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Understanding costs and health utilities in relation to symptom burden in a large European survey of patients with central disorders of hypersomnolence

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Background

- Narcolepsy type 1 (NT1), narcolepsy type 2 (NT2), and idiopathic hypersomnia (IH) are rare central disorders of hypersomnolence (CDH) characterised by excessive daytime sleepiness, cataplexy (NT1 only) and/or excessive need for sleep (IH).[1-3]
  - In Europe, narcolepsy prevalence estimates range from 22.2 to 39.7 per 100,000 individuals.[4-6]
  - Prevalence estimates for IH are difficult to determine due to an absence of biomarkers and lack of a clear consensus on diagnostic criteria.[7,8]
- Narcolepsy and IH are treated with behavioural interventions and pharmacological therapies.[2,3,9]
- Currently, little evidence is available on the health and economic consequences of CDH related to disease severity.

Objectives

- To estimate resource utilisation, costs and health utilities relative to symptom severity in NT1, NT2 and IH across 6 European countries.

Methods

Study design

- A cross-sectional, quantitative, observational survey study conducted in France, Germany, Italy, Sweden, Switzerland and the United Kingdom.

Participants

- Adults (≥18 years of age) with a self-reported diagnosis of NT1, NT2 or IH were recruited through specialist clinics, patient associations and disease registries.
- Participants enrolled in another clinical study were excluded.

Data collection

- One-year retrospective data were self-reported via a postal- or web-based questionnaire at a single time point during a period of 8 months.
- Data were collected on:
  - Clinical symptoms using validated scales (Epworth Sleepiness Scale [ESS], Narcolepsy Severity Scale [NSS-CT], IH Severity Scale [IHSS]).
  - Health-related quality of life using the EuroQoL-5 Dimensions-5 Levels (EQ-5D-5L).
  - Self-reported resource utilisation and work productivity.

Estimating costs and utilities

- Resource utilisation was annualised and multiplied with country-specific price vectors. For pooled analyses, costs were converted to Euros (€) using current exchange rates.
- Utility values were calculated from EQ-5D scores using published country-specific tariffs.

Developing disease severity groups

- Responses from participants who self-reported a diagnosis of NT1, NT2 or IH were analysed.
- To explore how disease severity impacts costs and utilities, we first constructed a linear composite of (standardised) total costs and health utilities using a principal component analysis. This composite explains the maximum amount of variability in both costs and utilities.
- Linear regression was used to model the composite of total costs and health utilities, including measures of symptom severity as well as demographic variables as explanatory variables. A stepwise approach was taken to variable inclusion, using AIC to select the optimal model.
- The final model was used to predict a score for each individual participant using the actual symptom severity values for each, but imputing sample means for other explanatory variables.
- Participants were divided into quintiles based on the model-predicted values, representing 5 groups of increasing severity.

Results

Participants

- 1,818 participants completed online (81%) or postal (19%) surveys. The mean age was 37.5 years (range 18–93) and 71% were female.
- Characteristics for the 1,818 participants who self-reported a CDH diagnosis across the 6 countries are shown in **Table 1**.

Table 1. Participant characteristics

	NT1 (n=929)	NT2 (n=204)	IH (n=362)	Other hypersomnolence (n=323)
Female, n (%)*	645 (69.5)	135 (66.5)	290 (80.1)	106 (65.8)
Treated, n (%)†	714 (91.3)	147 (84.5)	247 (79.4)	69 (60.5)
	Mean (range), years			
Age‡	37.0 (18–89)	39.9 (18–90)	36.7 (18–79)	39.5 (18–93)
Age at onset§	18.8 (0–65)	20.6 (1–73)	19.7 (0–56)	22.2 (0–60)
Age at diagnosis‖	25.6 (0–80)	29.6 (10–77)	29.4 (9–62)	30.5 (4–62)
	Mean (IQR)			
ESS total score¶	15.5 (12–19)	14.4 (11–18)	13.6 (10–17)	16.1 (14–19)
NSS-CT total score#	21.3 (14–28)	14.5 (9–20)	12.1 (7–17)	19.3 (13–25)
IHSS total score**	27.0 (20–34)	27.5 (22–35)	32.4 (27–38)	30.9 (24–38)
Cognitive impact††	5.7 (4–8)	5.7 (4–7)	6.0 (5–7)	6.6 (5–8)
Fatigue impact‡‡	6.8 (6–8)	6.8 (5–8)	7.3 (6–9)	7.4 (6–9)
Nap time, minutes§§	33.2 (20–40)	34.1 (20–35)	69.9 (30–90)	50.4 (20–60)
Daytime sleepiness‖‖	6.7 (5–8)	6.0 (5–7)	6.8 (6–8)	6.7 (5–8)
Country of residence, n (%)				
France	231 (24.9)	70 (34.3)	208 (57.5)	134 (41.5)
Germany	126 (13.6)	36 (17.6)	23 (6.4)	32 (9.9)
Italy	130 (14.0)	39 (19.1)	28 (7.7)	48 (14.9)
Sweden	266 (28.6)	22 (10.8)	32 (8.8)	55 (17.0)
Switzerland	81 (8.7)	13 (6.4)	35 (9.7)	18 (5.6)
United Kingdom	95 (10.2)	24 (11.8)	36 (9.9)	36 (11.1)

IQR, interquartile range. Percentages of participants are based on the total number of patients with CDH diagnoses. *n=928/203/362/161. †n=782/174/311/114. ‡n=926/203/361/152. §n=822/179/325/121. ‖n=826/181/324/118. ¶n=849/182/329/124. #n=621/141/262/82; maximum score for participants with NT2 or IH was lower than NT1, as they do not experience cataplexy. **n=649/155/281/98. ††n=756/170/297/109. ‡‡n=759/172/299/110. §§n=828/181/324/122. ‖‖n=921/204/362/131.

Disease severity groups

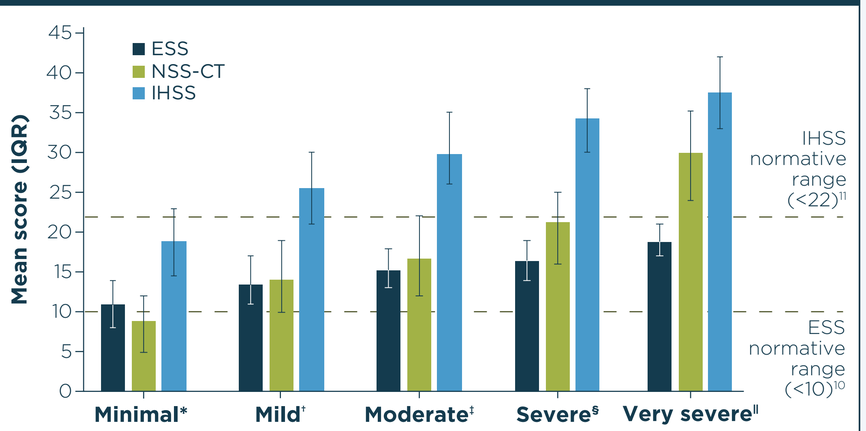
- Separation of the pooled study population into 5 disease severity groups was based on the linear regression model. Model coefficients are shown in **Table 2**.
- **Figure 1** shows the 5 disease severity groups across the validated clinical scales.

Table 2. Linear regression model coefficients for disease severity groups

	Estimate (SE)	t value	Pr(>|t|)
Intercept	−2.108 (0.179)	−11.78	P≤0.001
Cognitive impact	0.081 (0.014)	5.83	P≤0.001
Age at diagnosis	0.016 (0.004)	4.17	P≤0.001
ESS total	0.099 (0.025)	4.05	P≤0.001
NSS-CT total	0.014 (0.005)	2.97	P<0.01
Fatigue impact	0.034 (0.014)	2.39	P<0.05
Age of onset*	−0.009 (0.004)	−2.02	P<0.05
Nap time	0.001 (0.001)	1.91	0.057
Disturbed nighttime sleep	0.077 (0.041)	1.88	0.061
Daytime sleepiness	0.156 (0.098)	1.59	0.113

Residual SE, 0.9425 on 767 degrees of freedom. Multiple R-squared, 0.321; adjusted R-squared, 0.3131. F-statistic, 40.3 on 767 and 9 DF; P-value, 0.0000. *Item from NSS-CT.

Figure 1. Clinical burden in participants with NT1, NT2 and IH by disease severity group

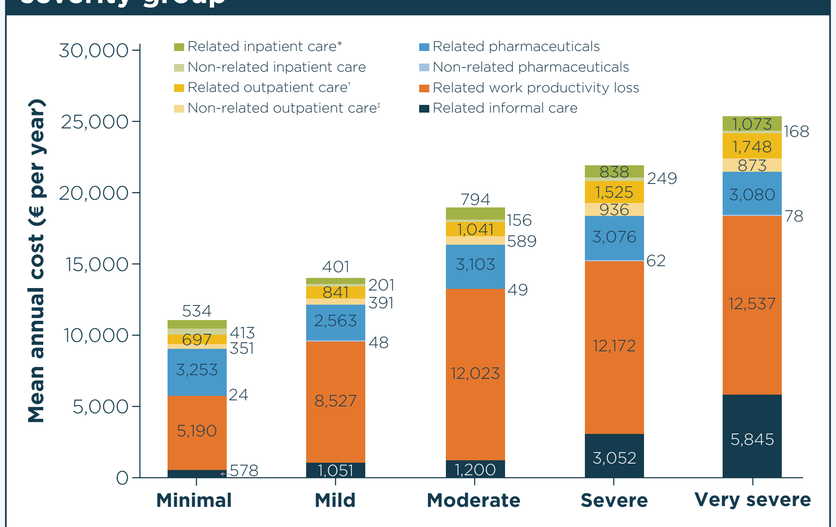


IQR, interquartile range. Data shown are based on the weighted combination of costs and utilities. NSS-CT does not have a normative range. *n=219/219/211. †n=217/219/209. ‡n=217/219/210. §n=217/219/205. ‖n=218/220/210.

Resource utilisation, total costs and utilities

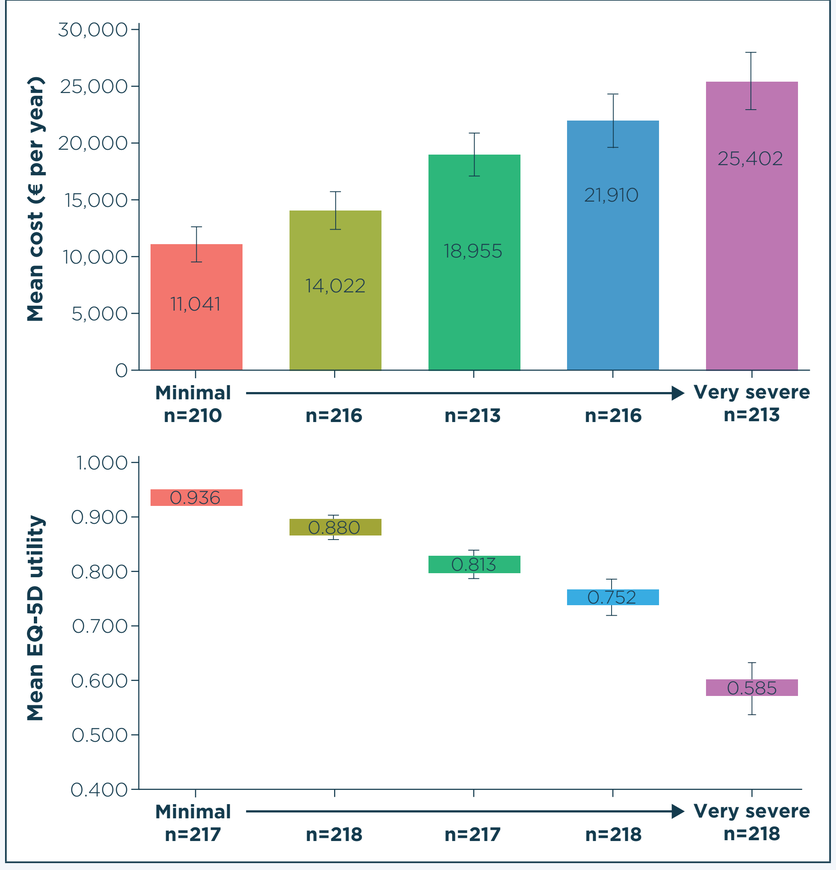
- Work productivity losses accounted for the highest annual costs across all disease severity groups (**Figure 2**).
- Higher costs and lower EQ-5D utility scores were associated with increases in residual symptoms, including excessive daytime sleepiness and overall disease severity, in participants with NT1, NT2 and IH (**Figure 3**).
- Total costs ranged from €11,041 per year in the mildest group to €25,402 in the most severe group, while utilities ranged from 0.936 to 0.585, respectively.

Figure 2. Resource utilisation costs by disease severity group



IQR, interquartile range. *Includes inpatient care and diagnostic procedures. †Includes outpatient care and diagnostic procedures, emergency room and daycare. ‡Includes outpatient care and diagnostic procedures.

Figure 3. Total costs and utilities by disease severity group for participants with NT1, NT2 and IH



Conclusions

- **This was the first study to describe the link between residual symptom burden, costs and utilities in a large European survey of people with NT1, NT2 and IH treated in routine care.**
- **Despite the majority of participants being treated, increasing disease severity, as defined by this study, was associated with increased total costs and decreased EQ-5D utility scores.**
- **Study limitations include a cross-sectional design, convenience sample, largely treated participants, no control group, and all data and diagnoses were self-reported.**
- **This study will support future modelling of the impact on costs and utilities from new therapies in NT1, NT2 and IH.**

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