RESEARCH ARTICLE OPEN ACCESS

Suicidal Ideation and Sleep Disturbances Among People With Huntington Disease

Evidence From the HDBOI Study

Idaira Rodríguez Santana,[1] Samuel A. Frank,[2] Tiago A. Mestre,[3] Astri Arnesen,[4] Jamie L. Hamilton,[5] Hayley Hubberstey,[6] Michaela Winkelmann,[7] Elena Hernandez-Jimenez,[1] Jeff Frimpter,[8] Ricardo Dolmetsch,[9] and Talaha M. Ali[9]

Correspondence
Dr. Santana
idaira.rodriguez@primeglobalpeople.com

Neurol Clin Pract. 2025;15:e200461. doi:10.1212/CPJ.0000000000200461

Abstract

Background and Objectives

Suicidal ideation and sleep disturbances are more common among people with Huntington disease (PwHD) than otherwise healthy peers; however, the scope and magnitude of these challenges are not well understood. This study evaluated suicidal thoughts and sleep disturbances among PwHD in Europe and the United States using data from the Huntington's Disease Burden of Illness (HDBOI) study.

Methods

The HDBOI study is a cross-sectional burden-of-illness study of PwHD in France, Germany, Italy, Spain, the United Kingdom, and the United States. Eligible participants were adults (18 years and older) with motor manifest Huntington disease (HD) ≥ 12 months before study recruitment. PwHD were categorized as having early-stage (ES), mid-stage (MS), or advanced-stage (AS) HD as reported by the treating physician. Data were collected by the physician, and a voluntary questionnaire was completed by the PwHD or a caregiver. All findings were analyzed descriptively. Differences were assessed using analysis of variance or χ^2 tests.

Results

A total of 2,094 PwHD were included; 1,602 (77%) were from Europe and 492 (23%) were from the United States, with 846 (40%) with ES, 701 (33%) with MS, and 547 (26%) with AS HD. PwHD reported current (13%, n = 272) or previous (28%, n = 575) suicidal ideation, which was more common with advanced HD (ES, 11%; MS, 14%; AS, 15%; $p < 0.05$). Of 482 questionnaire respondents, 91% (n = 437) reported difficulty sleeping, which was more common with AS HD ($p < 0.05$; [$p = 0.000$]).

Discussion

The HDBOI study showed a substantial burden of suicidal ideation and sleep disturbances among PwHD, which tended to worsen with disease severity.

Introduction

Huntington disease[1] is a progressive neurodegenerative disorder characterized by declining motor symptoms and cognition that has a substantial negative impact on mental health.[2,3] People with Huntington disease (PwHD) have an estimated life expectancy of 15–20 years after diagnosis of motor symptoms.[4] Common neuropsychiatric symptoms include irritability, depressed mood, apathy, and obsessive-compulsive behaviors that can present in all

[1]Prime HCD, Knutsford, United Kingdom; [2]Harvard Medical School/Beth Israel Deaconess Medical Center, Boston, MA; [3]The Ottawa Hospital Research Institute, Ontatio, Canada; [4]4European Huntington Association, Kristiansand, Norway; [5]5CHDI Management/CHDI Foundation, New York, NY; [6]Huntington's Disease Youth Organization, Kington, United Kingdom; [7]Deutsche Huntington-Hilfe, Duisburg, Germany; [8]Integrative Life Sciences, Morristown, NJ; and [9]UniQure, Lexington, MA.

The Article Processing was funded by the uniQure.

stages of the disease and may precede motor signs.[5] Progressive decline in voluntary and involuntary movement, behavior, and functioning ultimately requires substantial caregiver support for regular care and daily activities.

Sleep and circadian disturbances are more common among PwHD than otherwise healthy peers.[6] Sleep disturbances can affect up to 90% of HD population,[7] and poor sleep has been reported in the early stages of HD and even among asymptomatic HD gene expansion carriers.[8,9] A study using data from participants in the Netherlands found that night-time sleep impairment was significantly more prevalent in PwHD compared with controls (58.1% vs 34.9%). Differences in daytime sleepiness were explored but not statistically significant.[10] Sleep and circadian disturbances affect HD severity and progression[9,11] and can both worsen and be worsened by cognition and psychiatric symptoms.[12,13]

PwHD also have 9.2 times higher age-adjusted and sex-adjusted risk of death by suicide than otherwise healthy peers, particularly PwHD younger than 45 years.[14] An analysis of the prospective European HD Network study (REGISTRY) reported suicide to be the third most common cause of death among PwHD (6.6%) after pneumonia (19.5%) and infections (6.9%).[15]

While sleep disturbances, suicidal ideation, and elevated suicide risk have been documented in PwHD, a recent systematic review has underscored the need for further research to elucidate the etiology and the magnitude of these issues for PwHD.[16] This study evaluated the occurrence of suicidal ideation and sleep disturbances among PwHD in 5 European countries and the United States using data from the Huntington's Disease Burden of Illness (HDBOI) study.

Methods

HDBOI Study

The HDBOI study is a retrospective, cross-sectional burden-of-illness study of PwHD in France, Germany, Italy, Spain, the United Kingdom (EU5), and the United States. The HDBOI study collected information related to the clinical, humanistic, and economic burden of HD on PwHD and their caregivers[17,18]; this analysis focused on mental health-related outcomes from data collected between September 2020 and May 2021.

Eligible PwHD were adults (18 years and older) with a clinical diagnosis of motor manifest HD ≥ 12 months before the date of clinical consultation that was used for study recruitment (defined as the index date). PwHD who participated in a clinical trial for an HD treatment in the 12 months before the index date were not eligible. PwHD were categorized as having ES, mid-stage (MS), or advanced-stage (AS) HD as determined by the opinion of the treating physician based on published descriptors.[19]

Standard Protocol Approvals, Registrations, and Patient Consents

Ethical approval for the HDBOI study was granted by the Research Ethics Subcommittee at the University of Chester (RESC0420-1038). Electronic informed consent was obtained from all participants.

Variables and Outcomes

Data were collected from an electronic case record form completed by the treating physician and from a voluntary Patient Public Involvement Engagement (PPIE-P) questionnaire completed by the PwHD. For participants with a severe cognitive deficit, the primary caregiver (i.e., spouse/partner, relatives, or friends, with or without contractual agreement or formal payment) was asked to provide consent and to complete the PPIE-P questionnaire on the PwHD's behalf (proxy respondents). All questionnaires were administered using an online platform. Physicians retrospectively extracted sociodemographic and clinical information (including suicidal ideation) from the participants' medical records to complete the CRF. In parallel, PwHD (or proxy respondents) provided sociodemographic and clinical information as well as lifestyle changes and cross-sectional self-reported outcomes in the PPIE-P questionnaire.

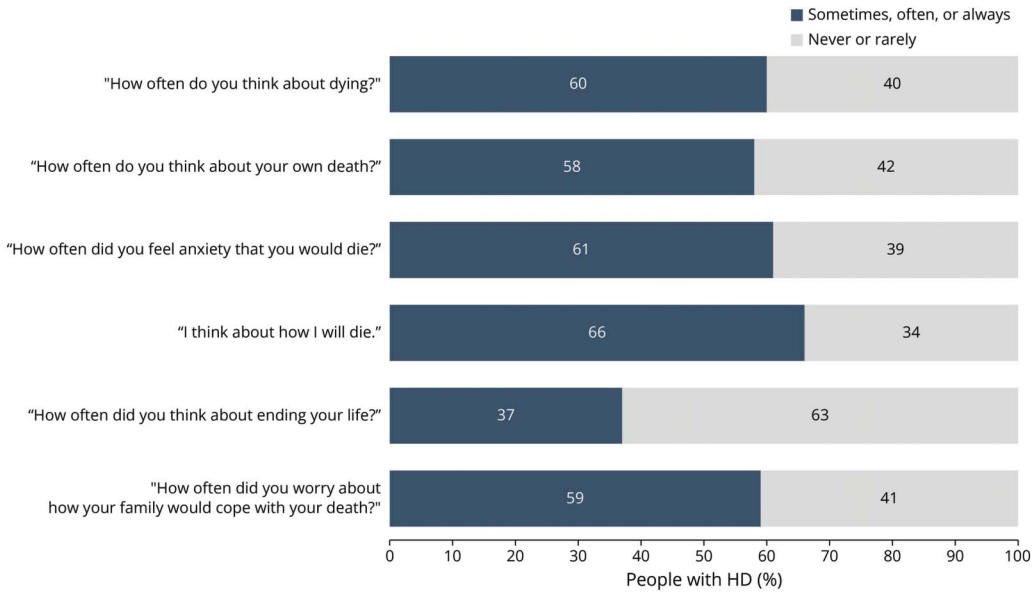
Questions related to sleep disturbances were included in the PPIE-P questionnaire where respondents were asked to describe their sleep, with 5 possible answers ranging from "no difficulty sleeping" to "hardly ever sleep at all." Suicidal ideation was assessed in a CRF question asking whether the PwHD were currently engaging, or have previously engaged, in suicidal ideation (considering, planning, and/or preparing to commit suicide) in relation to the study index date. Concerns about death and dying were assessed using the Huntington Disease Health-Related Quality of Life (HDQLIFE) instrument,[20-22] which was included in the PPIE-P questionnaire. The HDQLIFE Concern with Death and Dying instrument examines the impact that concerns and preoccupation with death and dying may have on health-related quality of life for PwHD.[21] The HDQLIFE short form consists of 6 questions (Figure 1) with 5 scoring answers ("never," "rarely," "sometimes," "often," "always").

The Health Measures Scoring Service[23] was used to score the HDQLIFE responses, where the scoring algorithm transforms the total raw score into a T-score for each participant. The Concern with Death and Dying scores are on a T metric (mean, 50; SD, 10) relative to an HD population, where higher scores indicate greater preoccupation with thoughts of death and dying.

Statistical Analysis

Descriptive statistics were used to summarize demographic and clinical characteristics for the overall study population and by subgroups based on HD stage. Study outcomes were

Figure 1 Grouped HDQLIFE Responses by All Respondents (n = 482)



PwHD reported, source: PPIE-P Questionnaire. PwHD = people with Huntington disease.

analyzed descriptively overall, by disease stage, and by country using measures of central tendency. Univariate comparisons were conducted when appropriate. No imputation of missing data was performed. Differences between outcomes were explored by disease stage; differences were assessed using analysis of variance tests. Differences in outcomes by disease stage were explored descriptively using χ^2 tests. Statistically significant associations $(p < 0.05)$ are indicated in text. All data were analyzed using STATA 16[24] (StataCorp LLC, College Station, TX) and R.[25]

Data Availability

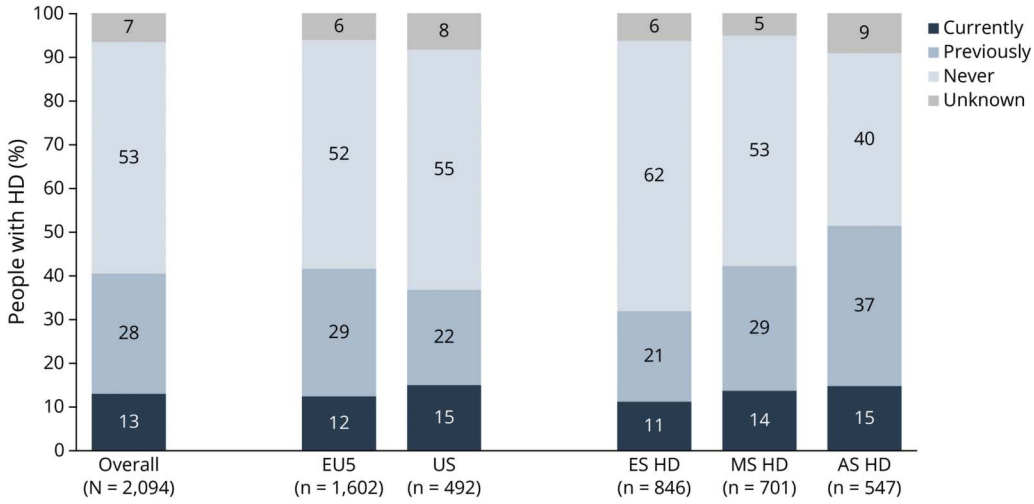
The data that support the findings of this study may be available from HCD Economics Ltd., but restrictions apply to the availability of these data, which were used under license for this study and so are not publicly available. Data may be

Table Study Population Characteristics

	All PwHD	EU5	United States	ES HD	MS HD	AS HD
PwHD, n (%)	2,094 (100)	1,602 (77)	492 (23)	846 (40)	701 (33)	547 (26)
PPIE-P respondents, n (%)	482 (23)	445 (28)	37 (8)	204 (24)	164 (23)	114 (21)
Self-report, n/N (%)	440/482 (91)	403/445 (91)	37/37 (100)	192/204 (94)	155/164 (95)	93/114 (82)
Caregiver proxy, n/N (%)	42/482 (9)	42/445 (9)	0/37 (0)	12/204 (6)	9/164 (5)	21/114 (18)
Age, y, mean (SD)	47.3 (13.7)	47.5 (13.7)	46.4 (13.7)	43.2 (12.9)	48.1 (13.6)	52.3 (13.3)
Sex, male, n (%)	1,253 (60)	952 (59)	301 (61)	492 (58)	397 (57)	364 (67)
Education, n (%)						
Primary or less	216 (10)	169 (11)	47 (10)	82 (10)	68 (10)	66 (12)
Secondary/high school	1,100 (53)	909 (57)	191 (39)	414 (49)	393 (56)	293 (54)
Bachelor's or postgraduate	640 (31)	444 (28)	196 (40)	294 (35)	201 (29)	145 (27)
Unknown	138 (7)	80 (5)	58 (12)	56 (7)	39 (6)	43 (8)

Abbreviations: AS = advanced-stage; ES = early-stage; EU5 = 5 European countries; HD = Huntington disease; MS = mid-stage; PwHD = people with Huntington disease.
Proportions may not sum to 100% because of rounding.

Figure 2 Suicidal Ideation Among PwHD (N = 2,094)



Note: Treating physicians indicated whether the PwHD is currently engaging, or has previously engaged, in suicidal ideation in relation to the study index date. Proportions may not sum to 100% due to rounding. Physician reported, source: CRF. HD = Huntington disease; PwHD = people with Huntington disease.

available from the authors on reasonable request and with permission of HCD Economics Ltd.

Results

Study Population

A total of 2,094 PwHD from the HDBOI study were eligible and included in this analysis, including 1,602 (77%) from the EU5 and 492 (23%) from the United States. Of the 2,094 PwHD, 60% (n = 1,253) were men and 846 (40%) were categorized as having ES HD, 701 (33%) as having MS HD, and 547 (26%) as having AS HD. The mean age of the study sample was 47.3 years (SD, 13.7). Participants in the EU5 were slightly older than those in the United States (47.5 vs 46.4 years), and age was higher with advanced disease progression (Table). Approximately half of all PwHD (53%) completed secondary/high school, and nearly one-third (31%) completed a bachelor's or postgraduate degree. A subset of the participants provided responses to the PPIE-P questionnaire (n = 482), and nearly all (91%, n = 440) PwHD responded on their own behalf, with 9% (n = 42) having caregivers provide proxy responses.

Suicidal Ideation

Of the total study sample, 13% (n = 272) and 28% (n = 575) of PwHD were currently displaying or had previously displayed suicidal ideation behaviors, respectively (Figure 2). Current suicidal ideation was more prevalent in PwHD in the United States compared with the EU5 (15% vs 12%; $p < 0.05$ [$p = 0.005$]) and increased with the PwHD's disease progression: 11% for ES, 14% for MS, and 15% for AS ($p < 0.05$ [$p = 0.000$]). Previously displayed suicidal ideation also increased with disease progression (Figure 2, $p < 0.05$, [$p = 0.000$]).

Death-Related and Suicide-Related Thoughts From the HDQLIFE Instrument

Responses to the HDQLIFE instrument (n = 482) showed that approximately more than half of the PwHD thought about dying (60%) or their own death (58%) "sometimes," "often," or "always" (Figure 1), which was higher in the United States (70% and 76%) than EU5 (59% and 56%) cohorts (Figure 3). Similarly, 61% of PwHD reported feeling anxiety that they would die, which was markedly higher in the United States (81%) than in EU5 (59%). Two-thirds of PwHD (66%) reported thinking about how they would die, and more than one-third (37%) reported thinking about ending their own lives (Figure 1). Recurrent suicidal thoughts were present in early stages of disease: 7.9% of people with ES HD think often or always about ending their lives, and the percentage increased to 11.6% for people with MS HD and to 20.2% for people with AS HD ($p < 0.05$ [$p = 0.002$]) (Figure 4).

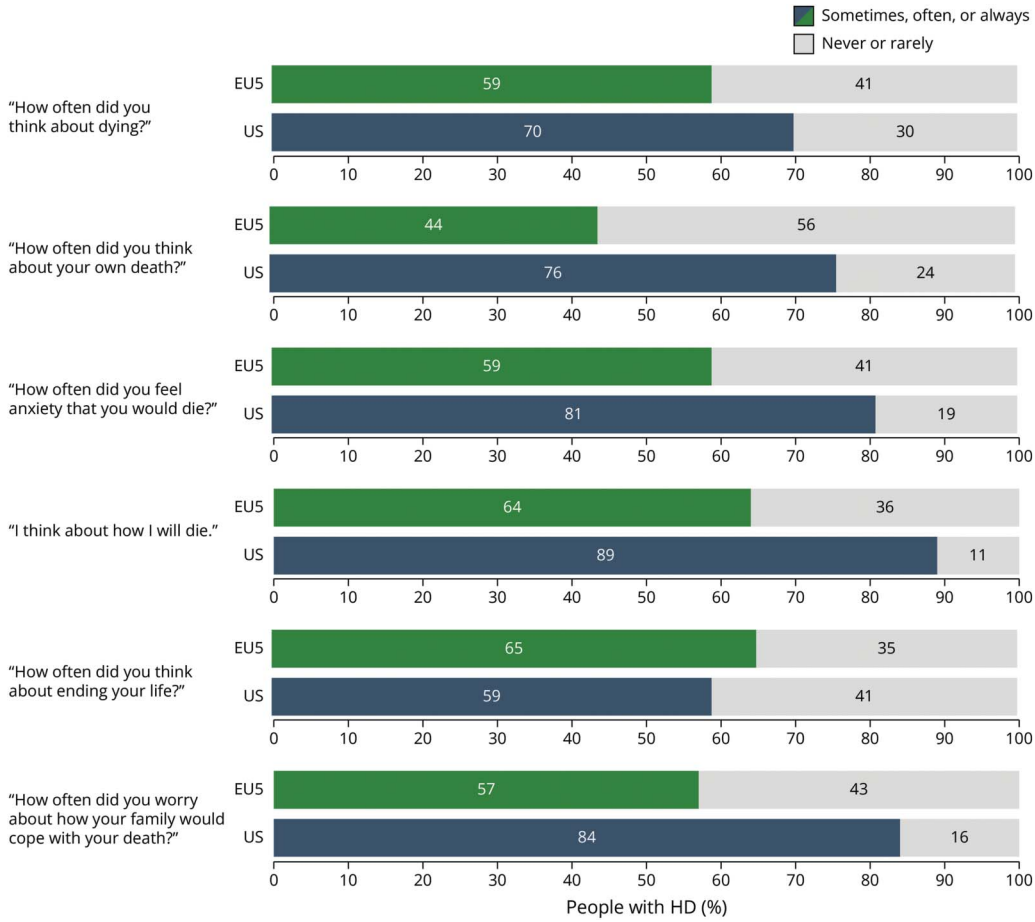
The mean T-score for the HDQLIFE instrument was 58.2 (n = 482) and higher in the United States than in EU5 (US, n = 37: 62.5 vs EU5, n = 445: 57.8); however, differences were not statistically significant ($p = 0.166$). Concerns with death and dying were present across levels of HD severity and cohorts, with mean T-scores of 57.8, 56.4, and 61.5 for people with ES, MS, and AS HD ($p < 0.05$ [$p = 0.000$]).

For the subsample of participants with caregivers as proxy respondents, the mean T-score was 63.0 (n = 42), higher than the self-reported mean of 57.7 (n = 440). However, the difference was not statistically significant ($p = 0.488$).

Sleep Disturbance

Of 482 respondents, nearly all (91%, n = 437) reported some level of difficulty sleeping, with approximately half (47%, n =

Figure 3 Grouped HDQLIFE Responses by Country



PwHD reported, source: PPIE-P Questionnaire. HD = Huntington disease.

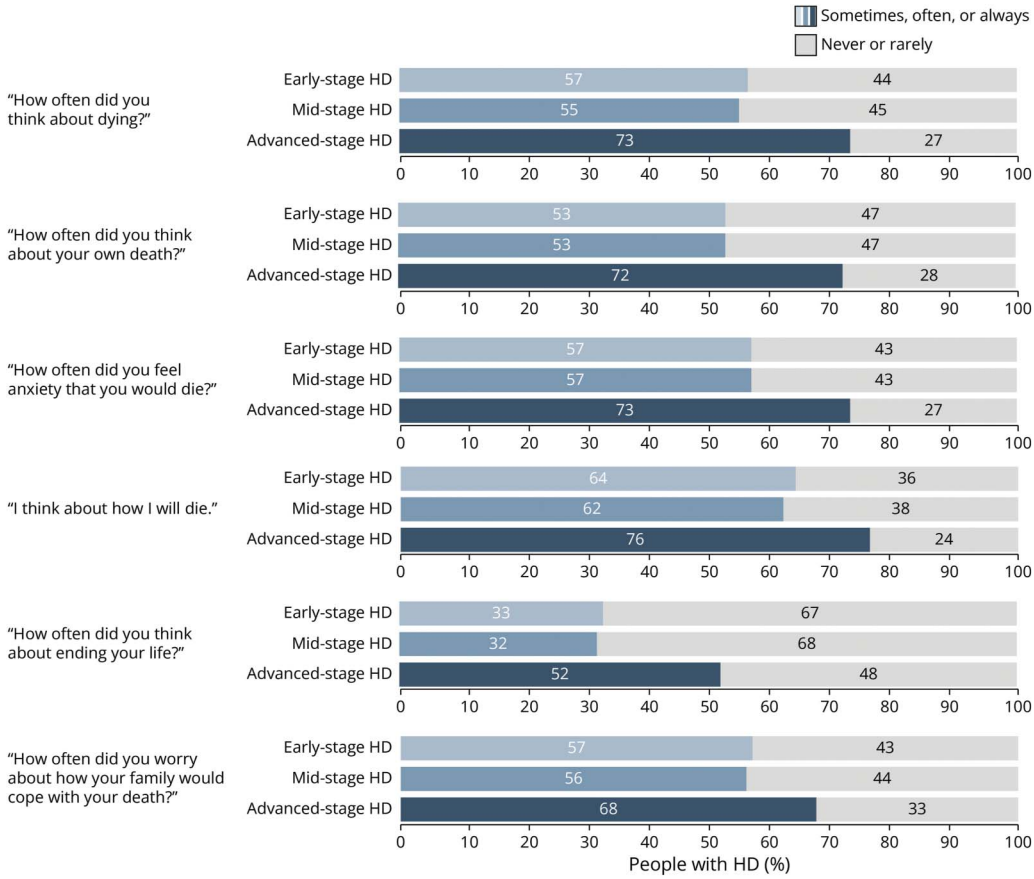
225) reporting moderate, severe, or worse difficulty sleeping (Figure 5). Significantly more people with AS HD reported moderate or severe difficulty sleeping than those with ES or MS HD ($p < 0.05$, [$p = 0.000$]). As expected, the proportion of PwHD reporting no difficulty sleeping was higher in the ES group and decreased as HD severity increased (ES, 14%; MS, 8%; AS, 4%; $p < 0.05$ [$p = 0.000$]). Observed differences between those in the United States compared with EU5 were not statistically significant ($p = 0.582$).

For the subsample of participants with caregivers as proxy respondents, 66.7% (N = 42) reported that the person with HD had moderate, severe, or worse difficulty sleeping. In comparison, 44.8% (N = 440) of the self-reported participants with HD reported similar difficulties. The difference between these groups was statistically significant ($p < 0.05$, $p = 0.006$).

Discussion

This analysis of more than 2,000 PwHD from the HDBOI study in the EU5 and United States showed a substantial burden of death-related and suicide-related thinking and sleep disturbances among PwHD, which tended to worsen with disease severity. More than 10% of PwHD reported active suicidal ideation and more than 25% reported previous suicidal ideation, both of which were significantly more prevalent with advanced disease. PwHD generally expressed anxiety and concern not only for their own mortality but for the impact of their passing on their families, which was reported by most of those with AS HD who had a mean age of 52 years. These findings highlight the importance of interventions aimed at ensuring that adequate mental health and suicide prevention services are available for PwHD and their families, although there is currently a relative lack of evidence regarding effective medical interventions to manage suicidal ideation and behavior among PwHD.[16] The HDBOI study showed that nearly all PwHD reported some level of difficulty sleeping and nearly half reported moderate or worse difficulties. Evidence of a significant relationship between sleep disturbances and psychiatric disorders emphasizes the need for early detection and treatment because effective treatment of psychiatric disorders may help with sleep normalization.[26] Sleep disturbances may be closely related to the timing of motor symptom onset among

Figure 4 Grouped HDQLIFE Responses by HD Severity

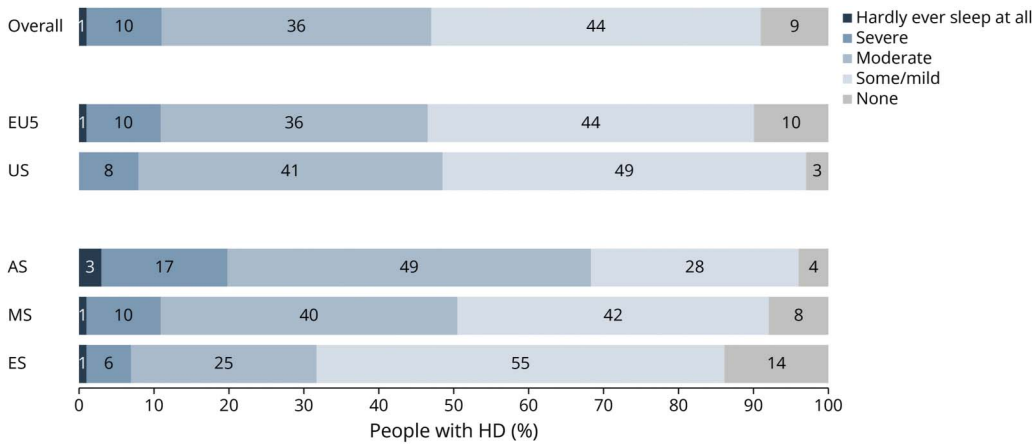


Proportions may not sum to 100% due to rounding. PwHD reported, source: PPIE-P Questionnaire. HD = Huntington disease.

PwHD, suggesting a potential mechanistic factor that may negatively affect sleep quality.[6] The complexities of HD affecting sleep patterns in this population necessitate the development of new assessment tools for sleep and alertness in HD.[7]

Findings from this study were consistent with and complementary to the existing literature. In an observational study using the Enroll-HD data set, involving 5,709 individuals with Huntington disease (PwHD), the research findings showed that current suicidal ideation ranged from 6% to 10%

Figure 5 Difficulty Sleeping Overall and by Country and HD Severity



Proportions may not sum to 100% due to rounding. AS = advanced-stage; ES = early-stage; MS = mid-stage; EU5 = five European countries; US = United States; HD = Huntington disease.

(HDBOI study, 13%) while previous suicidal ideation ranged from 19% to 31% (HDBOI study, 28%) among the participants.[27] Suicidal ideation may be related to neuropsychiatric symptoms and use of psychotropic medication among PwHD.[5,27] Feelings of entrapment associated with having an incurable, progressive neurodegenerative condition may also be an important risk factor of suicidal ideation.[5] These factors highlight the importance of holistic HD management and comprehensive clinical assessment for suicidal ideation behaviors and sleep disturbances including both clinician-rated and self-reported measures throughout the HD severity continuum.[28]

Owing to the progressive nature of debilitating clinical symptoms associated with HD, end-of-life concerns and sleep disturbances are known to be prevalent among PwHD, with rates of both being significantly higher than in the general population and those with other neurodegenerative conditions.[5,6,16] Sleep disturbances and suicidal risk tend to be elevated with more advanced stages of HD, although detectable even among those with ES HD.[5,6,16,29] In the HDBOI study, concerns with death and dying were indeed present in early stages of disease and the HDQLIFE T-scores did not increase significantly with more severe HD, which aligns with previous findings[29]; however, the T-scores in the HDBOI study were generally higher compared to those reported in an earlier study.[29]

Findings of this study should be interpreted in the context of certain strengths and limitations. To minimize bias and to provide representative estimates of the mental health burden of HD, we aimed to enroll a generalizable HD sample with adequate proportions of patients in each disease stage; however, these proportions were not available in the published literature. Because recruitment was driven through clinician office visits, very AS patients may have been underrepresented if they were admitted to long-term residential or nursing care homes. While patient-reported outcomes are particularly valuable in the context of burdensome, lifelong conditions such as HD, data collection may have been influenced by a selection bias in participation and completion of the questionnaires. Completion of the PPIE-P questionnaire was voluntary, although this subset of patients shared similar demographic characteristics to the larger cohort of participants (CRF sample). Disclosure of information about suicidal ideation or behavior may also be influenced by perceived stigma and, therefore, may be underreported.[5] In addition, available information in relation to PwHD's suicide-related thinking behavior was limited to the presented data and the HDBOI study did not capture any further details on the handling of these suicidal-related episodes. Although we discuss the link between sleep disturbances and psychiatric disorders based on existing literature, we could not perform related analyses because of limited data. Finally, there may have been a potential recall bias for PwHD and/or proxy respondents completing the PPIE-P quesrionnaire, although the number of questions requiring recall were kept to a minimum and the recall periods were relatively short.

This analysis of the HDBOI study offers an up-to-date perspective on the large burden of HD on death-related and suicide-related thinking and chronic difficulty sleeping. As the disease progresses, this burden increases, underscoring the need for intervention at earlier stages of HD. This work increases the evidence base for the international HD community that will enable stakeholders to make fully informed decisions and can lead to improvements in the management of HD.

TAKE-HOME POINTS

- This work aims to evaluate the presence of suicidal ideation and sleep disturbances among people with Huntington disease (PwHD) in 5 European countries (EU5) and the United States using data from the Huntington's Disease Burden of Illness study.
- End-of-life concerns and sleep disturbances are high among people with HD, and rates were significantly higher than in the general population and those with other neurodegenerative diseases.
- Sleep disturbances and suicidal risk increased at more advanced stages of the disease, although the suicidal risk is present from the early stages of disease.
- Our findings highlight the importance of holistic HD management and comprehensive clinical assessment for suicidal ideation behaviors and sleep disturbances to reduce the burden on PwHD.

Author Contributions

I. Rodríguez Santana: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data. S.A. Frank: drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data. T.A. Mestre: drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data. A. Arnesen: drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data. J.L. Hamilton: drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data. H. Hubberstey: drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data. M. Winkelmann: drafting/revision of the manuscript for content, including medical writing for content; analysis or interpretation of data. E. Hernandez-Jimenez: drafting/

revision of the manuscript for content, including medical writing for content; analysis or interpretation of data. J. Frimpter: drafting/revision of the manuscript for content, including medical writing for content. R. Dolmetsch: drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data. T.M. Ali: drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data.

Study Funding

This research article was sponsored by uniQure. The wider HDBOI study was supported by research funding from uniQure and Roche.

Disclosure

J.L. Hamilton, H. Hubberstey, and M. Winkelmann have no disclosures to declare. I. Rodríguez Santana is a paid employee of Prime HCD. E. Hernandez-Jimenez was a paid employee of Prime HCD during the development of the manuscript. S. Frank has received personal compensation from uniQure as a steering committee member, Huntington Study Group for data and safety monitoring board contract work and Sage Therapeutics for consulting; his work institution has received funding for research from Roche/Genentech, Triplet Therapeutics, CHDI Foundation, and Huntington Study Group/Prilenia Therapeutics. A. Arnesen has received consultancy fee from Prilenia as member of the Steering Committee. European Huntington Association has, in the past 2 years, received financial support from Roche, Novartis, Uniqure, Wave Life Sciences, PTC, Boston Scientific Foundation and European Federation for Neurologic Associations. T.A. Mestre has received speaker honoraria from AbbVie and the International Parkinson and Movement Disorder Society; consultancies from CHDI Foundation/Management, Sunovion, Valeo Pharma, and Rocher; advisory board memberships with AbbVie, Biogen, Sunovion, Roche, Medtronic, nQ; and research funding from the EU Joint Programme – Neurodegenerative Disease Research, uOBMRI, Roche, Ontario Research Fund, Canadian Institutes of Health Research, Michael J. Fox Foundation, Parkinson Canada, PDF/PSG, LesLois Foundation, PSI Foundation, and Parkinson Research. J. Frimpter provided editorial/writing support funded by HCD Economics. R. Dolmetsch was a paid employee of uniQure Inc during the development of the manuscript and T.M. Ali is a paid employee of uniQure Inc. Full disclosure form information provided by the authors is available with the full text of this article at Neurology.org/cp.

Publication History

Received by *Neurology: Clinical Practice* April 22, 2024. Accepted in final form February 24, 2025. Submitted and externally peer-reviewed. The handling editor was Associate Editor John P. Ney, MD, MPH.

References

1. Tabrizi SJ, Scahill RI, Owen G, et al. Predictors of phenotypic progression and disease onset in premanifest and early-stage Huntington's disease in the TRACK-HD study: analysis of 36-month observational data. *Lancet Neurol*. 2013;12(7):637-649. doi:10.1016/S1474-4422(13)70088-7
2. McColgan P, Tabrizi SJ. Huntington's disease: a clinical review. *Eur J Neurol*. 2018;25(1):24-34. doi:10.1111/ene.13413
3. Rosenblatt A, Kumar BV, Mo A, Welsh CS, Margolis RL, Ross CA. Age, CAG repeat length, and clinical progression in Huntington's disease. *Mov Disord*. 2012;27(2):272-276. doi:10.1002/mds.24024
4. America HsDSo. *A Physician's Guide to the Management of Huntington's Disease*. Accessed April 8, 2024. hdsa.org/product/a-physicians-guide-to-the-management-of-huntingtons-disease-3rd-edition/
5. van Duijn E, Fernandes AR, Abreu D, Ware JJ, Neacy E, Sampaio C. Incidence of completed suicide and suicide attempts in a global prospective study of Huntington's disease. *BJPsych Open*. 2021;7(5):e158. doi:10.1192/bjo.2021.969
6. Ogilvie AC, Nopoulos PC, Schultz JL. Sleep disturbances by disease type and stage in Huntington's disease. *Parkinsonism Related Disord*. 2021;91:13-18. doi:10.1016/j.parkreldis.2021.08.011
7. Fifel K, Videnovic A. Circadian and sleep dysfunctions in neurodegenerative disorders—an update. *Front Neurosci*. 2020;14:627330. doi:10.3389/fnins.2020.627330
8. Arnulf I, Nielsen J, Lohmann E, et al. Rapid eye movement sleep disturbances in Huntington disease. *Arch Neurol*. 2008;65(4):482-488. doi:10.1001/archneur.65.4.482
9. Lazar AS, Panin F, Goodman AO, et al. Sleep deficits but no metabolic deficits in premanifest H untington's disease. *Ann Neurology*. 2015;78(4):630-648. doi:10.1002/ana.24495
10. Aziz NA, Anguelova GV, Marinus J, Lammers GJ, Roos RA. Sleep and circadian rhythm alterations correlate with depression and cognitive impairment in Huntington's disease. *Parkinsonism Related Disord*. 2010;16(5):345-350. doi:10.1016/j.parkreldis.2010.02.009
11. Goodman AO, Rogers L, Pilsworth S, et al. Asymptomatic sleep abnormalities are a common early feature in patients with Huntington's disease. *Curr Neurol Neurosci Rep*. 2011;11(2):211-217. doi:10.1007/s11910-010-0163-x
12. Videnovic A, Lazar AS, Barker RA, Overeem S. The clocks that time us'--circadian rhythms in neurodegenerative disorders. *Nat Rev Neurol*. 2014;10(12):683-693. doi:10.1038/nrneurol.2014.206
13. Nassan M, Videnovic A. Circadian rhythms in neurodegenerative disorders. *Nat Rev Neurol*. 2022;18(1):7-24. doi:10.1038/s41582-021-00577-7
14. Alothman D, Marshall CR, Tyrrell E, Lewis S, Card T, Fogarty A. Risk of mortality from suicide in patients with Huntington's disease is increased compared to the general population in England. *J Neurol*. 2022;269(8):4436-4439. doi:10.1007/s00415-022-11085-z
15. Rodrigues FB, Abreu D, Damásio J, et al. Survival, mortality, causes and places of death in a European huntington's disease prospective cohort. *Mov Disord Clin Pract*. 2017;4(5):737-742. doi:10.1002/mdc3.12502
16. Kachian ZR, Cohen-Zimerman S, Bega D, Gordon B, Grafman J. Suicidal ideation and behavior in Huntington's disease: systematic review and recommendations. *J Affective Disord*. 2019;250:319-329. doi:10.1016/j.jad.2019.03.043
17. Rodriguez Santana I, Frank S, Doherty M, et al. Humanistic burden of huntington disease: evidence from the huntington disease burden of illness study. *Neurol Clin Pract*. 2022;12(6):e172-e180. doi:10.1212/CPJ.0000000000200095
18. Rodríguez-Santana I, Mestre T, Squitieri F, et al. Economic burden of huntington disease in Europe and the USA: results from the huntington's disease burden of illness study. *Eur J Neurol*. 2023;30(4):1109-1117. doi:10.1111/ene.15645
19. Wild E, Tabrizi S, Bates G, Jones L. Premanifest and early Huntington's disease. In: Bates G, Tabrizi S, Jones L, eds. *Huntington's Disease*. Oxford University Press; 2014.
20. Carlozzi NE, Boileau NR, Chou KL, et al. HDQLIFE and neuro-QoL physical function measures: responsiveness in persons with huntington's disease. *Mov Disord*. 2020;35(2):326-336. doi:10.1002/mds.27908
21. Carlozzi NE, Boileau NR, Paulsen JS, et al. End-of-life measures in huntington disease: HDQLIFE meaning and purpose, concern with death and dying, and end of life planning. *J Neurol*. 2019;266(10):2406-2422. doi:10.1007/s00415-019-09417-7
22. Carlozzi NE, Ready RE, Frank S, et al. Patient-reported outcomes in Huntington's disease: quality of life in neurological disorders (Neuro-QoL) and Huntington's disease health-related quality of life (HDQLIFE) physical function measures. *Mov Disord*. 2017;32(7):1096-1102. doi:10.1002/mds.27046
23. *HealthMeasures. Home*. Accessed 8 April. healthmeasures.net/
24. Stata. *Statistical Software for Data Science*. Accessed April 8, 2024. stata.com/
25. Foundation TR. *The R Project for Statistical Computing*. Accessed April 8, 2024. r-project.org/.
26. Herzog-Krzywoszanska R, Krzywoszanski L. Sleep disorders in huntington's disease. *Front Psychiatry* 2019;10:221. doi:10.3389/fpsyt.2019.00221
27. Honrath P, Dogan I, Wudarczyk O, et al. Risk factors of suicidal ideation in Huntington's disease: literature review and data from Enroll-HD. *J Neurology*. 2018;265(11):2548-2561. doi:10.1007/s00415-018-9013-6
28. Wesson M, Boileau NR, Perlmutter JS, et al. Suicidal ideation assessment in individuals with premanifest and manifest Huntington disease. *J Huntingtons Dis*. 2018;7(3):239-249. doi:10.3233/JHD-180299
29. Carlozzi N, Downing N, McCormack M, et al. New measures to capture end of life concerns in Huntington disease: meaning and Purpose and Concern with Death and Dying from HDQLIFE (a patient-reported outcomes measurement system). *Qual Life Res*. 2016;25(10):2403-2415. doi:10.1007/s11136-016-1354-y

How to cite this article: Rodríguez Santana I, Frank SA, Mestre TA, et al. Suicidal ideation and sleep disturbances among people with huntington disease: evidence from the HDBOI study. *Neurol Clin Pract.* 2025;15(3):e200461. doi: 10.1212/CPJ.0000000000200461