ORIGINAL ARTICLE

Burden and drivers of health-related quality of life among French and Italian caregivers of Huntington's disease patients

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Competing interest
None declared

Funding information
The study was cofounded by University of Lyon and an unrestricted grant from Neurosearch

Received: 21 January 2015
Accepted: 18 December 2015

The Rare Diseases and Orphan Drugs Journal has received funding from the European Union Seventh Framework Programme (FP7/2007-2013) under Grant Agreement n. 305690 RARE-Bestpractices project www.rarebestpractices.eu.
Sole responsibility lies with the authors and the European Commission is not responsible for any use that may be made of the information contained therein.

Abstract

Objective. To assess the impact of Huntington's disease (HD) on caregivers and identify the main determinants of French and Italian caregivers' burden, and Health-Related Quality of Life (HRQoL).

Methods. This cross-sectional, observational study included patients and their caregivers who were identified by national HD patients associations in France and Italy. Data on HD characteristics and QoL of patients and caregivers was collected using the Huntington Self-Assessment Instrument (HSAI), SF-36 and EQ-5D.

Results. The study included 175 patient caregiver pairs from France and 126 pairs from Italy. Mean age (±SD) of patients was 54.5 (±11.6). Average ages at the onset of the first symptoms and at HD diagnoses were 44.8 (±12.4) years and 46.7 (±12.0) years, respectively. The mean age (±SD) of caregivers in France and Italy was 61.31 (11.36) and 51.14 (13.18) respectively. 44% and 55% of caregivers were unsatisfied with their own happiness and 38% and 45% were unsatisfied with overall QoL in France and Italy respectively. No correlation was found between patients and caregivers HRQoL. Correlations of HDQoL-C scores with patients EQ-5D utility score ranged from 0.16 to 0. 25 and with patients SF-36 ranged from 0.11 to 0.34. Caregivers HRQoL was driven by patient voluntary movement disorder (p=0.01), patient depression/anxiety issues (p<0.01) and patient psychotic disorder (p<0.01).

Conclusion. This study captured the predictors of burden in HD caregivers and provides further insights into HD caregivers. Predictors were found to be voluntary movement disorders, depression/anxiety, and psychotic disorders, thus highlighting further insights for a correct therapeutic approach.

Key words

Caregiver, Health-Related Quality of Life, Huntington's disease.

Background

Huntington's disease (HD) is a rare and chronic neurodegenerative disease causing motor and non-motor disorders that result in progressive disability [1,2]. The disease has a large impact on patients' physical well-being but also on psychosocial functioning, including emotional health, social function, and cognitive dysfunction [3]. As a result, HD affects the Health-Related Quality of Life (HRQoL) of patients but also of their caregivers [4]. As with other caregivers of adults with impairments in cognition and emotional functioning, HD caregivers reported multiple aspects of emotional distress [5]. Caregivers of HD patients described being a carer as 'experiencing the disintegration of one's life' [6]. Besides worrying about everyday coping, carers are also concerned about the risk of their children inheriting the disease. There is a paucity of studies conducted to capture the HRQoL of caregivers of HD patients [4,6-8]. In addition, none of these studies used a validated instrument to quantify the experiences of caregivers of HD patients. In order to expand our knowledge of caregiver burden in different cultures, Italian and French caregivers of HD patients were assessed using a battery of validated instruments. The objective of this study was to assess the impact of HD on caregivers and identify the main determinants of French and Italian caregivers' burden, and HRQoL. It was hypothesized that the degree of burden in caregivers would be correlated with severity of patients' disorders, in particular physical dysfunctions.

Method

Study

The European HD burden study (Euro-HDB) was an international, cross-sectional observational study in six European countries (France, Germany, Italy, Spain, Sweden and UK) and was later extended to Poland and USA. The survey was designed as self-reported interviews. A non-random convenience sampling was used. Patients and their caregivers were contacted by the national HD patient associations: the *Association Huntington France* in France and the *Lega Italiana Ricerca Huntington e malattie correlate onlus (www.lirh.it)* with the support of a neurologist in Italy. The associations were responsible for sending self-reported questionnaires to their members, as well as an information letter explaining the study objectives. The response rate was roughly 70% considering patients who were reached through patient associations. Patients aged at least 18 years old with a well-established diagnosis of HD were asked to participate in the survey and to ask their main caregiver to participate as well. If agreed, patients and caregivers had to fill in two extensive questionnaires, one addressed to the patient and one addressed to the caregiver, and send them back anonymously to the associations. Patients and caregivers were explained that participating to this survey was not compulsory and they gave their consent implicitly by sending back their questionnaires. This study was designed to have no interference on either patient care or caregivers and patients' day to day lives. The recruitment for the study in France and Italy took place from October 2009 to February 2010.

2.2. Assessments

Patients and caregivers completed the Huntington Self-Assessment Instrument (HSAI). In addition, patients were asked to complete the SF-36 and the EuroQoL-5D instruments.

The HSAI is a comprehensive instrument that assesses all HD characteristics. It consists of two questionnaires, one for the patient and one for the caregiver. Both are made up of four parts: background information assessment, the Huntington clinical self-reported instrument (H-CSRI), a disease-specific HRQoL assessment and the Huntington resource utilization interview (H-RUI). This instrument was co-developed and validated in Italian and French.

The H-CSRI is the first clinimetric patient-assessed scale for patients with HD. It includes three subscales:

1. motor subscale including thirteen Likert-type items in four dimensions: voluntary movement, stiffness, chorea, precise movement;
2. the functional subscale including seven Yes/No questions;
3. the behavioural subscale including thirteen Likert-type items in four dimensions: depression/anxiety, temper, psychotic disorder, and cognition.

Higher scores on the function scales indicate more severe symptoms than lower scores. This instrument showed satisfactory validation as demonstrated using classical test and item response assessments [9].

Patients' severity was also measured by the independence scale, a scale included in the Unified Huntington's Disease Rating Scale [10]. It is presented as a checklist of common daily tasks graduated from *'patient doesn't need special care'* to *'patient has a tube fed and has a total bed care'*. It is rated from 0 to 100. Higher scores on the function scales indicate better functioning than lower scores. In this study, caregivers were asked to complete it.

The disease-specific HRQoL assessment of patients was made by the Huntington Quality of Life Instrument (H-QoL-I). It is the first self-reported specific instrument developed to assess the HRQoL of patients with HD. It includes eleven five-point Likert scale items, split into three dimensions: motor functioning (four items), psychology (four items) and socializing (three items). Higher scores on the function scales indicate better HRQoL than lower scores. It demonstrated very good psychometric properties: acceptable construct and external validity and good reliability [11].

The disease-specific HRQoL assessment of caregivers was made by the Huntington's disease Quality of Life Battery for Carers (HDQoL-C) short- version. The HDQoL-C is a multidimensional, disease-specific and subjective HRQoL tool that incorporates the individual's physical health, psychological state, level of independence, social relationships and personal beliefs [12]. The shortened version comprised two components relative to QoL: the satisfaction with life component including three items (section 1) and the feelings about living with HD including seventeen items (section 2). Response choices were presented as a rating scale from dissatisfied or never (scored 0) to satisfied or always (scored 10), respectively, for the first and second component. A total score summarizing the two components is also calculated. For aggregated scores, higher scores on the function scales indicate better HRQoL than lower scores. This instrument showed good internal consistency, reliability and congruent validity [13].

The SF-36 instrument is a standardized generic questionnaire comprising 36 questions designed to assess self-perceived health status. It is a psychometric measure that produces a profile of eight dimensions: physical functioning, role-physical limitations, bodily pain, general health, vitality, mental health, role-emotional limitations, social functioning. Standard scoring algorithms allow aggregation of scores from the eight subscales in two distinct, higher-order summary scores: Physical Component Summary (PCS) and Mental Component Summary (MCS) [14]. Higher scores on the function scales indicate better HRQoL than lower scores. The instrument is available in Italian and French. Validation of this instrument is very well documented [15-17].

The EuroQoL-5D self-assessment questionnaire mea-

sures five dimensions of quality of life: mobility, personal care, routine occupations, pain and discomfort, anxiety and depression. Each of these domains is noted on three level Likert-type items: no problem, minor problems, and major problems. The instrument is available in Italian and French. Validation of this instrument is very well documented [18,19].

Data analysis

The EuroQol-5D scores were converted to utility scores from -0.594 to 1 using the UK social tariff [20].

Impact of HD on caregivers is described through the means and Standard Deviation (SD) of HDQoL-C items and aggregated scores.

Pearson's correlations between the two sections and total HDQoL-C scores and 1/the SF-36 scores (the eight dimensions scores and the two summary component scores), 2/the H-QoL-I scores (the three subscales and the total scores) and 3/EuroQol-5D utility score were calculated to investigate the relationship between caregivers' HRQoL and patients' HRQoL.

In order to identify the determinants of caregiver HRQoL, regression analyses were run using the HDQoL-C total score as a dependent variable. Potential drivers were patients' clinical impairments related to the following aspects: motor disorders, depression and anxiety, psychotic disorders, cognition, and temper. Motor disorders, which were composed of voluntary movement disorders, fall and balance disorders, and chorea, were analysed all together as an aggregated variable but also separately as three distinct variables. Analyses were adjusted for age, sex and occupational categories. Several forms of models were tested: traditional linear model, Poisson model, log model and negative binomial model. The model with the lower Root Mean Squared Error (RMSE) was retained.

Results

One hundred and seventy five patient-caregiver pairs in France and 126 pairs in Italy were included in this study. Patient characteristics did not differ between patients from France and Italy. Patient mean age (±SD) was 54.5 (±11.6) years old. Average ages at the onset of the first symptoms and at HD diagnoses were 44.8 (±12.4) years and 46.7 (±12.0) years, respectively. In 90% of the cases, patients reported a performed genetic confirmatory test. All levels of patients' severity were represented (Figure 1). Demographic characteristics of caregivers are shown in Table 1. French caregivers were older than Italian caregivers (61 versus 51 years old, in average) and most of the caregivers did not work (55% for France, 56% for Italy).The vast majority of caregivers were close relatives of the patients, and most of them cared for HD patients on a permanent basis, with a mean duration of caregiving of 16.3 (±19.3) and 9.1 (±7.9) years, respectively for France and Italy.

Caregivers reported taking care of patients' toilet visits, eating, dressing, grooming, walking and bathing for an average time of three hours and a half a day (2.7; 5.0 hours a day respectively for France and Italy). Likewise, they reported four hours per day to take care of shopping,

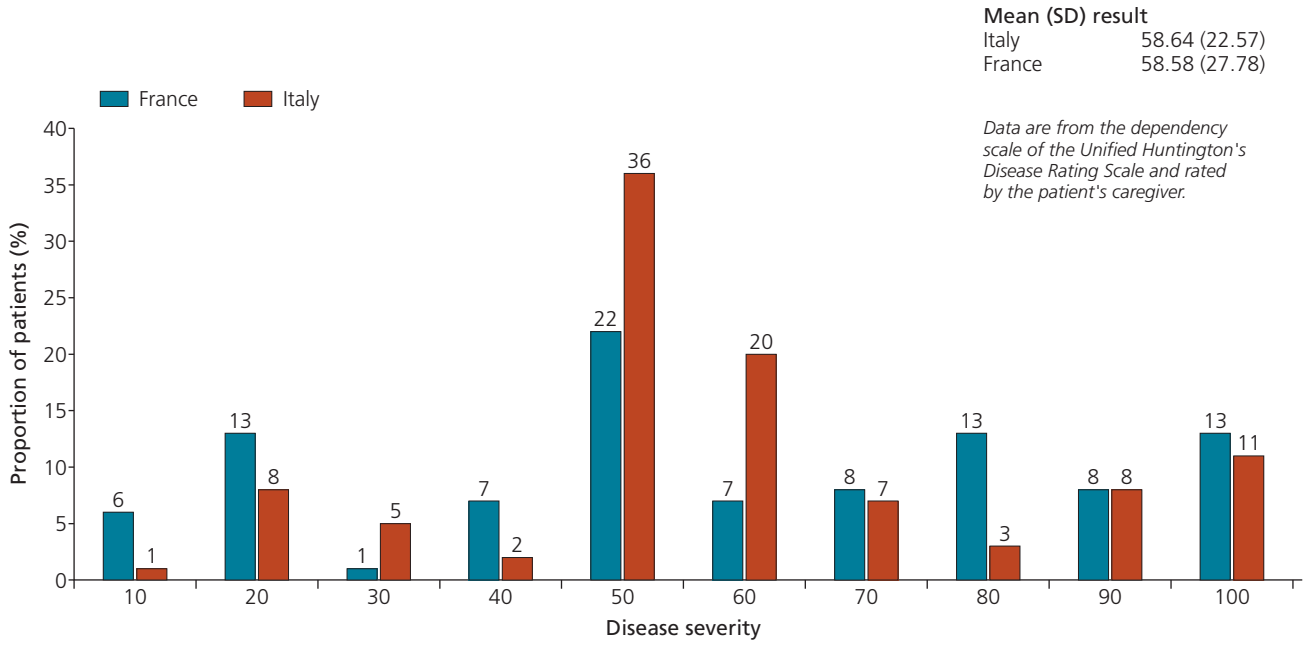

Figure 1. Distribution of patients' severity.

Table 1. Caregivers' characteristics

Characteristics	France n. = 175	Italy n. = 126
Demographic		
Men, n (%)	69 (39%)	50 (40%)
Age (years)	61.31 (11.36)	51.14 (13.18)
Occupational activity		
Workers, n (%)	77 (45%)	55 (32%)
Retired, n (%)	83 (48%)	33 (19%)
Unemployed, n (%)	12 (7%)	38 (22%)
Marital status		
Married/cohabiting, n (%)	139 (80%)	102 (81%)
Never married, n (%)	3 (2%)	13 (10%)
Divorced/separated, n (%)	8 (5%)	4 (3%)
Widowed, n (%)	23 (13%)	7 (6%)
Family situation		
Main carer, n (%)	133 (78%)	110 (90%)
Carer lives with HD patient, n (%)	118 (68%)	101 (80%)
Number of years since HD knowledge in family	22.3 (20)	13 (9.8)
Have children at risk, n (%)	92 (56%)	68 (55%)
Relation with HD patient		
Husband/wife, n (%)	118 (70%)	75 (60%)
Child, n (%)	19 (11%)	12 (10%)
Sibling, n (%)	11 (7%)	10 (8%)
Parent, n (%)	16 (9%)	18 (15%)
Friend, n (%)	1 (1%)	2 (2%)
Other, n (%)	3 (2%)	7 (6%)
Carer background		
Carer has previously cared any other HD-affected person, n (%)	44 (25%)	27 (21%)
Duration of caring (in years)	**16.3 (19.3)**	**9.1 (7.9)**

food preparation and housekeeping (2.7; 5.1 hours a day, respectively); almost five hours per day to assist patients in their care (1.2; 6.8 hours a day, respectively) and five hours and a half per day to supervise patients (2.9; 6.0 hours a day, respectively).

With regards to their own happiness, 44% and 45% of caregivers declared themselves to be unsatisfied respectively in France and in Italy. Similarly, 38% and 45% declared themselves to be unsatisfied with their overall quality of life. They reported [mean (±SD)] to be stressed [5.51 (±2.91); 6.38 (±3.39)], exhausted [5.53 (±3); 5.49 (±2.89)], and felt that their needs were not important to others [6.49 (±2.64); 5.15 (±3.64] respectively for France and Italy. Most importantly, they were very worried about the genetic consequences of HD [7.89 (±2.86); 8.18 (±3.38)]. However, they reported as well to have hope for the future [5.63 (±3.28); 5.63 (±2.85)] and especially they believe that a cure for HD will be found one day [5.75 (±3.06); 7.06 (±2.57)]. They felt they could cope [5.7 (±2.78); 6.95 (±3.4)] and even felt that HD made them a stronger person [5.35 (±3.11); 6.45 (±2.92)]. The French HDQoL-C scores were 53.21 (±25.14) and 48.75 (±14.78) respectively for satisfaction regarding different areas of life and feelings with regards to different aspects of life dimensions. The equivalent Italian HDQoL-C scores were 49.33 (±28.93) and 53.94 (±16.43). There was no difference in the global HDQoL-C scores between the two countries (p=0.77).

HRQoL of caregivers was not found to be related to HRQoL of patients as illustrated by Figure 1, displaying the HDQoL-C total score in function of the EuroQoL-5D utility score, but also by the Pearson's correlations between patient and caregiver HRQoL scores. Indeed, HDQoL-C scores were found to be weak to moderately correlated with the generic patient HRQoL assessments. Correlations between HDQoL-C scores and the EuroQoL-5D utility score ranged from 0.16 to 0.25. Correlations between HDQoL-C scores and the eight domains of SF-36 instruments varied from 0.11 to 0.34 (Table 2). Similarly, HDQoL-C scores were found to be weakly to moderately correlated by the specific patient HRQoL instrument (H-QoL-I) with a range of 0.24 to 0.34.

Analysis of determinants retained the traditional linear model which modelled the dependent variable, i.e. HDQoL-C total score, as normally distributed using an identity link function. The RMSE was 15.56 (range: 15.56-16.55), 16.02 (range: 16.02-16.89) respectively for France and Italy. Drivers of caregiver's HRQoL, explained by the total HDQoL-C score, were found to be patient voluntary movement disorder (p=0.01, p=0.03 respectively for France and Italy), patient depression/anxiety issues (p<0.01), patient psychotic disorder (p<0.01). Figure 2 illustrates the relationship between the caregiver's HRQoL and patient voluntary movement disorder. Patient cognition, temper and chorea were not found to be determinants of caregivers' HRQoL independent of other clinical characteristics (Table 3).

Discussion

HD is characterized by progressively worsening motor, cognitive, behavioural and psychiatric symptoms. Emergence and sequence of symptoms vary from one patient to another but HD is fatal for all. As the disease progresses, motor disturbance becomes more and more generalised and patients' concentration on cognitive tasks becomes increasingly difficult until the complete physical dependence. In parallel, the burden for family increases in a substantial way [2]. The literature is scarce on issues of caregivers' of HD patients with no previous studies conducted on the topic in France and Italy.

Table 2. Pearson's correlations between caregivers' HRQoL, as measured with the HDQoL-C instrument and patients HRQoL, as measured with the EQ-5D, SF-36 and H-QoL-I instruments

	EQ5D	SF36										H-QoL-I			
HDQoL-C	Utility	PF	RP	BP	GH	VT	MF	RE	SF	PCS	MCS	PF	Psych.	Social.	Total
Section 1	0.25	0.22	0.24	0.11$^{\mu}$	0.31	0.34	0.26	0.28	0.32	0.25	0.27	0.31	0.26	0.29	0.33
Section 2	0.16	0.15*	0.18	0.1$^{\mu}$	0.28	0.26	0.21	0.20	0.20	0.21	0.25	0.24	0.24	0.30	0.30
Total	0.24	0.21	0.24	0.12$^{\mu}$	0.33	0.34	0.27	0.26	0.29	0.25	0.28	0.31	0.27	0.31	0.34

All correlations were significant at 1% level except where indicated by * or $^{\mu}$.
*: significant at 5%; $^{\mu}$: non-significant.
Section 1: satisfaction regarding different areas of life. Section 2: feeling regarding different aspects of life.
BP, bodily pain; GH, general health; MCS, mental component summary; MH, mental health; PCS, physical component summary ; PF; physical functioning; Psych., psychology; RE, role limitations due to emotional problems; RP, physical problems; SF, social functioning; Social. , socializing; VT, vitality.

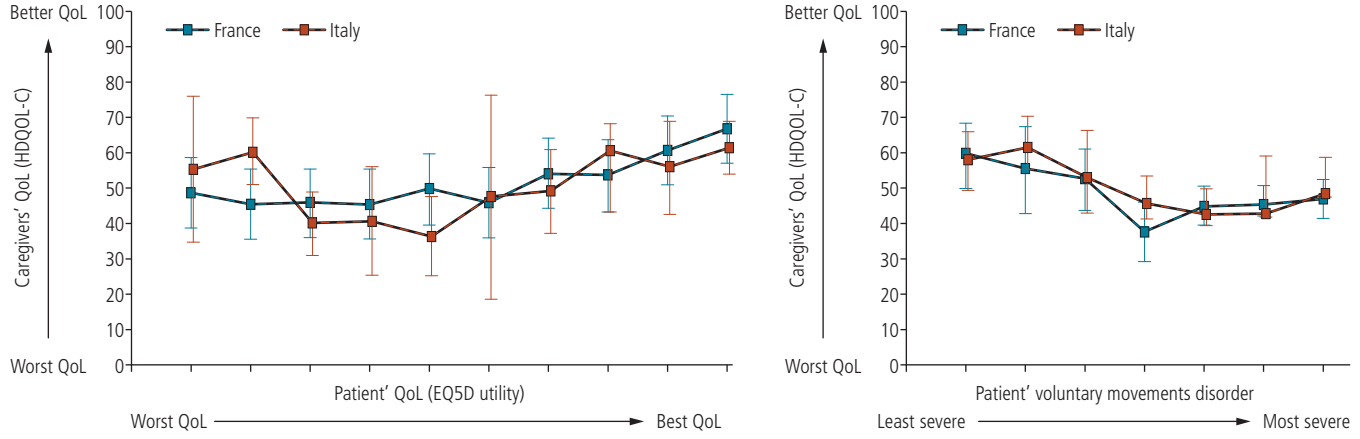

Figure 2. HDQoL-C total score according to patients' QoL (left panel); HDQoL-C total score according to patients' voluntary movement disorder (right panel).

Table 3. Results of regression model on HDQoL-C

		France			Italy		
Variables	Degree of freedom*	Chi-square test	β coefficient	p-value	Chi-square test	β coefficient	p-value
Voluntary movements	1	6.33	-1.96	0.01	5.80	-1.47	0.03
Fall/balance	1	0.32	0.25	0.57	2.40	0.52	0.051
Chorea	1	1.6	0.63	0.21	1.26	0.79	0.26
Depression/anxiety	1	11.37	-1.45	<0.01	8.28	-1.59	<0.01
Temper	1	3.44	1.81	0.06	1.43	1.67	0.23
Psychotic disorder	1	8.29	-1.73	<0.01	6.66	-1.23	<0.01
Cognition	1	1.8	-0.68	0.18	1.32	-0.46	0.25
Sex (Female)	1	2.24	-5.51	0.13	2.69	-7.89	0.10
Occupational activity	7	19.39	positives	<0.01	13.67	positives	0.05
Age	1	0.81	0.18	0.37	1.01	0.22	0.31

*Results from the regression model with the dependent variable, HDQoL-C total score, normally distributed and with the use of an identity link function (RMSE 15.56; 16.02 respectively).

This study found that HD patients are assisted by their family, in particular by their husband or wife (70%) but also by their children (10%). Caregivers spent a substantial amount of time caring for HD patients, as they reported caring their relative for almost 10 hours a day in France and almost the entire day (i.e. 23 hours) in Italy; those times did not include time dedicated for transportation. As a result, Italian relatives reported spending more than twice the time caring for patients on average than French relatives. Across both Italian and French results, global caregiver HRQoL was highly affected and in particular caregivers felt stressed and exhausted; they believed that their needs were not important to others and above all they were very worried about the genetic consequences of HD.

Caregiver HRQoL was found to be indirectly correlated through patient clinical scores. As such, caregivers' HRQoL worsens as the patient's clinical characteristics deteriorate, especially in terms of voluntary movement disorders, depression/anxiety and psychotic disorders. A previous study investigated the determinants of HD patients and caregiver self-report QoL and established that patient and caregiver QoL was associated with functional capacity and cognitive scores [4]. Unfortunately, it was complicate to directly compare the results from the two studies, as previous researchers investigated QoL and not HRQoL and as such the assessments were very different. In this present study, the association between functional capacity and HRQoL was not directly analysed. However, it was found that voluntary movement disorders were associated with lower HRQoL, which could be considered a good determinant of functional capacity. Finally, although Ready et al (2008) previously found that neuropsychiatric symptoms were not associated with caregivers' QoL, the authors explained that this unexpected result was possibly a type II error due a low study power.

This study had a number of strengths and weaknesses. Strong points included the use of validated HD-specific instruments and the inclusion of patients and caregivers with wide range of age, years of evolution and stages of the disease. Another point of strength was the large number of patients and caregivers who participated in this study, given that HD is an orphan disease. This was possible due to the design of the study and the collaboration with patients associations. However, this design potentially led to a biased selection due to recruitment from only patient associations and thus institutionalized patients were possibly under-represented. Also, it is important mentioning that results could have been different if clinical severity had been assessed by clinicians instead of patients themselves. Several studies reported divergence in patient and professional views of clinical outcomes [21,22]. However, because patient reported outcome questionnaire was developed based on the clinician questionnaire, it is likely that patient assessment and clinician assessment are very correlated even not the same and results would not have been dramatically different. But this should be carefully investigated in future studies.

Conclusion

In conclusion, this study provides further insights into HD caregivers and captures the predictors of burden in HD caregivers. Predictors were found to be voluntary movement disorders, depression and anxiety, and psychotic disorders. Further research needs to be conducted to more fully understand those determinants and confirm these findings.

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