Journal of Huntington's Disease 11 (2022) 179–193
DOI 10.3233/JHD-210505
IOS Press

Research Report

Disease Burden of Huntington's Disease (HD) on People Living with HD and Care Partners in Canada

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Pre-press 23 March 2022

Abstract.
Background: Huntington's disease (HD) has been shown to reduce health-related quality of life (HRQoL) and affect healthcare resource utilization (HRU) among patients and care partners internationally but has not been studied specifically in the Canadian context.
Objective: To characterize the burden of HD on individuals with HD and care partners of individuals with HD in Canada.
Methods: An online survey was distributed (September 14–November 23, 2020) through patient organizations to collect data on demographic and clinical characteristics, as well as: HRQoL, measured using the 36-Item Short-Form Health Survey (SF-36v1); HRU, measured using the Client Service Receipt Inventory (CSRI); and care partner burden, measured using the Caregiver Strain Index (CSI) and Huntington's Disease Quality of Life Battery for Carers (HDQoL-C). Descriptive statistics were used to report data and compare subgroups.
Results: A total of 62 adult individuals with HD (or their proxies) and 48 care partners met defined eligibility criteria. The mean [standard deviation] age was 51.2 [13.8] and 58.1 [13.9] years for individuals with HD and care partner respondents, respectively. For individuals with HD, the greatest HRQoL burden (i.e., lowest score) was for the SF-36v1 Role – Physical scale (46.8 [42.9]). HRU was higher for some services (e.g., general practitioner visits) for respondents who had experienced motor onset transition. Among care partners, 55.3% experienced high strain, as indicated by the CSI. The HDQoL-C showed the greatest HRQoL burden in feelings about life (45.1 [17.9]).
Conclusion: This study quantified the substantial burden on individuals with HD and care partners in Canada, addressing a critical knowledge gap that can affect the availability of and access to healthcare services.

Keywords: Huntington's disease, health-related quality of life, care giving burden, burden of illness, chronic disease, neurodegenerative diseases

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INTRODUCTION

The cognitive, behavioural, and motor symptoms of Huntington's disease (HD) substantially impact health-related quality of life (HRQoL) in individuals with HD. European studies have demonstrated lower HRQoL among individuals with mild to moderate HD compared with population norms [1–3]. Certain neuropsychiatric symptoms occur in individuals with HD at a higher rate than in the general population (e.g., anxiety, depression, irritability, obsessive-compulsive disorder), which can significantly impact an individual's quality of life [1, 4–6]. Depression, cognitive disturbances or impairment, and a decline in functional abilities related to HD have been shown to reduce HRQoL [1, 7–10]. Multiple European studies have also shown the progression of HD negatively impacts HRQoL [11–13].

Symptoms of HD can also impact healthcare resource utilization (HRU) and employment. A data mining study evaluating healthcare and associated service utilization among patients participating in the European REGISTRY study reported increased inpatient hospital service use with increased HD stage [14]. Another study examining the societal cost of HD in the United Kingdom showed that increasing hospital and residential care costs were associated with increasing HD stage [15]. Watkins et al. (2018) evaluated the relationship between employment and both HD-associated cognitive and motor decline and showed that cognitive symptoms had a significant association with function at work, as well as the decision to leave work [16].

Several studies evaluating HRQoL and HRU for individuals with HD have been conducted in the United States [1] and Europe, with multiple studies utilizing European Huntington's Disease Network REGISTRY [10, 14, 17, 18] data. Unfortunately, data relevant to Canadian populations are far more limited. The Enroll-HD [19] and TRACK-HD [20, 21] cohort studies included Canadian patients; however, Canadian patients were analyzed in combination with the overall study population and therefore do not provide results specific to the Canadian context. Crucially, data from outside of Canada may not be generalizable to the Canadian setting. The World Health Organization defines quality of life as the concept individuals have of their position in life, which includes perspective from their culture, as well as their evaluative systems, expectations, priorities, available infrastructure, and other factors [22, 23]; the jurisdiction from where HRQoL data originate is therefore important. Similarly, healthcare resources available to individuals with HD also vary between countries [24, 25], suggesting HRU associated with HD in Canada may be unique.

The burden of HD extends beyond the individuals with the disease. Although the literature available on care partners of individuals with HD is limited, most evidence points towards a compromised HRQoL through their caregiving role [1, 13, 26]. Care partners most commonly report feelings of isolation, emotional distress, and difficulties coping, in addition to financial pressure [1, 27–29]. The autosomal dominant inheritance of HD [1] provides a unique challenge. Care partners themselves may be affected by HD if the individual in their care is a close relative (e.g., parent or sibling), which may lead to feelings of anxiety, hopelessness, and uncertainty about the future; all of these could impact the care partner's HRQoL [1, 30]. Another important consideration is the potential effect of anosognosia—that is, the impairment of an individual's awareness of deficits and their potential impact—which may affect approximately 25–50% of individuals with any stage of HD and is associated with increased caregiver burden [31–34].

Within the Canadian context, a retrospective database study by Mitchell et al. (2015) evaluated informal caregivers of home care clients with neurological conditions in Manitoba and Ontario, using the routinely-collected Resident Assessment Instrument for Home Care (RAI-HC) [35]. The authors showed caregiver distress was twice as prevalent among caregivers of individuals with neurological conditions (28.0%) as among caregivers of individuals without neurological conditions (13.4%), and that HD was associated most strongly with caregiver distress, relative to other neurological conditions [35]. Another study conducted in Eastern Canada interviewed individuals in families affected by HD [26]. Etchegary (2011) found that individuals were frustrated with the limited HD knowledge available through their family physicians, that they encountered several challenges trying to access relevant healthcare and community support, and that they had suggestions for improving care [26].

There are notable country-specific differences in HD-related care and access to healthcare, as well as patient and care partner support resources. Information specific to Canada is limited, and data from other jurisdictions may not be sufficiently generalizable to the Canadian setting to be useful. Characterizing the Canadian societal burden for individuals with HD

and their care partners will not only address a critical gap in the current literature but will also be vital for improving access to healthcare resources and supports for the Canadian HD community. We conducted a real-world evidence (RWE) study to examine the impact of the disease on individuals with HD and care partners of individuals with HD in Canada.

MATERIALS AND METHODS

Study population and design

We conducted a cross-sectional online survey to collect real-world data from individuals in Canada who had a self-reported diagnosis of HD or were self-reported unpaid care partners with healthcare decision-making responsibilities for individuals with HD. Professional care partners (i.e., those employed as a care partner) were not eligible to complete the survey. Eligible respondents were required to meet the following screening criteria: 1) have lived in Canada (excluding Newfoundland and Labrador) for the previous 12 months; 2) be ≥ 21 years of age for individuals with HD, or over the age of majority (≥ 18 years- or ≥ 19 years-old based on the province or territory of residence) for care partners; 3a) indicate a self-reported diagnosis of HD or identify as a proxy of an individual with HD; or 3b) for unpaid care partners, specify three or more responsibilities that were part of their caregiving role (see Supplementary Material). Of note, although both individuals with HD and their care partners were invited to participate in the study, the availability of a dyad was not part of the inclusion criteria. Responses from individuals with HD and care partners were considered independently.

Individuals were invited to participate in the survey through the email distribution lists, social media pages (Facebook and Twitter), and website postings of the *Huntington Society of Canada* (HSC) and *Société Huntington du Québec* (SHQ). After consenting to participate, respondents were identified as either: an individual with HD; a proxy respondent (helper or representative that completed the survey on behalf of the individual with HD if they were unable to complete the survey on their own); or a care partner of an individual with HD. Respondents were screened for eligibility and those who were deemed ineligible were redirected out of the survey and excluded. All responses to the screening criteria were further verified by the research team to confirm eligibility prior to analysis. The surveys were available in both English and French (Canada) and were completed between September 14, 2020, and November 23, 2020.

The survey for individuals with HD (or their proxies) focused on demographic and clinical characteristics, as well as HRQoL, HRU, and employment, all from the perspective of individuals with HD. The care partner survey focused on: demographic characteristics of care partners completing the survey; demographic and clinical characteristics of the individual with HD for whom they provide care; care partner-related burden associated with HD; and care partner HRQoL. For both surveys, self-reported motor transition status was determined based on the question: "Have you/the person living with HD transitioned to early-stage motor onset (i.e., stage 1 or 2)?". To estimate HD stage, a rating scale was developed for this survey that was similar to the Shoulson-Fahn functional capacity scale [36, 37]. The survey rating scale, which was adapted from the Unified Huntington's Disease Rating Scale (UHDRS) Total Functional Capacity (TFC), included the following domains for the assessment of abilities: occupation, finances, domestic chores, activities of daily living, and care level. Answers from respondents were scored and used to estimate HD stage, since the TFC scale can be converted into stages that correspond to the Shoulson-Fahn functional capacity scale. The full rating scale is provided in Supplementary Table 1. Responses were categorized into four stages, rather than five stages as used in the clinical Shoulson-Fahn functional capacity rating scale. Despite the similarities between our survey-specific rating scale and the Shoulson-Fahn functional capacity rating scale, they are not directly comparable.

The 36-Item Short-Form Health Survey (SF-36v1) is the recommended measure of HRQoL in individuals with HD [38]. It was therefore selected to assess HRQoL in this study, following the receipt of permission by the RAND Corporation. The results of the SF-36v1 were also mapped to the EuroQol 5 Dimensions (EQ-5D) to generate an EQ-5D utility score.

The Client Service Receipt Inventory (CSRI) used in this study was developed by adapting the validated CSRI [39] tools from the Enroll-HD Study [40] and for Parkinson's Disease [41]. For this study, a six-month recall period was assessed using the CSRI. This was done to better capture HRU outcomes (e.g., hospitalizations) that may not be used frequently because of the cross-sectional study

design. Since the survey was open to respondents between September–November 2020, which would have captured a period of employment and utilization during the Coronavirus disease 2019 (COVID-19) pandemic, additional questions were added to the survey to assess the impact of the COVID-19 pandemic on employment status, income, and HRU.

Care partner HRQoL and burden were assessed using the Huntington's Disease Quality of Life Battery for Carers (HDQoL-C) and the Caregiver Strain Index (CSI). The HDQoL-C is a validated and recommended tool for measuring quality of life in family care partners of individuals with HD that was developed with feedback from this population [38, 42, 43]. Permission to use the HDQoL-C and CSI were provided by Dr. Aimee Aubeeluck at the University of Nottingham and by the Oxford University Press, respectively.

The survey was administered via Qualtrics© software (Qualtrics, Provo, UT), a platform compliant with the General Data Protection Regulation and Personal Information and Electronic Documents Act. Respondents were not provided any type of compensation for completing the survey. This study was approved by the Health Research Ethics Board of Alberta Community Health Committee (HREBA-CHC) for the province of Alberta, and the Advarra Institutional Review Board (IRB) for the rest of Canada (excluding Newfoundland & Labrador).

Statistical analysis

The results presented include responses received and deemed eligible (i.e., those which met all required screening criteria) for the study. Responses from individuals with HD and proxies were combined for analysis.

Data are reported using descriptive statistics. For continuous variables, measures of central tendency (means and medians) and dispersion (standard deviation [SD], interquartile range [IQR], range) are reported. Where appropriate, distributions are reported. Any categorical variables are described with frequencies and percentages. Due to small sample size, in instances where responses have <10 individuals or where residual identification is feasible, response data have been suppressed to preserve respondent anonymity. In such cases, the general trends are discussed, but exact values are not presented.

The individual SF-36v1 scales were scored following the steps outlined in the SF-36 Interpretation and Scoring Guide [44]. In addition, the SF-36v1 Physical Component Summary and Mental Component Summary scores were calculated using the approach outlined by Ware et al. (1994) in the SF-36 Physical and Mental Health Summary Scales: A User's Manual utilizing Canadian normative values [45, 46]. SF-36v1 scales have been transformed to a 0–100 scale, where a lower score represents higher burden. The results of the SF-36v1 were also mapped to the EQ-5D using methodology (Model 3) outlined by Rowen et al. (2009) [47] to generate an EQ-5D utility score on a 0–1 scale, where 1 represents full health.

The CSRI was reported descriptively, as suggested by the Personal Social Services Research Unit of the University of Kent [48].

The HDQoL-C was scored according to the user guide of the HDQoL-C [42]. The HDQoL-C summary scores have been transformed to a percent score for Sections 2–4, where a 100% score represents optimum satisfaction with life and an optimum quality of life. The CSI was scored on a scale of 0–13 by summing the number of "Yes" responses; a score of seven or more indicates a high level of stress and burden.

HRQoL responses from individuals with HD (or their proxies) were stratified by motor transition status and respondent type (individuals with HD vs. proxy response), while care partner responses were stratified by motor transition status, where possible. Non-parametric statistical testing was used to compare results between subgroups due to non-normal distributions and small sample sizes. *P*-values for differences in categorical variables are based on the exact Pearson chi-squared test, while *p*-values for differences in continuous variables are based on the Kruskal-Wallis test. Differences with a *p*-value of <0.05 were considered statistically significant. All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

After responding to the screening questions, 62 individuals with HD (or their proxies) and 48 care partners met study inclusion criteria (Supplementary Figure 1). Participants that met the screening criteria may not have responded to every survey question or could have stopped responding to questions at any point in the survey, as forced responses were not permitted by the HREBA-CHC and Advarra IRB. Therefore, sample sizes may vary between questions.

Individual with HD/proxy survey

Demographics

The mean [SD] age of respondents with HD was 51.2 [13.8] years, and respondents were primarily male ($n = 44$; 72.1%) (Table 1). Just over one-third of respondents ($n = 22$; 35.5%) were estimated to have Stage 1 HD. The number of respondents trended downward across Stages 2–4, with the lowest number of respondents for Stage 4 ($n < 10$). Over half ($n = 34$; 57.6%) of the respondents with HD reported they had not experienced motor transition.

HRQoL

Overall, the lowest mean SF-36v1 score (indicating greatest HRQoL burden) was in the Role – Physical scale (46.8 [42.9]). Based on the Canadian SF-36 norms, the mean summary scores for the Physical and Mental Health Components among individuals with HD were 42.9 [13.4] and 42.8 [11.9], respectively (Table 2). The mean mapped EQ-5D utility score was 0.72 [0.24].

The SF-36v1 results were stratified by motor transition status (Fig. 1 and Supplementary Table 2). Among those who had not transitioned, the highest mean score was for the Physical Functioning scale (81.9 [30.0]) and the lowest scores were for Vitality (59.8 [19.7]) and Role – Emotional scales (59.8 [43.1]). Among those who had experienced motor transition, the highest mean score was for the Bodily Pain scale (71.9 [35.0]), while the lowest was for the Role – Physical scale (17.1 [26.4]). There were statistically significant differences in scores by motor transition status for each scale except Mental Health and Bodily Pain, with the largest differences in the Physical Functioning and Role – Physical scales. Compared with those who had transitioned, those who had not experienced motor transition had significantly higher mean values for both the Physical Component Summary score (48.7 [11.3] vs. 35.0 [11.5]; $p < 0.01$) and mapped EQ-5D utility score (0.82 [0.15] vs. 0.57 [0.27]; $p < 0.01$).

When comparing individuals with HD and proxy respondents ($n = 13$), statistically significant differences were observed for mapped EQ-5D utility score, the Physical Component Summary score, and across most SF-36v1 scales, except for Mental Health and Bodily pain (Supplementary Table 3).

Employment and CSRI

Among individuals with HD, 31.0% ($n = 18$) were retired, and 25.9% ($n = 15$) were employed; the remaining 43.1% ($n = 25$) were unemployed/other/homemaker/did not respond (Table 3). Most respondents ($n = 49$; 87.5%) reported that COVID-19 did not affect their employment status. Among those who were employed ($n = 15$), most respondents reported having full-time employment, and did not require time off work due to HD ($n < 10$; data not shown). However, among those who were unemployed, most left their jobs due to HD ($n < 10$; data not shown). The most reported main income source for all respondents with HD was government benefits ($n = 17$; 30.4%); the most reported gross annual income range was $25,000–$50,000 Canadian dollars ($n = 18$; 32.1%). Approximately half ($n = 31$; 55.4%) of the overall respondents reported receiving government benefits, of which the majority received disability benefits ($n = 25$; 80.6%). Employment results stratified by transition status (sample sizes were $n < 10$) are not presented to protect patient confidentiality.

Overall, for individuals with HD, the majority did not use hospital or residential services within the prior six months (Table 4). Most respondents ($n = 38$; 71.7%) reported that their use of hospital and residential services stayed the same during the COVID-19 pandemic. When stratified by motor transition status, statistically significantly higher ($p < 0.05$) use of neurology outpatient and nursing or residential home services was observed among respondents who had experienced motor transition.

The most frequently used primary and community care services (Table 4) were general practitioner (GP) or internist/family doctor visits (in-person), followed by telemedicine visits (with any healthcare practitioner). No significant differences were observed when stratified by motor transition status. Over half of all respondents ($n = 29$; 56.9%) reported that their use of primary and community care services remained the same during the COVID-19 pandemic.

Among individuals with HD who use informal care services (Table 4), the most used services were help in or around the house (e.g., cooking, cleaning, laundry) and help outside the house (e.g., shopping, transport) ($n = 16$; 31.4% and $n = 12$; 23.5%, respectively). Respondents who had experienced motor transition had statistically significant ($p < 0.05$) greater frequency of use of help in/around the house and help outside the house compared with those who had not experienced motor transition.

Only a small proportion of individuals with HD reported using adaptive equipment (Table 4). Among those who did, the most frequently used equipment

Table 1
Self-reported demographic characteristics of individuals with HD (from individual with HD/proxy[a]- or care partner-completed surveys)[b]

Characteristic	Individual with HD/proxy survey		Care partner survey	
	Respondents (n)	Estimate	Respondents (n)	Estimate
Age of individual with HD	62		NA	
Mean (SD)		51.2 (13.8)	–	–
Median (IQR)		51.0 (42.0 – 60.0)	–	–
Sex of individual with HD, *n* (%)	61		48	
Female		17 (27.9)		27 (56.3)
Male		44 (72.1)		21 (43.8)
Years since clinical HD diagnosis	62		48	
Years since clinical diagnosis, mean (SD)	59	9.9 (7.3)	47	11.7 (7.3)
Years since clinical diagnosis, median (IQR)	59	8.0 (4.0 – 16.0)	47	10.0 (7.0 – 17.0)
Received genetic testing results for HD?	62		48	
Years since genetic test results, mean (SD)	57	10.4 (7.8)	44	11.5 (7.1)
Years since genetic test results, median (IQR)	57	8.0 (4.0 – 18.0)	44	10.0 (6.0 – 16.0)
Symptoms Related to HD, *n* (%)[c]				
Movement/motor disorders	46		46	
Impaired gait, posture, and balance		32 (69.6)		46 (100.0)
Difficulty with speech or swallowing		31 (67.4)		41 (89.1)
Involuntary jerking or writhing movements (chorea)		27 (58.7)		41 (89.1)
Bumping into objects/people/walls		27 (58.7)		34 (73.9)
Dropping objects		24 (52.2)		35 (76.1)
Muscle problems or posturing		19 (41.3)		27 (58.7)
Experiencing falls		17 (37.0)		31 (67.4)
Vision problems		< 10		< 10
Cognitive disorders	41		47	
Slowness in processing thoughts or "finding" words		36 (87.8)		44 (93.6)
Difficulty organizing, prioritizing or focusing on tasks		33 (80.5)		42 (89.4)
Difficulty in learning new information		27 (65.9)		37 (78.7)
Lack of flexibility or the tendency to get stuck on a thought, behavior, or action (perseveration)		23 (56.1)		39 (83.0)
Lack of awareness of one's own behaviors and abilities		14 (34.1)		36 (76.6)
Lack of impulse control that can result in outbursts, acting without thinking, and sexual promiscuity		10 (24.4)		19 (40.4)
Neuropsychiatric disorders	40		43	
Fatigue/loss of energy		33 (82.5)		39 (90.7)
Feelings of sadness or apathy		27 (67.5)		28 (65.1)
Insomnia		22 (55.0)		26 (60.5)
Feelings of irritability or angry outbursts		19 (47.5)		26 (60.5)
Frequent thoughts of death, dying, or suicide		< 10		< 10
HD Stage[d] *n* (%)	62		48	
1		22 (35.5)		< 10
2		13 (21.0)		< 10
3		< 10		19 (39.6)
4		< 10		19 (39.6)
No score		10 (16.1)		< 10
Motor Transition Status, *n* (%)	59		47	
Have not transitioned/Non-respondent		34 (57.6)		12 (25.5)
Transitioned		25 (42.4)		35 (74.5)

HD, Huntington's disease; IQR, interquartile range; NA, not asked in the care partner survey; SD, standard deviation. Cells representing < 10 individuals are suppressed to reduce the risk of re-identification of individuals. [a]A proxy respondent was defined as a helper/representative that completed the survey on behalf of the individual with HD if they were unable to complete the survey independently. [b]The individuals with HD/proxy or care partner surveys responses are not patient-care partner dyads. [c]Percentages for different symptoms are based on individuals with HD who answered 'Yes' to the section. [d]HD stage was estimated based on self-reported answers to a survey-specific rating scale (details in Supplementary Table 1). Of note, although the survey rating scale is similar to the clinical Shoulson-Fahn functional capacity rating scale, it is not directly comparable.

was grab rail/stair rails and handrails. Most utilization of adaptive equipment was reported by respondents who had experienced motor transition, with significantly greater use ($p < 0.05$) reported for grab rail/stair rails, handrails, medication reminder dispensers, and outdoor railings.

Table 2
SF-36v1 scale and summary scores[a] for individuals with HD

Scale	All Respondents		
	n	Mean (SD)	Median (IQR)
Bodily Pain	49	74.1 (27.3)	74.0 (61.0 – 100.0)
Mental Health	48	65.7 (18.4)	68.0 (52.0 – 80.0)
Physical Functioning	49	61.4 (39.0)	75.0 (15.0 – 100.0)
Social Functioning	49	59.7 (29.7)	62.5 (37.5 – 87.5)
General Health	48	55.0 (22.8)	56.0 (41.0 – 71.0)
Vitality	48	53.1 (22.6)	52.5 (37.5 – 70.0)
Role – Emotional Scale	49	46.9 (44.1)	33.3 (0.0 – 100.0)
Role – Physical Scale	49	46.8 (42.9)	50.0 (0.0 – 100.0)
Physical Component Summary Score	48	42.9 (13.4)	47.5 (29.8 – 53.5)
Mental Health Component Summary Score	48	42.8 (11.9)	42.6 (37.0 – 53.5)
Mapped EQ-5D Utility Score[b]	48	0.72 (0.24)	0.77 (0.62 – 0.90)

HD, Huntington's disease; IQR, interquartile range; SD, standard deviation. [a]Individual SF-36v1 scales were scored following the SF-36 Interpretation and Scoring Guide [44]. Physical Component Summary and Mental Component Summary scores were calculated using the approach outlined by Ware et al. (1994) in the SF-36 Physical and Mental Health Summary Scales: A User's Manual utilizing Canadian normative values [45, 46]. SF-36v1 scales have been transformed to a 0–100 scale, with a lower score representing a higher burden. [b]The SF-36 was mapped to the EQ-5D using methodology outlined by Rowen et al. (2009) [47] to generate a utility score from 0-1, with a score of 1 representing full health.

Care partner survey

Characteristics of care partners for individuals with HD

Most care partners were female ($n = 31$; 75.6%), with a mean age of 58.1 [13.9] years. Nearly half were the primary care partner for the individual with HD ($n = 35$; 85.4%) and 46.3% ($n = 19$) were unemployed (Table 5). The mean number of years caring for a (primary) family member with HD was 10.2 [8.7] years and most care partner respondents had not previously cared for any other person affected by HD ($n = 32$; 78.0%).

Characteristics of individuals with HD receiving care from a care partner are reported in Table 1. Most care partner respondents reported that the individuals in their care had experienced motor transition ($n = 35$; 74.5%) and were estimated as HD Stage 3 ($n = 19$; 39.6%) or Stage 4 ($n = 19$; 39.6%).

Care partner burden and HRQoL

The mean CSI score was 6.9 [3.8], with 55.3% ($n = 21$) of respondents having a score greater than or equal to seven, indicating high strain (Table 5). The categories of the CSI that were most affected included "It is upsetting to find the person I care for has changed so much from his/her former self" ($n = 30$; 75.0%), "I feel completely overwhelmed" ($n = 27$; 67.5%), and "Some behaviour is upsetting" ($n = 26$; 65.0%) (Supplementary Table 4). When stratified by motor transition status, the only category for which significant differences in scores were observed was for the "Some behaviour is upsetting" category, although the sample size for individuals with HD who had not experienced motor transition was small ($n < 10$; data not shown).

Care partner respondents reported HDQoL-C mean percent summary scores of 46.5 [16.3] for Section 2 (feelings about role as a caregiver), 62.1 [21.3] for Section 3 (satisfaction with different areas of life), and 45.1 [17.9] for Section 4 (feelings about different areas of life) (Table 5; Supplementary Table 5). Care partner respondents of individuals with HD who had not experienced motor transition had lower summary scores across all sections of the HDQoL-C when compared with care partners of individuals with HD who had experienced motor transition; however, these differences did not reach statistical significance ($n < 10$; data not shown).

DISCUSSION

This study has sought to address important gaps in understanding the impact HD has on HRQoL, employment and HRU for individuals with HD, and the care partners of individuals with HD, in Canada.

Respondents with HD reported substantial impairment in HRQoL, with the greatest burden observed with respect to the SF-36v1 Role – Physical scale and the least burden observed with respect to the Bodily Pain scale. Our results suggest that motor transition is associated with greater burden, particularly

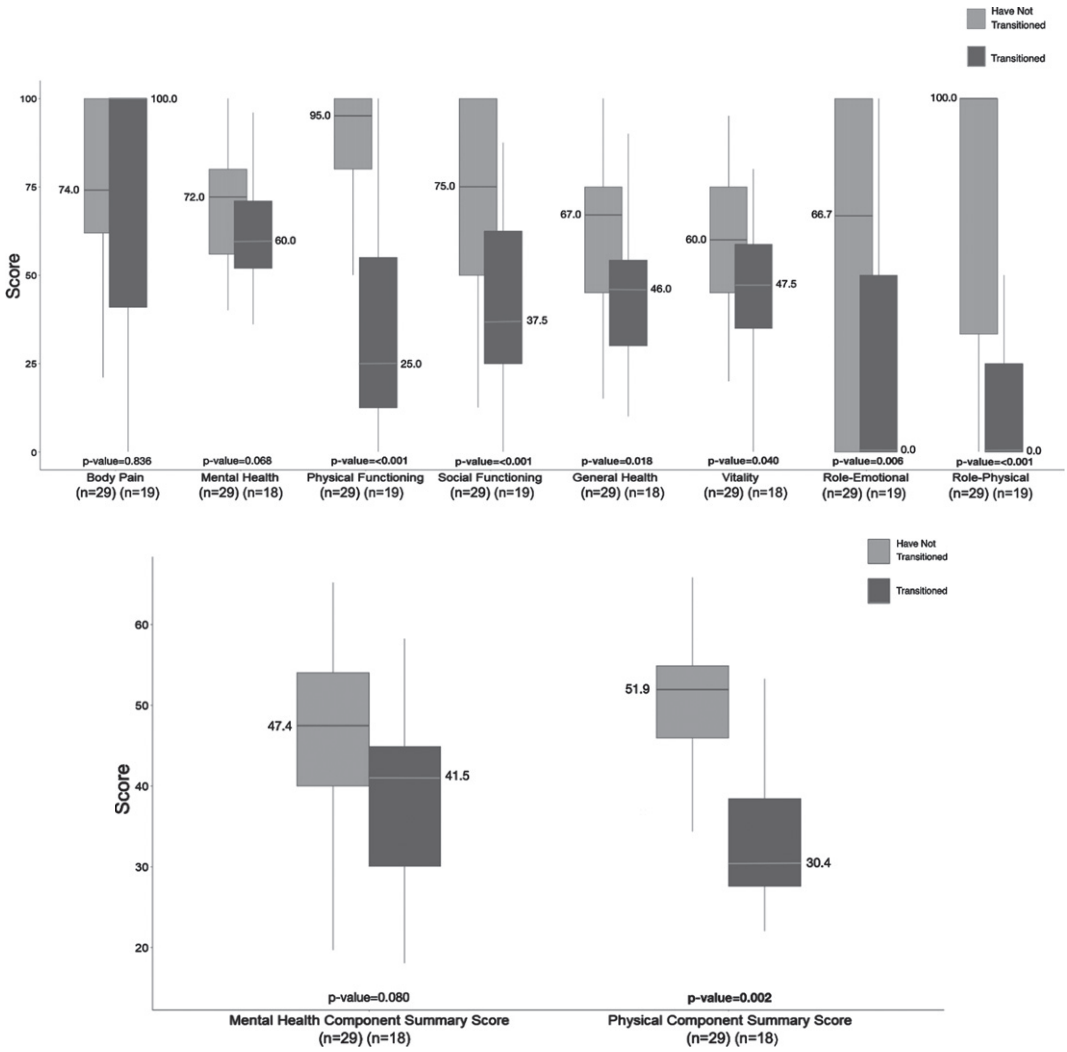

Fig. 1. Median SF-36v1 scale scores[a] (A) and summary scores[a] (B) stratified by motor transition status[b] in individuals with HD. HD, Huntington's disease. *P*-values for continuous variables are based on the Kruskal-Wallis test comparing mean ranks of respondents based on self-reported motor transition status. Bold *p*-values indicate significance ($p < 0.05$). [a]Individual SF-36v1 scales were scored following the SF-36 Interpretation and Scoring Guide [44]. Physical Component Summary and Mental Component Summary scores were calculated using the approach outlined by Ware et al. (1994) in the SF-36 Physical and Mental Health Summary Scales: A User's Manual utilizing Canadian normative values [45, 46]. SF-36v1 scales have been transformed to a 0–100 scale, with a lower score representing a higher burden. [b]Motor transition status was self-reported and determined based on the question: "Have you/the person living with HD transitioned to early-stage motor onset (i.e., stage 1 or 2)?".

for the SF-36v1 Role – Physical and Physical Functioning scales, as compared with the Mental Health and Bodily Pain scales. The literature is extremely limited, but these findings generally align with those from the study completed by van Walsem et al. (2017), where individuals in Norway with advanced disease (Stage 4 and 5 HD) reported the lowest HRQoL, while individuals with moderately advanced disease (Stage 3) had the most variable HRQoL [12]. Of note, the progression of HD is associated with cognitive impairments, some of which may impact the responses provided on patient-reported outcome measures. While cognitive impairments associated with late-stage HD have been shown to negatively impact the psychometric properties (e.g., reliability and validity) of some patient-reported outcome measures for HRQoL, the reliability of the HDQLIFE^{TM} still meets established clinical standards, therefore, remains a valuable measure for evaluating HRQoL throughout the progression of HD [49].

Table 3
CSRI[a] results for individuals with HD - Employment and income

Characteristic	Respondents (*n*)	Estimate
Employment status, *n* (%)	**58**	
Employed (paid, voluntary, or sheltered)		15 (25.9)
Unemployed		< 10
Student		0 (0.0)
Homemaker		< 10
Retired		18 (31.0)
Other		14 (24.1)
Non-respondents		< 10
ALL RESPONDENTS		
Employment status result of COVID-19, *n* (%)	**56**	
Yes		< 10
No		49 (87.5)
Non-respondents		< 10
Main income source, *n* (%)	**56**	
Salary/Wage		16 (28.6)
Government benefits		17 (30.4)
Pension		12 (21.4)
Family support (e.g., from spouse)		< 10
Other		< 10
Gross annual income, *n* (%)	**56**	
$10,000 or less		< 10
$10,000 – 25,000		14 (25.0)
$25,000 – 50,000		18 (32.1)
$50,000 – 75,000		11 (19.6)
$75,000 – 100,000		< 10
$100,000 or more		< 10
Non-respondents		< 10
Receive any government benefits, *n* (%)	**56**	
Yes		31 (55.4)
No		25 (44.6)
Benefits received, *n* (%)	**31**	
Employment Insurance		< 10
Sickness Benefits		< 10
Disability Benefits		25 (80.6)
Compassionate Care Benefits		< 10
Parents of Critically Ill Children Benefits		0 (0.0)
Housing Benefits		< 10
Other		< 10
Private insurance coverage, *n* (%)	**56**	
Yes		28 (50.0)
No		28 (50.0)

CSRI, Client Service Receipt Inventory; HD, Huntington's disease; IQR, interquartile range; SD, standard deviation. Cells representing < 10 individuals are suppressed to reduce the risk of re-identification of individuals. [a]The CSRI results are reported as indicated by the Personal Social Services Research Unit of the University of Kent [48].

The mean score on the SF-36v1 Bodily Pain scale in our study (74.1 [27.3]) was at the bottom end of the range of mean SF-36 Pain scale scores seen in the literature (74.1–88.3) [3, 8, 50–53]. Such a finding is not unusual. Sprenger et al. (2019) showed that individuals with HD had significantly lower pain burden (mean: 84, 95% confidence interval [CI]: 81–86) compared to the general population (70.8 [25.5]) [52, 54], which could be attributed to medications taken, associated comorbid conditions, anosognosia, or other factors not yet identified [52]. More severe HD could result in other symptoms, by comparison, having a more significant impact on quality of life than pain, which could result in pain being reported less frequently [52, 55].

HRQoL was observed to be significantly lower for most scales among proxy respondents when compared with non-proxy respondents, which may be related to most proxy respondents in the overall survey ($n = 14$; 77.8%) answering on behalf of individuals who had transitioned (data not shown). While proxy respondents were supposed to answer the questionnaire on behalf of the patient, there may be some bias with respect to the lower HRQoL, as proxies tend to underestimate HRQoL using the SF-36v1 [56, 57]. However, since anosognosia can be associated with HD [33], in some cases proxies may be in a better position to capture HRQoL than patients.

Approximately one quarter (25.9%; $n = 15$) of individuals with HD were employed, and most employed patient respondents reported not requiring time off work due to HD ($n < 10$; data not shown). However, among unemployed individuals with HD, most reported leaving the workforce due to HD ($n < 10$). By comparison, the employment rate in the Canadian population in 2020 for those between 25–54 years of age was 79.5%, and for those 55 years of age or older was 33.9% [58, 59], indicating HD may negatively impact employment when compared to the general Canadian population. There is limited evidence reporting the impact of HD on employment, but a study by Watkins et al. (2018) indicated that cognitive symptoms had a significant association with functional capacity at work, as well as the decision to leave work [16]. As HD progresses, increasing cognitive symptoms can result in work environments being more challenging to navigate and may lead to individuals deciding to leave the workforce.

The proportion of respondents receiving care from GPs and telemedicine is higher in our study compared with the results of a survey study in the United States, which reported only one in five individuals with HD were currently receiving medical or community care [60]. However, this may be due to differences between the healthcare systems. Additionally, reported telemedicine use may have been greater due to our survey being conducted during the

Table 4
CSRI[a] results for patients with HD: Hospital and residential services in the last 6 months

Utilization	For all HD Patients[b]		N (%) reporting "Yes" to services[c]		
	Yes *n* (%)	No *n* (%)	Have not transitioned (*N* = 30)	Transitioned (*N* = 22)	*p*[d]
Hospital and Residential Services (*n* = 53)					
Neurology outpatient	23 (43.4)	25 (47.2)	< 10	15 (75.0)	0.001
Other hospital outpatient	16 (30.2)	32 (60.4)	< 10	< 10	0.758
Hospital emergency room	< 10	42 (79.2)	< 10	< 10	0.144
Nursing or residential home	< 10	43 (81.1)	< 10	< 10	0.010
Ambulatory/same day surgery	< 10	46 (86.8)	< 10	< 10	0.176
Inpatient hospital stays	< 10	46 (86.8)	< 10	< 10	1.000
Frequency of use of services due to COVID-19					
Increased	< 10		–	–	–
Decreased	12 (22.6)		–	–	–
Stayed the Same	38 (71.7)		–	–	–
Non-respondent	< 10		–	–	–
Primary and Community Care Services (*n* = 51)					
GP or internist/family doctor	34 (66.7)	15 (29.4)	20 (69.0)	14 (73.7)	0.759
Telemedicine (i.e., telephone appointments with healthcare practitioners)	19 (37.3)	26 (51.0)	12 (44.4)	< 10	1.000
Social worker	11 (21.6)	31 (60.8)	< 10	< 10	0.164
Psychiatrist	< 10	29 (56.9)	< 10	< 10	1.000
OT	< 10	36 (70.6)	< 10	< 10	0.208
Practice nurse (nurse practitioner or physician assistant)	< 10	33 (64.7)	< 10	< 10	0.677
Other services	< 10	31 (60.8)	< 10	< 10	0.439
Frequency of use of services due to COVID-19					
Increased	< 10		–	–	–
Decreased	15 (29.4)		–	–	–
Stayed the Same	29 (56.9)		–	–	–
Non-respondent	< 10		–	–	–
Investigations/Diagnostic Tests (*n* = 51)					
Blood test	22 (43.1)	27 (52.9)	11 (39.3)	11 (55.0)	0.381
MRI	< 10	42 (82.4)	< 10	< 10	1.000
CT/CAT scan	< 10	44 (86.3)	< 10	< 10	1.000
Genetic test	< 10	48 (94.1)	< 10	0 (0.0)	1.000
EEG	< 10	47 (92.2)	0 (0.0)	< 10	0.426
Informal Care (*n* = 51)					
Help in/around the house (e.g., cooking, cleaning, laundry)	16 (31.4)	34 (66.7)	< 10	12 (60.0)	< 0.001
Help outside the house (e.g., shopping, transport)	12 (23.5)	37 (72.5)	< 10	10 (50.0)	0.002
Personal care (e.g., washing, dressing)	< 10	41 (80.4)	< 10	< 10	0.429
Childcare	< 10	45 (88.2)	< 10	< 10	1.000
Other	< 10	35 (68.6)	< 10	< 10	0.132
Equipment, Aids, Devices, & Adaptations to the Home (*n* = 51)					
Grab rail/stair rail	17 (33.3)	31 (60.8)	< 10	13 (65.0)	< 0.001
Handrails	16 (31.4)	32 (62.7)	< 10	13 (65.0)	< 0.001
Calendar clock	13 (25.5)	35 (68.6)	< 10	< 10	0.324
Medication reminder dispenser	12 (23.5)	36 (70.6)	< 10	< 10	0.012
Outdoor railing	11 (21.6)	37 (72.5)	< 10	< 10	0.002

CSRI, Client Service Receipt Inventory; CT/CAT, computed tomography; EEG, electroencephalogram; GP, general practitioner; HD, Huntington's disease; IQR, interquartile range; MRI, magnetic resonance imaging; OT, occupational therapist; SD, standard deviation. Cells representing < 10 individuals are suppressed to reduce the risk of re-identification of individuals. [a]The CSRI results are reported as indicated by the Personal Social Services Research Unit of the University of Kent [48]. [b]Percentages may not equal 100% since non-respondent results are not shown. [c]Percentages are calculated using the number of respondents who answered each question item as the denominator, which is not always equal to the number of eligible respondents for each stratum (noted in the subsection headings). [d]*P*-values for categorical variables are based on the chi-squared test comparing respondents based on self-reported transition status.

COVID-19 pandemic, as demonstrated in a primary care study from Ontario during the first four months of the pandemic [61].

The findings of this study also highlight that there is substantial strain associated with being a care partner of someone with HD, with more than half (*n* = 21;

Table 5
Self-reported demographic and quality of life characteristics of care partners for individuals with HD

Characteristic	Respondents (n)	Estimate
Age	48	
Mean (SD)		58.1 (13.9)
Median (IQR)		59.5 (48.0 – 68.0)
Sex, *n* (%)	41	
Male		< 10
Female		31 (75.6)
Non-respondent		< 10
Marital status, *n* (%)	41	
Single		< 10
Married		20 (48.8)
Partnership		< 10
Separated		< 10
Divorced		< 10
Widowed		< 10
Non-respondent		< 10
Years that presence of HD in your family known	36	
Mean (SD)		21.3 (14.2)
Median (IQR)		20.0 (10.0 – 31.5)
Years caring for a (primary) HD affected family member	36	
Mean (SD)		10.2 (8.7)
Median (IQR)		7.0 (4.5 – 14.0)
Main carer for the person with HD, *n* (%)	41	
Yes		35 (85.4)
No		< 10
Non-respondent		< 10
Affected person is my, *n* (%)	41	
Sibling		< 10
Spouse/Partner		25 (61.0)
Parent		< 10
Child		< 10
Other		< 10
Non-respondent		< 10
Previously cared for any other HD affected person, *n* (%)	41	
Yes		< 10
No		32 (78.0)
Non-respondent		< 10
Current Employment, *n* (%)	41	
Yes		19 (46.3)
No		19 (46.3)
No due to the COVID-19 pandemic		< 10
Non-respondent		< 10
Total Caregiver Strain Index Score[a] (n)	38	
Mean (SD)		6.9 (3.8)
Median (IQR)		8.0 (3.0 – 10.0)
Respondents with high stress/ burden (score ≥ 7), *n* (%)		21 (55.3)
HDQoL-C Summary Scores[b]		
Section 2 - Feelings about role as a caregiver[c]	36	
Mean (SD)		46.5 (16.3)
Median (IQR)		48.9 (35.0 – 56.1)
Section 3 - Satisfaction with different areas of life	38	
Mean (SD)		62.1 (21.3)
Median (IQR)		60.0 (46.3 – 78.8)
Section 4 - Feelings about different areas of life	34	
Mean (SD)		45.1 (17.9)
Median (IQR)		48.8 (32.4 – 55.9)

COVID-19, Coronavirus disease; HD, Huntington's disease; HDQoL-C, Huntington's Disease Quality of Life Battery for Carers; IQR, interquartile range; SD, standard deviation. Cells representing < 10 individuals are suppressed to reduce the risk of re-identification of individuals. [a]The Caregiver Strain Index was scored from 0–13 by summing the number of "Yes" responses. A score of ≥ 7 indicates a high level of stress and burden. [b]The HDQoL-C was scored according to the HDQoL-C User Guide. HDQoL-C summary scores were transformed to a percent score for Sections 2–4, where a 100% score represents optimum quality of life. [c]Responses may be skewed as the data analyzed from the survey excluded one level of response.

55.3%) of respondents scoring greater than seven on the CSI. These findings are consistent with other studies that used the modified CSI. Williams et al. (2009) reported that the emotional aspect of caregiving for individuals with HD can cause substantial distress and impact the care partner's own life, through the loss of the relationship with their spouse, for example, if that is the individual for whom they provide care [27]. This type of emotional distress would likely impact perceived care partner burden [27]. Other studies in the Canadian context have also shown the stress experienced by those providing care to individuals with HD related to caregiving responsibilities, as well as the challenges associated with accessing relevant healthcare and community services [26, 35].

Using the HDQoL-C, we found that care partners reported the highest score for Section 3 (satisfaction with different areas of life), with lower scores in Section 2 (feelings about role as a caregiver) and Section 4 (feelings about different areas of life). Results from our study are in line with those of studies from other jurisdictions using the HDQoL-C [13, 62]. Cox et al. (2010) reported the mean score for American caregivers on the HDQoL-C was 55%, which was characterized as suboptimal quality of life [62]. Similar results were seen in France and Italy using the short-version of the HDQoL-C [13], where nearly half of caregiver respondents reported being unsatisfied with their own happiness (France 44%, Italy

45%) and with their general quality of life (France 38%; Italy 45%). Furthermore, the HDQoL-C short-version scores that were reported by French and Italian caregivers for the "satisfaction with life" and "feelings about living with HD" sections [13] are in a similar range to those observed in our study.

The similarity of the HRQoL scores for this Canadian sample and those reported from other countries in the current literature [12, 13, 16, 27, 52, 60, 62] demonstrates the consistent and substantial impact of HD on the HRQoL of both individuals with HD and care partners of persons with HD, despite differences in the resources and supports available across countries. However, these results also illustrate the importance of obtaining country-specific estimates for resource use and indirect costs, as these have been shown to vary internationally across healthcare systems [14, 15].

This study had several strengths. Both individuals with HD and care partners of individuals with HD were surveyed and several aspects of disease burden were measured. Respondents resided in seven of the thirteen Canadian provinces and territories, provided responses in both English and French, and results were also stratified by motor transition status. This provides information about the burden of disease across Canada, and in different phases of disease progression. Furthermore, there were limited missing data from the survey respondents, with over 80% of respondents who were eligible completing the surveys in their entirety. Our study provides relevant real-world context for the burden HD places on affected individuals, which expands the current literature that primarily evaluates HRQoL in the context of international clinical trials.

However, some limitations should also be noted. This was a cross-sectional survey study, which can be subject to response, recall, and selection biases. Response bias is an important consideration, since respondents may alter their responses or behavior because they know they are part of a study. Recall bias may have also impacted the accuracy of the results as respondents were asked to recall details related to their HRQoL (up to four weeks) and HRU (up to 6 months) prior to completing the survey. Selection bias is another aspect to consider; since no incentives were provided for participating in this survey, it is possible that the motivation to participate may differ based on the current impact of HD on individuals and care partners (e.g., those who are more heavily affected may be more interested in participating). Due to the anonymous nature of the survey, it is not possible to verify and confirm that respondents were indeed individuals diagnosed with HD or care partners of individuals with HD. Proxy responses were permitted for respondents with HD. Although proxies were supposed to provide answers on behalf of individuals with HD, this could not be verified in their survey responses.

The survey included questions to identify motor transition status; however, we cannot attribute any differences in outcomes to motor transition status, due to the cross-sectional design. Furthermore, due to the small sample sizes, adjustments for confounding variables could not be completed. In our study, over half of the respondents with HD reported they had not yet experienced motor transition, while nearly three quarters of care partner respondents reported the individual in their care had transitioned. This difference is likely due to the screening criteria applied to respondents completing the care partner survey, which may have resulted in more care partners of transitioned or later stage individuals with HD being included in the study. It may have also been possible that due to anosognosia, individuals with HD may not have been fully aware of their symptoms, which could have resulted in an underreporting of their motor transition status.

There was also a limited number of survey respondents for both study surveys, which limited the ability to report results by motor transition status and HD stage. This may have reduced the precision of the estimates obtained. It is important to note that although we obtained a limited sample size, it is similar to the sample sizes of two other Canadian studies that recruited for interviews of HD care partners [26, 27]. Other publications utilizing similar survey tools, such as the SF-36 [52] and HDQoL-C [63], have also achieved comparable relative sample sizes. We therefore believe the sample size of our study is aligned with the current literature.

Lastly, this survey collected answers on HRQoL and HRU for individuals with HD and care partners during the COVID-19 pandemic, which itself may have impacted HRQoL. However, most individuals with HD who responded indicated the COVID-19 pandemic did not significantly impact their employment or HRU. The COVID-19 pandemic may have also affected the sample size obtained for this study. We worked with the *Huntington Society of Canada* and *Société Huntington du Québec* to launch the survey following the first wave in Canada. However, the pandemic circumstances may have prevented potential survey respondents from participating due to

impacts on financial situations, mental health, and/or access to care, among other factors.

Due to the nature of HD progression, there are substantial differences among individuals that have progressed to different stages of HD, as well as between those who have or have not experienced motor transition. We attempted to address this in our survey study, but due to the limited sample size obtained, some stratifications of interest needed to be withheld to preserve patient confidentiality. Larger studies evaluating the differences in HRQoL and HRU associated with different stages of HD and motor transition status in Canada would be of great interest.

In conclusion, the current study identified a substantial burden on the HRQoL and HRU on both individuals with HD and care partners, with lower HRQoL and higher HRU reported among individuals who experienced motor transition. These findings add to a very limited evidence base regarding the impact of HD on HRQOL, HRU, and employment, particularly in the Canadian context. Despite differences in infrastructure and available resources to support patients and their care partners, similar HRQoL impacts have been observed in other countries. To our knowledge, this is the first study to investigate the burden of illness of HD on individuals with HD and care partners in Canada. Burden of illness information is applied throughout a broad range of Canadian public health policy and practice [64], demonstrating how crucial understanding the burden of HD is for improving healthcare access and support for those diagnosed with the disease and their care partners in Canada.

ACKNOWLEDGMENTS

This is a study sponsored by Hoffmann-La Roche Ltd. We thank Wayne Khuu (Medlior) for his work in cleaning the data and reviewing the study results, and Khushboo Gurjar (Medlior) for her work in creating the Qualtrics surveys.

CONFLICT OF INTEREST

ES, MM, PE, SM, EG, and TC are employed by Medlior Health Outcomes Research Ltd. which received funding for the study from Hoffmann-La Roche Ltd. JWW, NB, and BM are employed by Hoffmann-La Roche Ltd., who funded this study. JWW, NB, and BM also hold Hoffmann-La Roche Ltd. stock. TM reports speaker honorarium from Abbvie, and International Parkinson and Movement Disorder Society; consultancies from CHDI Foundation/Management, Sunovion, Valeo Pharma, Roche, nQ Medical and Merz; advisory board from Abbvie, Biogen, Sunovion, Medtronic; and research funding from EU Joint Programme - Neurodegenerative Disease Research, uOBMRI, Roche, Ontario Research Fund, CIHR, MJFF, Parkinson Canada, PDF/PSG, LesLois Foundation, PSI Foundation, Parkinson Research Consortium and Brain Canada.

SUPPLEMENTARY MATERIAL

The supplementary material is available in the electronic version of this article: https://dx.doi.org/10.3233/JHD-210505.

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