic zones.[4-9]
- **Direct medical costs** during each phase (pre-diagnosis and 1-year follow-up) were estimated based on the mean number of visits and tests (laboratory, imaging and neurophysiologic), the mean length of hospital stays, and corresponding unit costs.[10] Pharmacological costs were not included.
- **Direct non-medical** costs were estimated based on the average distance travelled by patients for each visit and test, the type of transportation used (car, taxi, bus, or ambulance), and the cost per kilometre for each mode.[11-13]
- **Indirect costs** Indirect costs were calculated from productivity losses, measured in days of sick leave or medical-related absenteeism among employed patients and their caregivers, multiplied by the cost per workday.[14]
- **Intangible costs**, estimated using a willingness to pay (WTP) approach, captured the disease's impact on patients' and caregivers' daily lives (Figure 2).
- Results were expressed as total costs for the prevalent population and mean cost per patient (€,2025).

RESULTS

- Patients with ATTRv-PN was estimated at 746 and 35% of them need caregiver.

PRE-DIAGNOSIS

- Based on the survey data, the mean time from symptom onset to diagnosis was estimated to be 2.5 years (median: 2; IQR: 1-3).
- Direct medical costs were estimated at €4,569,876 (€6,126/patient; 38% visits, 24% tests, 39% hospitalizations) (Table 1).
- Direct non-medical costs were estimated to be €325,820 (€437/patient) (Table 1).
- Indirect costs were estimated at €327,609 (€439/patient) (Table 1).

1-YEAR FOLLOW-UP

- Direct medical costs were estimated at €2,455,689 (€3,292/patient; 60% visits, 9% tests, 32% hospitalizations) during 1-year of follow-up
- Direct non-medical costs associated to the transport of patient to visits and tests were estimated at €243,299 (€326/patient).
- Indirect costs were estimated at €640,376 (€858/patient) in 1-year of follow-up.
- ATTRv-PN symptoms caused the greatest impact on patients' daily lives, reflected in significant intangible costs (€440,182; €590/patient). For caregivers, the emotional burden accounted for the highest intangible costs (€174,067; €667/caregiver).

Figure 2: WTP associated with the disease impact on patients and caregivers.

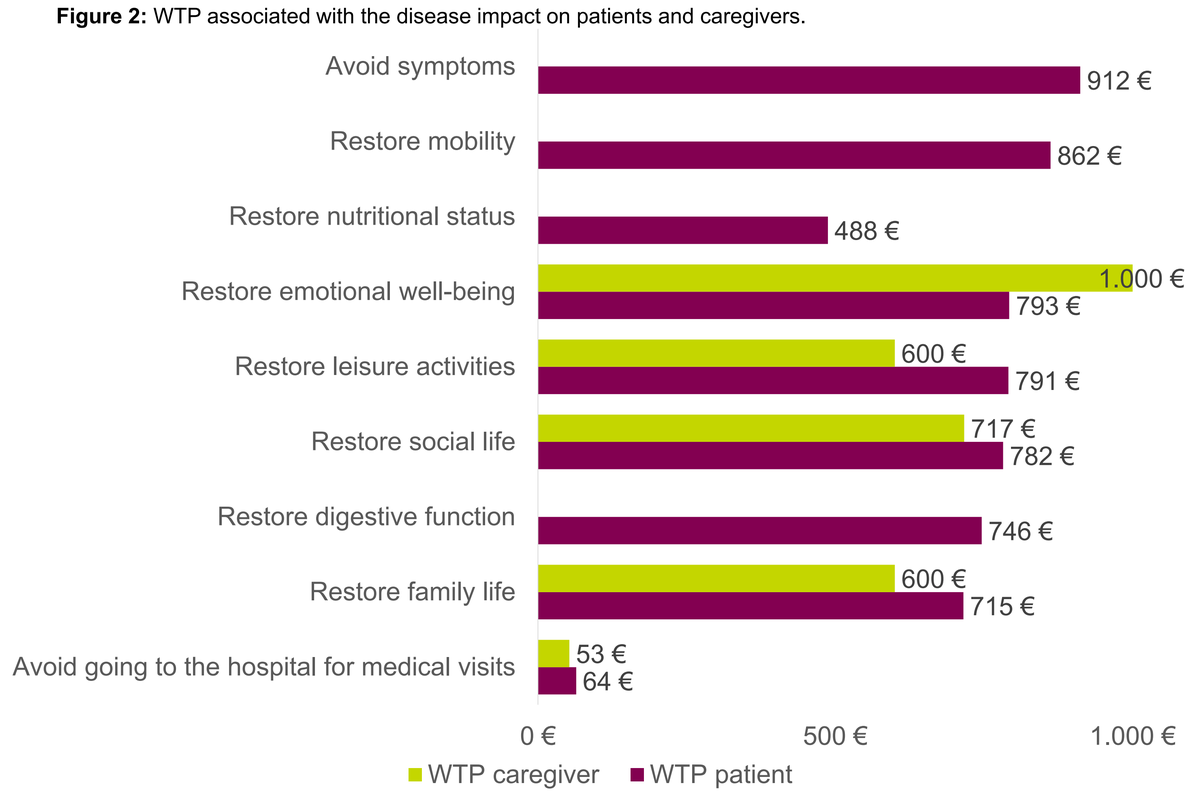


Table 1: Costs estimated in each phase.

	Pre-diagnosis		1-year follow-up	
	Cumulative	**Per patient**	**Cumulative**	**Per patient**
Visits	€1,718,106	€2,303	€1,461,192	€1,959
Tests	€1,082,532	€1,451	€210,807	€283
Hospitalization	€1,769,238	€2,372	€783,690	€1,051
Direct healthcare costs	**€4,569,876**	**€6,126**	**€2,455,689**	**€3,292**
Direct non-healthcare costs	**€325,820**	**€437**	**€243,299**	**€326**
Loss of productivity-patient	€327,609	€439	€640,376	€858
Loss of productivity-caregiver	--	--	€95,238	€128
Indirect costs	**€327,609**	**€439**	**€735,614**	**€986**
Intangible costs-patient	**--**	**--**	€3,074,993	€4,122
Intangible costs-caregiver	**--**	**--**	€579,934 €	€2,221
Intangible costs	--	--	**€3,654,927**	**€4,899**
Total costs	**€5,223,305**	**€7,002**	**€7,089,529**	**€9,503**

LIMITATIONS

Pharmacological costs were not included in the analysis, and intangible costs were only considered in the follow-up, not in the pre-diagnosis phase, so the total economic burden of the disease may be underestimated.

CONCLUSIONS

- **ATTRv-PN imposes a substantial social and economic burden on Spanish NHS, and a significant impact on patients' and caregivers' daily lives.**
- **The high pre-diagnosis costs reveal the impact of diagnostic delays and emphasize the need for early diagnosis and comprehensive care.**
- **These findings provide valuable insights that can inform health policy and resource allocation to improve ATTRv-PN care.**

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Conflict of interest

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