Work and Activity Impairment in Huntington Disease

Shoshana Reshef,[1] Erin Furr Stimming,[2] Victor Sung,[3] Rosa Willock,[4] Rinat Ribalov,[5] Sarah Brighton,[4] Sam Leo[6]

[1]Teva Branded Pharmaceutical Products R&D, Inc., Epidemiology and Global Health Economics and Outcomes Research, Parsippany, NJ, United States; [2]UTHealth, McGovern Medical School, Houston, TX, United States; [3]University of Alabama at Birmingham, Birmingham, AL, United States; [4]HCD Economics Ltd, Cheshire, United Kingdom; [5]Teva Pharmaceutical Industries Ltd., Global Health Economics and Outcomes Research, Tel Aviv, Israel; [6]Teva Branded Pharmaceutical Products R&D, Inc., Global Health Economics and Outcomes Research, Parsippany, NJ, United States

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Introduction

- Huntington disease (HD) is a rare, genetic, and highly complex neurodegenerative disease with increasing prevalence in Australia, North America, and Western Europe (including the United Kingdom) during the past 50-plus years[1]
- The most common motor symptom in adult-onset HD is chorea, which negatively affects patients' quality of life and overall functional status[2]
- HD is commonly associated with impaired employment and work productivity[3]; however, there is a paucity of real-world data assessing employment status in relation to chorea severity and HD stage

Objective

- To describe employment status and work and activity impairment in individuals with HD by chorea severity and HD stage

Methods

Study Design and Data Source

- Data for this retrospective observational study were obtained from Enroll-HD—a large, global research platform following individuals with or at risk of HD, and their families and non-HD caregivers. Data cut for the period of 2013–31 October 2020 were used for this analysis

Study Population and Assessments

- Participants aged ≥18 years were categorized by HD status into 3 subpopulations: pre-motor manifest (pre-manifest), motor-manifest (manifest), and genotype negative or family control (non-HD)
- Participants in the manifest subpopulation were classified by:
  - HD stage based on Total Functional Capacity (TFC) scores at baseline according to Shoulson and Fahn Staging scores (adapted from Johnson[4]) (**Table 1**)
  - Chorea severity categories based on Unified Huntington's Disease Rating Scale® Total Maximal Chorea (TMC) scores grouped into evenly divided ranges (0–7, 8–14, 15–21, 22–28) for analysis (0 = no chorea, 28 = most severe)
- Employment status and work productivity were assessed via the Work Productivity and Activity Impairment Questionnaire (WPAI)[5]

Table 1. HD Stages

HD stage	TFC score	Shoulson and Fahn Staging score[4]
Early	7–13	Stage 1–2
Middle	3–6	Stage 3
Late	0–2	Stage 4–5

HD = Huntington disease, TFC = Total Functional Capacity

Analysis

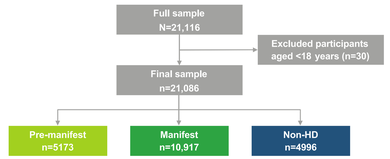
- Mean (SD) or frequency (as proportion) of baseline characteristics were calculated for the pre-manifest, manifest, and non-HD subpopulations
- Mean (SD) or frequency (as proportion) for employment and work productivity measures were calculated for the pre-manifest and non-HD subpopulations, as well as the manifest subpopulation by HD stage and chorea severity category

Results

Participants

- A total of 21,086 participants in the Enroll-HD dataset were selected for analysis (**Figure 1**)

Figure 1. Analysis Population



HD = Huntington disease

Baseline Characteristics

- The manifest subpopulation included a smaller proportion of women, and patients were older on average, weighed less, and had lower mean body mass index compared with the pre-manifest and non-HD subpopulations (**Table 2**)
- Marital status, area of residence, and International Standard of Education (ISCED) level showed no patterns across the 3 subpopulations, except that the manifest subpopulation seemed to have been more educated up to the upper secondary education level (**Table 2**)

Table 2. Baseline Characteristics (Pre-Manifest, Manifest, and Non-HD Subpopulations)

	Pre-manifest n=5173	Manifest[a] n=10,903	Non-HD n=4996
Age at enrollment, years, mean (SD)	39.8 (12.1)	53.0 (12.8)	46.7 (14.8)
Female, n (%)	3099 (59.9)	5602 (51.4)	3056 (61.2)
Weight, kg, mean (SD)	76.4 (18.3)	72.0 (16.4)	79.8 (19.7)
BMI, kg/m^2, mean (SD)	26.2 (5.6)	24.9 (5.0)	27.7 (6.2)
Marital status, n (%)			
Married	2517 (48.7)	6069 (55.7)	3098 (62.0)
Partnership	887 (17.2)	713 (6.5)	588 (11.8)
Single	1337 (25.9)	2089 (19.2)	835 (16.7)
Divorced	315 (6.1)	1412 (13.0)	246 (4.9)
Legally separated	63 (1.2)	189 (1.7)	25 (0.5)
Widowed	51 (1.0)	417 (3.8)	200 (4.0)
Missing	3 (0.7)	14 (0.1)	4 (0.1)
Area of residence, n (%)			
City	2367 (45.8)	4125 (37.8)	2323 (46.5)
Town	1738 (33.6)	4152 (38.1)	1543 (30.9)
Village	776 (15.0)	1987 (18.2)	761 (15.2)
Rural	286 (5.5)	627 (5.8)	362 (7.3)
Missing	6 (0.1)	12 (0.1)	7 (0.1)
Education level, n (%)			
ISCED 0 (early childhood education)	4 (0.1)	34 (0.3)	11 (0.2)
ISCED 1 (primary education)	44 (0.9)	490 (4.5)	145 (2.9)
ISCED 2 (lower secondary education)	503 (9.7)	1960 (18.0)	461 (9.2)
ISCED 3 (upper secondary education)	1359 (26.3)	3698 (33.9)	1372 (27.5)
ISCED 4 (post-secondary non-tertiary education)	1126 (21.8)	1863 (17.3)	1045 (20.9)
ISCED 5 (short-cycle tertiary education)	1948 (37.7)	2516 (23.1)	1788 (35.8)
ISCED 6 (Bachelor's or equivalent)	173 (3.3)	261 (2.4)	153 (3.1)
Missing	16 (0.3)	61 (0.6)	21 (0.4)

BMI = body mass index, HD = Huntington disease, ISCED = International Standard of Education, TMC = Total Maximal Chorea
[a]Based on patients with TMC scores, 14 patients were missing TMC scores.

Key Results

Unemployment

- The proportion of unemployed participants increased from pre-manifest (24.3%) and non-HD (29.0%) subpopulations, and increased in the manifest subpopulation as HD progressed—TFC early (68.1%), TFC middle (98.4%), and TFC late (99.6%)—and as chorea severity increased–TMC 0–7 (71.4%), TMC 8–14 (80.2%), TMC 15–21 (92.3%), and TMC 22–28 (96.3%) (**Table 3**)

Work productivity

- Among employed participants, work missed because of HD was similar in the pre-manifest and non-HD subpopulations (~1.9% in both groups), and increased in the manifest subpopulation as HD progressed—TFC early (mean [SD], 11.1% [28.5]), TFC middle (19.6% [36.7]), and TFC late (53.0% [not calculable because n=1])—and as chorea severity increased—TMC 0–7 (9.3% [26.1]), TMC 8–14 (13.5% [31.3]), TMC 15–21 (17.2% [34.1]), and TMC 22–28 (73.0% [18.4]) (**Table 3**)
- Overall activity impairment was similar in the pre-manifest and non-HD subpopulations (~5 in both groups), and increased in the manifest subpopulation as HD progressed—TFC early (mean [SD], 31.5% [28.7]), TFC middle (59.4% [29.2], and TFC late (82.4% [24.2])—and as chorea severity increased—TMC 0–7 (34.5% [31.5]), TMC 8–14 (41.4% [31.7]), TMC 15–21 (55.4% [31.8]), and TMC 22–28 (66.1% [30.3]) (**Table 3**)

Table 3. Baseline Employment and Work Productivity by HD stage and Chorea Severity (Pre-Manifest, Manifest, and Non-HD Subpopulations)

		Pre-manifest subpopulation		Manifest subpopulation[a]												Non-HD subpopulation	
				HD stage						Chorea severity category							
				TFC early		TFC middle		TFC late		TMC 0–7		TMC 8–14		TMC 15–21		TMC 22–28	
		n	n (%)	n	n (%)	n	n (%)	n	n (%)	n	n (%)	n	n (%)	n	n (%)	n	n (%)	n	n (%)
Employment status	Full-time	5173	2933 (56.7)	7441	1549 (20.8)	2330	15 (0.6)	1120	0	5055	944 (18.7)	4374	565 (12.9)	1310	57 (4.4)	164	2 (1.2)	4996	2680 (53.6)
	Part-time		765 (14.8)		642 (8.6)		16 (0.7)		1 (<0.1)		388 (7.7)		233 (5.3)		36 (2.8)		3 (1.8)		649 (13.0)
	Self-employed		208 (4.0)		165 (2.2)		1 (<0.1)		0		99 (2.0)		61 (1.4)		6 (0.5)		0		203 (4.1)
	Unemployed		1255 (24.3)		5069 (68.1)		2292 (98.4)		1116 (99.6)		3610 (71.4)		3506 (80.2)		1209 (92.3)		158 (96.3)		1447 (29.0)
	Missing		12 (0.2)		16 (0.2)		6 (0.3)		3 (0.3)		14 (0.3)		9 (0.2)		2 (0.2)		1 (0.6)		17 (0.3)
Unemployment reason	Sick leave	1255	153 (12.2)	5069	963 (19.0)	2292	498 (21.7)	1116	232 (20.8)	3610	753 (20.9)	3506	687 (19.6)	1209	222 (18.4)	158	30 (19.0)	1447	74 (5.1)
	Retirement		300 (23.9)		2538 (50.1)		1282 (55.9)		667 (59.8)		1744 (48.3)		1938 (55.3)		705 (58.3)		103 (65.2)		636 (44.0)
	Working in the home		219 (17.5)		353 (7.0)		116 (5.1)		51 (4.6)		243 (6.7)		202 (5.8)		67 (5.5)		9 (5.7)		304 (21.0)
	Unemployed		412 (32.8)		1163 (22.9)		389 (17.0)		157 (14.1)		826 (22.9)		663 (18.9)		209 (17.3)		13 (8.2)		272 (18.8)
	Training/ college		171 (13.6)		44 (0.9)		4 (0.2)		3 (0.3)		38 (1.1)		11 (0.3)		3 (0.3)		0		159 (11.0)
	Missing		0		8 (0.2)		3 (0.1)		6 (0.5)		6 (0.2)		5 (0.1)		3 (0.3)		3 (1.9)		2 (0.1)
Social/ disability benefits[b]	Yes	712	279 (39.2)	3701	2231 (60.3)	1671	1288 (77.1)	824	658 (79.9)	2570	1630 (63.4)	2601	1749 (67.2)	914	698 (76.4)	116	99 (85.3)	908	356 (39.2)
	No		431 (60.5)		1451 (39.2)		367 (22.0)		155 (18.8)		918 (35.7)		835 (32.1)		212 (23.2)		15 (12.9)		539 (59.4)
	Missing		2 (0.3)		19 (0.5)		16 (1.0)		11 (1.3)		22 (0.9)		17 (0.7)		4 (0.4)		2 (1.7)		13 (1.4)
Reductions to work[c]	Yes	3906	194 (5.0)	2356	554 (23.5)	32	18 (56.3)	1	1 (100.0)	1431	299 (20.9)	859	244 (28.4)	99	28 (28.3)	5	4 (80.0)	3532	91 (2.6)
	No		3710 (95.0)		1790 (76.0)		13 (40.6)		0		1124 (78.6)		612 (71.3)		69 (69.7)		1 (20.0)		3437 (97.3)
	Missing		2 (0.1)		12 (0.5)		1 (3.1)		0		8 (0.6)		3 (0.4)		2 (2.0)		0		4 (0.1)
WPAI[d]		n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)	n	mean (SD)
1: % work missed because of HD		1920	1.9 (12.1)	1140	11.1 (28.5)	18	19.6 (36.7)	1	53.0 (–)	680	9.3 (26.1)	422	13.5 (31.3)	55	17.2 (34.1)	2	73.0 (18.4)	1409	1.8 (10.6)
2: % impairment while working because of HD		1662	3.7 (12.2)	918	20.6 (25.0)	16	37.5 (31.1)	0	–	546	18.3 (23.6)	348	24.0 (26.8)	38	27.9 (28.4)	2	45.0 (7.1)	1186	2.8 (11.1)
3: % overall work impairment because of HD		1658	4.2 (13.6)	915	22.7 (27.4)	15	40.0 (33.5)	0	–	543	20.2 (25.6)	347	26.1 (29.1)	38	31.1 (32.1)	2	85.5 (7.8)	1181	3.6 (12.9)
4: % activity impairment because of HD		2556	5.5 (15.9)	3533	31.5 (28.7)	920	59.4 (29.2)	293	82.4 (24.2)	2228	34.5 (31.5)	1922	41.4 (31.7)	545	55.4 (31.8)	56	66.1 (30.3)	2049	4.9 (16.5)

– = no responses recorded, HD = Huntington disease, TFC = Total Functional Capacity, TMC = Total Maximal Chorea, WPAI = Work Productivity and Activity Impairment
[a]26 patients were missing TFC scores; 14 patients were missing TMC scores.
[b]If retired/unemployed.
[c]Whether the participant has stopped or reduced work as a result of their health.
[d]Calculated for patients with non-missing data only.

Conclusion

- **These results indicate markedly increased unemployment when moving from pre-manifest (24.3%) to early-stage manifest (68.1%) HD as well as work and activity impairment, demonstrating substantial disease burden even during the earliest stages of HD, with increased burden as HD stage increased**
- **This indicates a dramatic increase in disease burden as HD progressed and chorea severity increased**
- **These results are consistent with previous studies and provide additional evidence to support the large societal impact of HD and chorea and suggest that chorea severity correlates with work and activity impairment**

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