

Unmet Needs for Insomnia Patients - Humanistic Burden in Europe

Joana E. Matos,¹ François-Xavier Chalet,² Cédric Vaillant,² Graeme Roberts²
¹Kantar Health, New York, United States, ²Idorsia Pharmaceuticals Ltd, Allschwil, Switzerland

Introduction

- The diagnosis of DSM-5 insomnia disorder includes the following criteria: (1) dissatisfaction with sleep quality or quantity; (2) complaint of one or more of the following sleep difficulties: difficulty initiating sleep, difficulty maintaining sleep, early morning awakening, or a nonrestorative sleep; (3) significant distress or interference with personal functioning in daily living caused by the sleep difficulty; (4) the sleep difficulty occurs at least three times a week; (5) the sleep difficulty is present for at least 3 months; and (6) the sleep difficulty occurs despite adequate opportunity and circumstances for sleep
- Insomnia is a highly prevalent condition, with >30% of adults worldwide experiencing symptoms of insomnia, >10% experiencing daytime impairment due to insomnia, and approximately 6% experiencing insomnia disorders lasting ≥1 month.¹⁻³ Prevalence estimates of insomnia disorder in Europe vary from 5.7% in Germany to 19.0% in France^{4,5}
- In the long term, insomnia disorder is associated with numerous serious health conditions, such as psychiatric disorders, cardiovascular diseases, and reduced quality of life⁶

Study Objective

- To assess the humanistic burden of insomnia disorder in treated and untreated patients in Europe (United Kingdom [UK], Germany, France, Spain, Italy), using real-world data

Methods

Design

- A retrospective, cross-sectional survey
- Study sample was identified from the 2020 Europe National Health and Wellness Survey (NHWS) (France, Germany, Italy, Spain, and the UK)

Data source

- The NHWS is a large, nationally representative, self-administered, internet-based general health survey
- All respondents were aged 18 or older, consented to participate in the survey, and could read and write in the primary language of the country at the time of the survey
- NHWS respondents are identified primarily through existing general-purpose (i.e., not healthcare-specific), web-based consumer panels
- Targeted sampling is used to ensure the demographic composition of the NHWS sample is representative of the corresponding adult population in each of the five European countries with respect to gender and age
- The 2020 Europe NHWS protocol and questionnaire were reviewed by Pearl Institutional Review Board (Indianapolis, IN, USA; 19-KANT-204) and granted exemption status

Study sample

The following questions were used to identify respondents for the study sample:

- "Which of the following [conditions (e.g., condition=insomnia)] have you experienced in the past twelve months?"
- "Which of your [conditions listed below (e.g., condition=insomnia)] have been diagnosed by a physician?"
- "Which of your [conditions listed below (e.g., condition=insomnia)] do you currently use a prescription medication to treat?"

Inclusion criteria

- Experienced insomnia in past 12 months

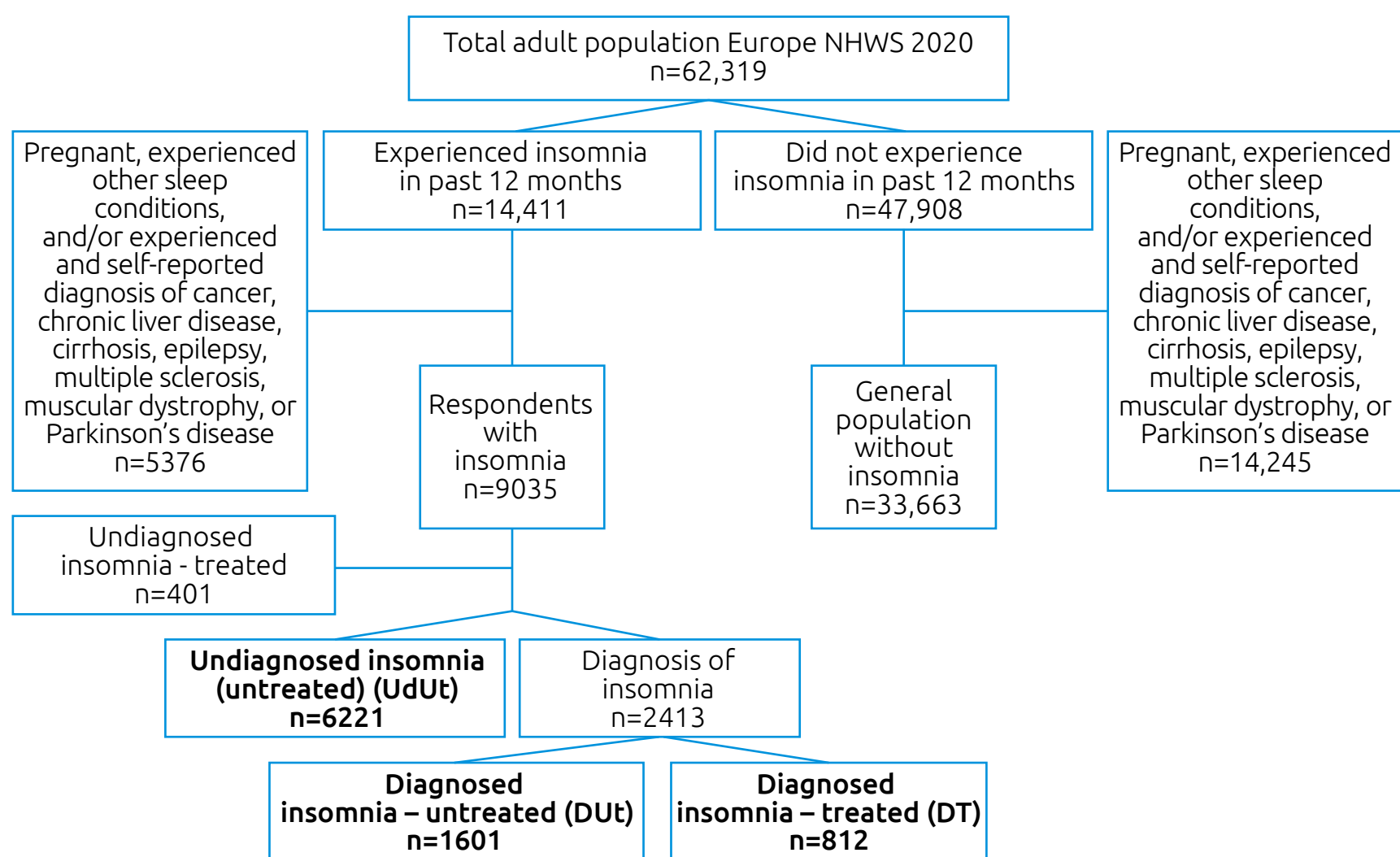
Exclusion criteria

- Experienced or diagnosed with narcolepsy, sleep apnea, or other sleep difficulties (other than insomnia, narcolepsy, or sleep apnea) in the past 12 months; and/or
- Experienced and self-reported diagnosis of another serious condition (any type of cancer, chronic liver disease, cirrhosis, epilepsy, multiple sclerosis, muscular dystrophy, Parkinson's disease); and/or
- Currently pregnant

Study cohorts (Figure 1)

- Self-report of a physician diagnosis of insomnia (herein 'diagnosed') and treated with prescription medication (DT)
- Diagnosed insomnia and not treated with prescription medication (DUT)
- Not diagnosed with insomnia ('undiagnosed') and not treated with prescription medication (UdUt)

Figure 1 Study sample from the 2020 Europe NHWS



Abbreviations: DT, diagnosed treated; DUT, diagnosed untreated; NHWS, National Health and Wellness Survey; UdUt, undiagnosed untreated

Study measures

Patient characteristics:

- Socio-demographics: age, sex, marital status, education, employment status
- Health behaviors: smoking, exercise
- Health status:
 - Body mass index (BMI)
 - Charlson Comorbidity Index (CCI)⁷
 - Self-reported medical diagnosis of
 - Anxiety
 - Depression
 - Pain conditions (diabetic neuropathic, fibromyalgia, headache, migraine, general pain)
 - Post-traumatic stress disorder (PTSD)

Insomnia-related factors:

- Time since first experience (months)
- Time since diagnosis (months); among those with a diagnosis)
- Days experienced insomnia in past 12 months
- Insomnia Severity Index (ISI)
 - No clinically significant insomnia (score = 0–7)
 - Subthreshold insomnia (score = 8–14)
 - Clinical insomnia (moderate severity) (score = 15–21)
 - Clinical insomnia (severe) (score = 22–28)

- Health status: EuroQol-5 Dimensions 5-level (EQ-5D-5L)⁸ is a self-reported current health status index. Higher scores on the EQ-5D-5L indicate better health-related quality of life (HRQoL). The EQ-5D-5L is comprised of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression

Statistical analyses

- Patient demographic and clinical characteristics were described using frequencies and percentages for categorical variables and means and standard deviations (SD) for continuous variables
- Bivariate analyses of respondent characteristics, insomnia-related factors and health status were evaluated by chi-square tests for categorical variables and ANOVA for continuous variables
- Multivariable analyses were conducted on the sub-group of patients with diagnosed insomnia to examine the health status burden according to ISI category (reference=no clinically significant insomnia). Generalized linear models specifying a normal distribution and identity function, adjusted for confounding factors: country, age, gender, marital status, education, employment status, smoking status, alcohol consumptions, BMI, self-reported medical diagnosis of anxiety, depression, or PTSD, self-reported medical diagnosis of a pain condition, CCI, and days experiencing insomnia in past 12 months

Results

Study sample characteristics

- Across the five European countries studied, 9035 respondents (14.5%) reported experiencing insomnia in the past 12 months, of which 26.7% (n=2413) had a diagnosis of insomnia and 68.9% (n=6221) did not (UdUt) (**Figure 1**)
- In the study sample of 8634 respondents, 27.9% (n=2413) reported having a diagnosis. Among these patients with diagnosed insomnia, 33.7% (n=812) were treated with prescription medication (DT), 66.3% (n=1601) were not treated with prescription medication (DUT) (**Figure 1**)
- The average age in the study was 45.7±16.0 (UdUt), 48.0±16.0 (DUT), and 50.5±15.0 (DT) (**Table 1**)
- Approximately two-thirds of respondents with insomnia were female, more than half were married or living with a partner and did not have a university degree (**Table 1**)
- Over one-third of respondents with a diagnosis of insomnia reported current smoking (DT=39.8%; DUT=33.5%) compared with 27.9% of those without a diagnosis of insomnia (**Table 1**)
- The CCI was 0.46±0.84 and 0.40±0.77 in the diagnosed groups compared to 0.22±0.58 in the undiagnosed group (**Table 1**), denoting a lower comorbidity level in the undiagnosed
- Diagnoses of anxiety, depression, pain, and PTSD were substantially less prevalent in UdUt than DT patients (p<0.001) (**Figure 2**). Among those with diagnosed insomnia, differences were observed for anxiety (DUT 42.6% vs DT 49.9%; p=0.001) and for PTSD (DUT 3.4% vs DT 5.5%; p=0.011), with similar percentages of patients with depression and pain

Insomnia-related factors

- Insomnia severity differed by respondent group (**Figure 3**)
 - A higher proportion of DT (50.9%) had moderate to severe insomnia (ISI≥15), when compared with DUT (43.8%) or UdUt (25.1%)
 - Distributional differences were observed within the insomnia-diagnosed groupings (p=0.012)
- On average, DT patients reported a longer experience with insomnia than the DUT or UdUt groups (10.6, 8.3, and 6.1 years respectively; p<0.001 for each group in comparison with DT) (**Table 2**)
- Time from diagnosis was 11.0 years for the treated group and 9.6 years for the untreated group (p<0.001) (**Table 2**)
- On average, DT patients had experienced significantly more 246.5±136.6 days of insomnia in the previous 12 months compared with DUT (201.0±137.7 days) and UdUt (144.0±133.7 days) (p<0.001) (**Table 2**)

Conclusions

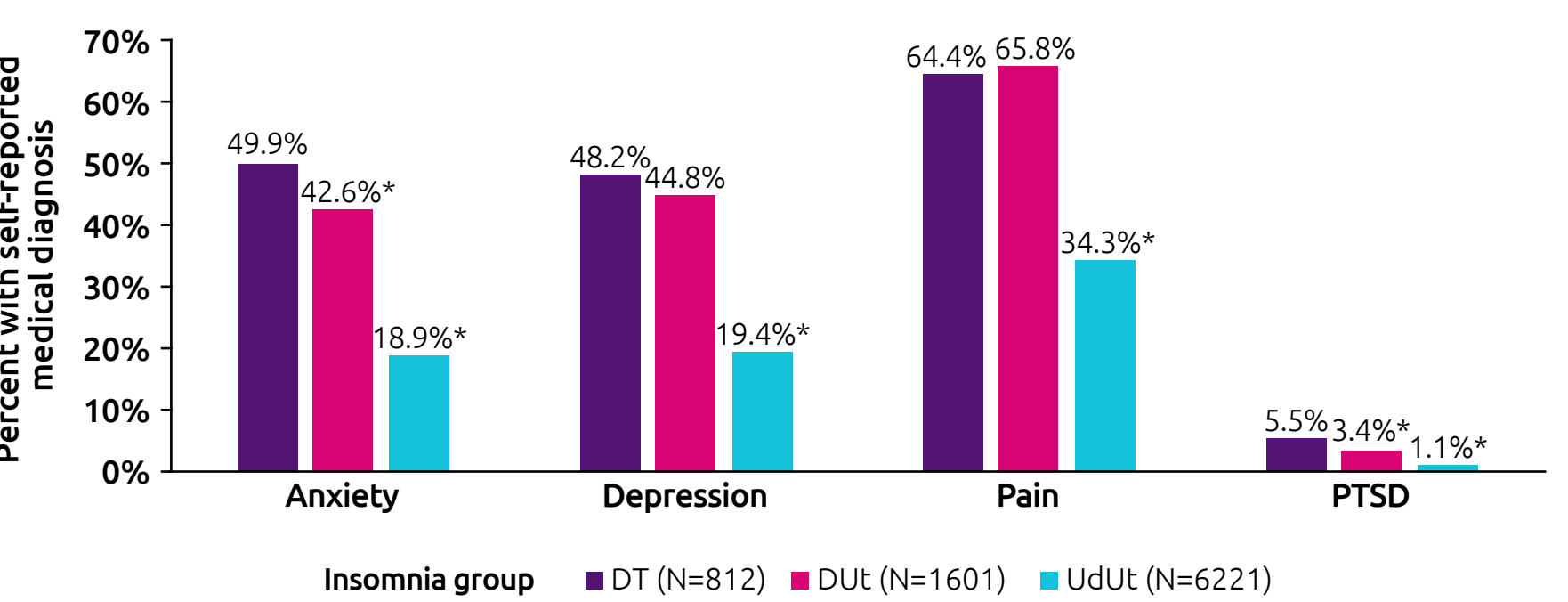
- Insomnia is reported in 14.5% of this representative sample from five large European countries, of which most did not receive pharmacological treatment
- In Europe, a large percentage of patients continue experiencing moderate to severe insomnia (based on the ISI) despite treatment
- The humanistic burden of insomnia disorder is significantly related to disease severity and not treatment status
- The health status of patients is significantly impaired as a result of their self-reported insomnia severity
- The results indicate an unmet need for better management, such as improved treatments to reduce the impact of insomnia on the lives of patients

Table 1 Characteristics of respondents with insomnia: 2020 Europe NHWS (N=8634)

	DT (N=812)		DUT (N=1601)		UdUt (N=6221)	
	n/mean	%/SD	n/mean	%/SD	n/mean	%/SD
Age, years	50.5	15.0	48.0	16.0	45.7	16.0
Female	503	61.9%	1064	66.5%	4041	65.0%
Marital status ^a						
Married/living with partner	513	63.2%	924	57.7%	3628	58.3%
Single/divorced/separated/widowed	299	36.8%	671	41.9%	2564	41.2%
Education ^b						
≥4-year university degree ^c	329	40.5%	636	39.7%	2826	45.4%
<4-year university degree ^c	474	58.4%	941	58.8%	3338	53.7%
Employment status						
Employed full- or part-time/self-employed	432	53.2%	868	54.2%	3679	59.1%
Not employed	181	22.3%	380	23.7%	1421	22.8%
Retired	199	24.5%	353	22.0%	1121	18.0%
Smoking status						
Current smoker	323	39.8%	536	33.5%	1733	27.9%
Former smoker	220	27.1%	437	27.3%	1747	28.1%
Never smoked	269	33.1%	628	39.2%	2741	44.1%
Alcohol consumption						
None	235	28.9%	437	27.3%	1319	21.2%
<4 times per week	478	58.9%	996	62.2%	4056	65.2%
≥4 times per week	99	12.2%	168	10.5%	846	13.6%
BMI, kg/m ²	26.1	5.6	26.0	6.0	25.4	5.7
CCI	0.46	0.84	0.40	0.77	0.22	0.58

Abbreviations: BMI, body mass index; CCI, Charlson Comorbidity Index; DT, diagnosed treated; DUT, diagnosed untreated; NHWS, National Health and Wellness Survey; SD, standard deviation; UdUt, undiagnosed untreated.
^aRespondents who declined to answer comprised: ≤0.5% for marital status; ≤1.5% for education; ^bThe category "4-year university degree or higher" groups "University degree complete" and "Higher than University degree (postgraduate, Master's etc)" levels; ^cThe category "less than 4-year university degree" groups "Less than secondary school" and "Secondary school complete" levels

Figure 2 Anxiety, depression, and pain among respondents with insomnia: 2020 Europe NHWS (N=8634)



Abbreviations: DT, diagnosed treated; DUT, diagnosed untreated; PTSD, post-traumatic stress disorder; UdUt, undiagnosed untreated
*In comparison to respondents in the DT group at p≤0.001

Table 2 Insomnia-related characteristics of respondents with insomnia: 2020 Europe NHWS (N=8634)

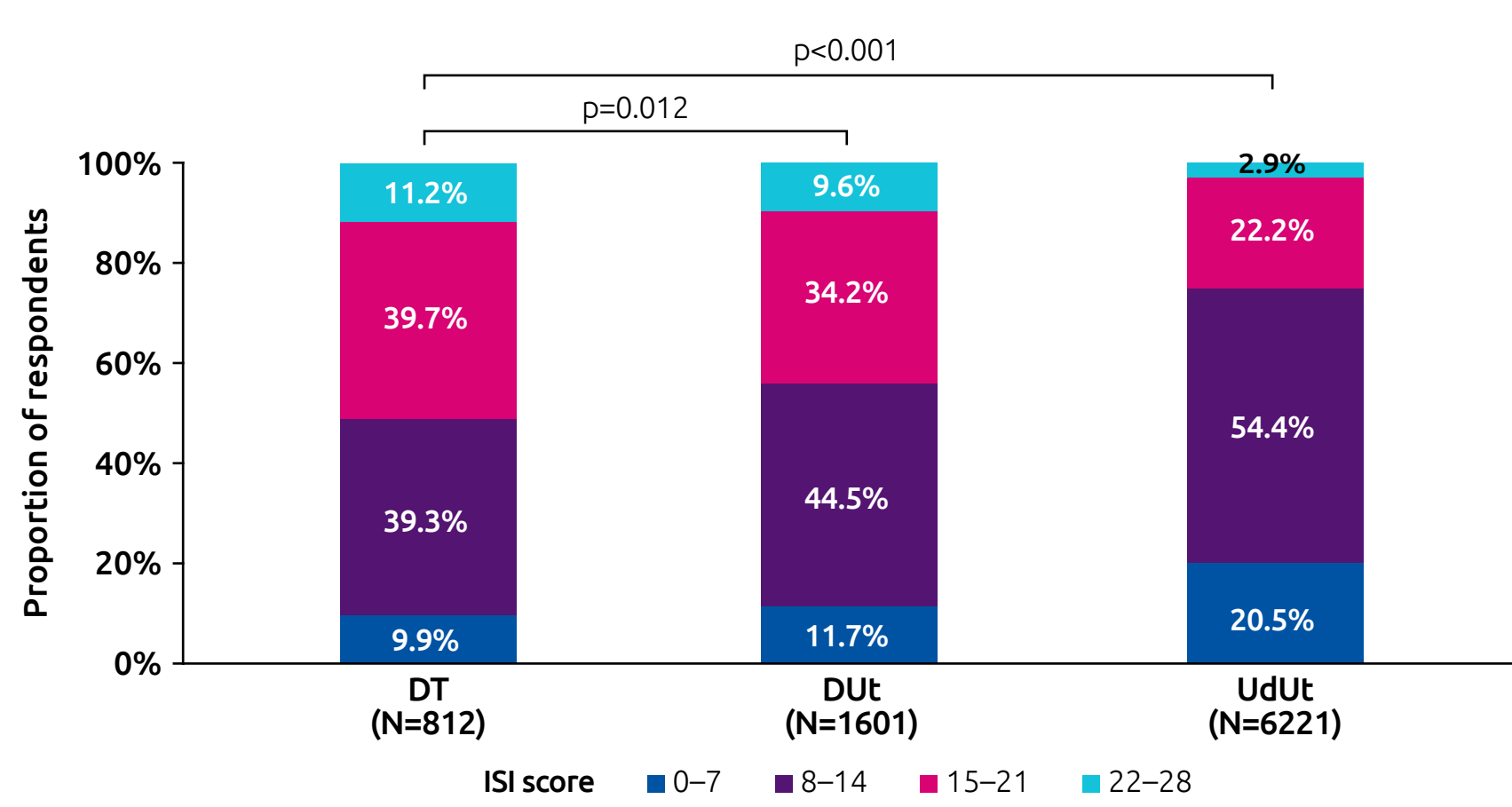
	DT (N=812) mean±SD	DUT (N=1601) mean±SD	UdUt (N=6221) mean±SD	p-value
Insomnia - time since first experienced (years)	10.6±11.0	8.3±10.1	6.1±8.6	<0.001
Insomnia - time since diagnosis (years)	11.0±10.3	9.6±10.8	n/a	<0.001
Insomnia - total days experienced in last 12 months	246.5±136.5	201.0±137.7	144.0±133.7	<0.001

Abbreviations: DT, diagnosed treated; DUT, diagnosed untreated; n/a, not applicable; NHWS, National Health and Wellness Survey; SD, standard deviation; UdUt, undiagnosed untreated

Strengths and Limitations

- The NHWS is a nationally representative patient-reported outcome survey across five major countries in Europe
- While the NHWS is broadly representative of the adult population for the corresponding five European countries, these data may not be representative of the population with insomnia
- The NHWS is a cross-sectional study, thus causality cannot be inferred
- All data in this study are self-reported; therefore, responses are subject to recall bias and cannot be verified by a third party (e.g., medical chart)

Figure 3 Insomnia severity of respondents with insomnia: 2020 Europe NHWS (N=8634)

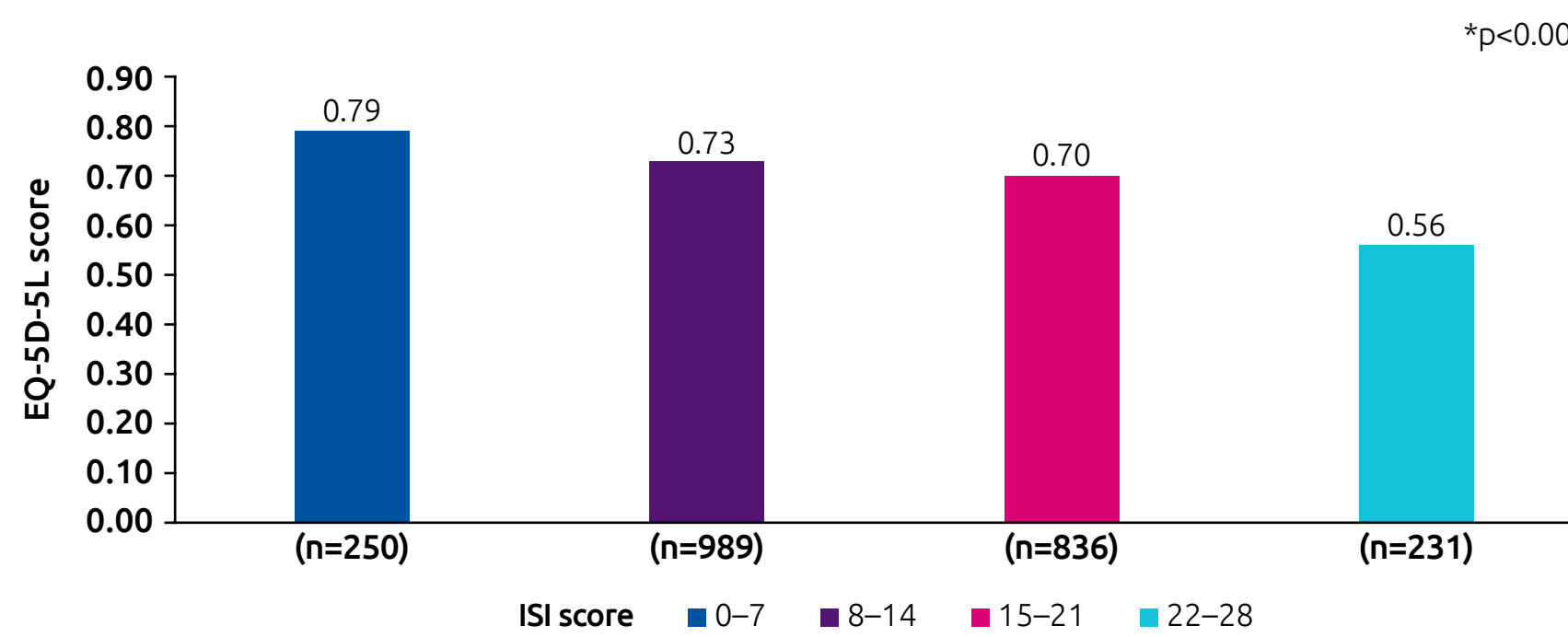


Abbreviations: DT, diagnosed treated; DUT, diagnosed untreated; ISI, Insomnia Severity Index; NHWS, National Health and Wellness Survey; UdUt, undiagnosed untreated

Health status

- EQ-5D-5L scores were different across cohorts, with DT having the poorer self-reported health status (i.e., lower scores) (0.68±0.26) compared with DUT (0.72±0.24, p=0.002) or UdUt (0.80±0.19, p<0.001)
- In multivariable analyses of the association with health status and adjusting for confounding factors, diagnosis-treatment groups were not significant factors (p=0.321), whereas insomnia severity (ISI) (continuous) was significant (p<0.001)
- Among those with diagnosed insomnia, multivariable results showed a statistically significant difference in mean EQ-5D-5L scores according to ISI categories. Specifically, those with no clinically significant insomnia had a mean±standard error (SE) of 0.79±0.01, and those with severe insomnia had a mean±SE of 0.56±0.01 (**Figure 4**)

Figure 4 Adjusted mean health status by insomnia severity according to ISI categories



Abbreviations: ISI, Insomnia Severity Index.
*Adjusted means differ between all ISI groups at p<0.001.

References

- Reynolds CF, O'Hara R. *Am J Psychiatry*. 2013;170:1099–1101.
- Roth T. *J Clin Sleep Med*. 2007;3(5 Suppl):S7–S10.
- Zhang Y, et al. *Sleep Med Rev*. 2019;45:1–17.
- Léger R, et al. *J Sleep Res*. 2000;9:35–42.
- Schlack R, et al. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz*. 2013;56:740–748.
- Riemann D, et al. *J Sleep Res*. 2017;26:675–700.
- Quan H, et al. *Am J Epidemiol*. 2011;173:676–682.
- Herdman M, et al. *Qual Life Res*. 2011;20:1727–1736.

Acknowledgements

This study was supported by Idorsia Pharmaceuticals Ltd, Allschwil, Switzerland
All authors contributed to and approved the presentation; editorial and design assistance were provided by Katerina Pipili, PhD, and Matthew Weddig, of Spark Medica Inc, funded by Idorsia Pharmaceuticals Ltd