

Huntington's Disease Burden of Illness (HDBOI): study methodology, sample representativeness and fieldwork risk mitigation strategy during the COVID-19 pandemic



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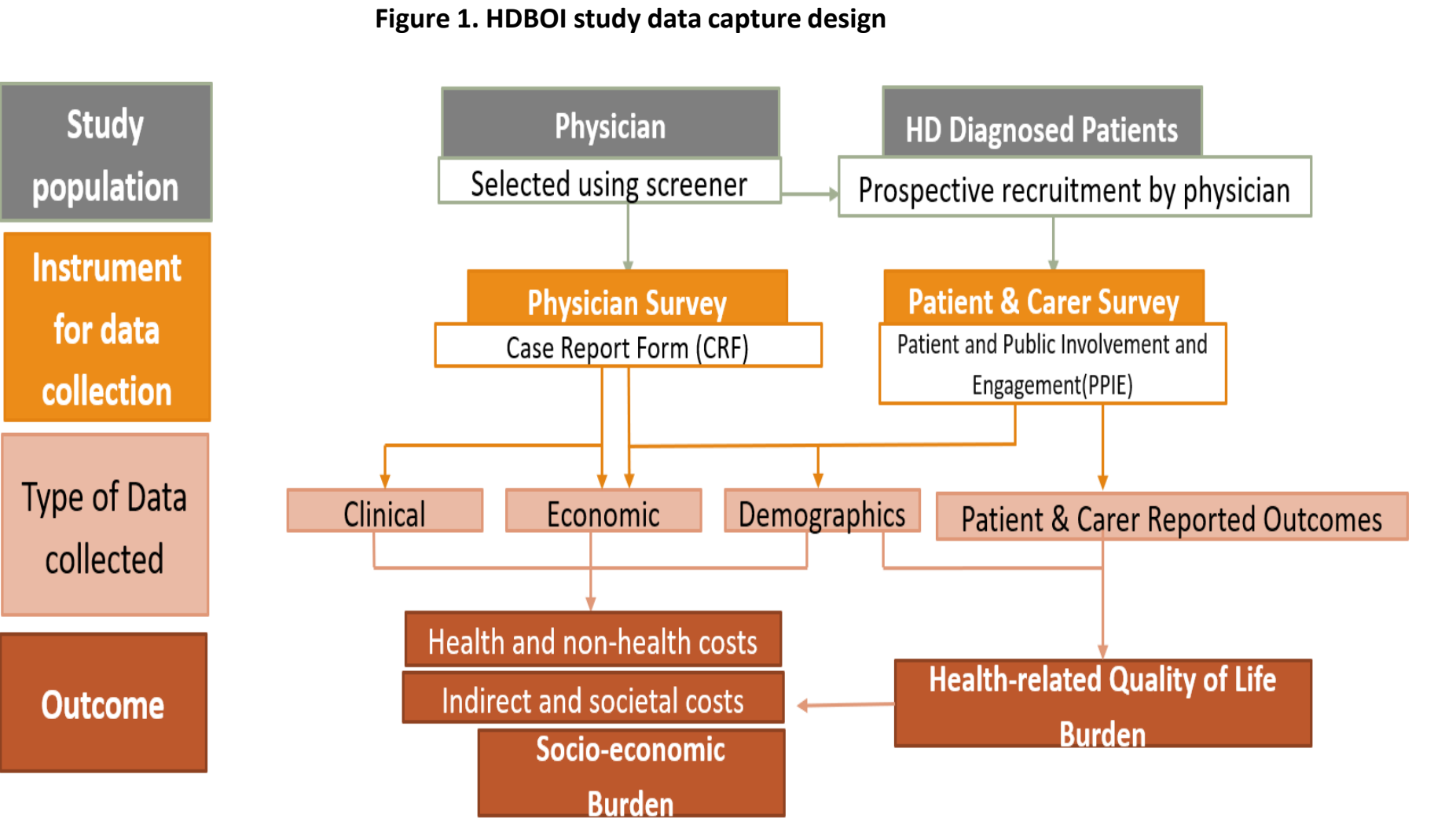
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Introduction

- The overall prevalence of Huntington's Disease (HD) is increasing¹ and the economic and humanistic burden associated with the condition is substantial.^{2,3} Recent research estimates annual costs associated with HD in the UK equates to £195 million per year.²
- There is limited evidence available providing a comprehensive assessment of the clinical, economic, and humanistic burden of HD by disease stage and on a large scale.
- The Huntington's Disease Burden of Illness (HDBOI) study aims to provide an up-to-date assessment of the burden of HD from a multinational perspective.
- This study also examines the impact of the COVID-19 pandemic on HD patients' health resource use (HRU) and health-related quality of life (HRQoL).

Methods

- The HDBOI is a retrospective, cross-sectional dataset that captures demographic, clinical, and HRU of a cohort of HD patients, reported by treating physicians in multiple centres across the USA, Germany, Spain, Italy, France, and the UK.
- Patients and caregivers reported information on HRQoL, non-medical and indirect costs associated with HD via optional questionnaires, Patient and Public Involvement and Engagement (PPIE) (See **Figure 1**).



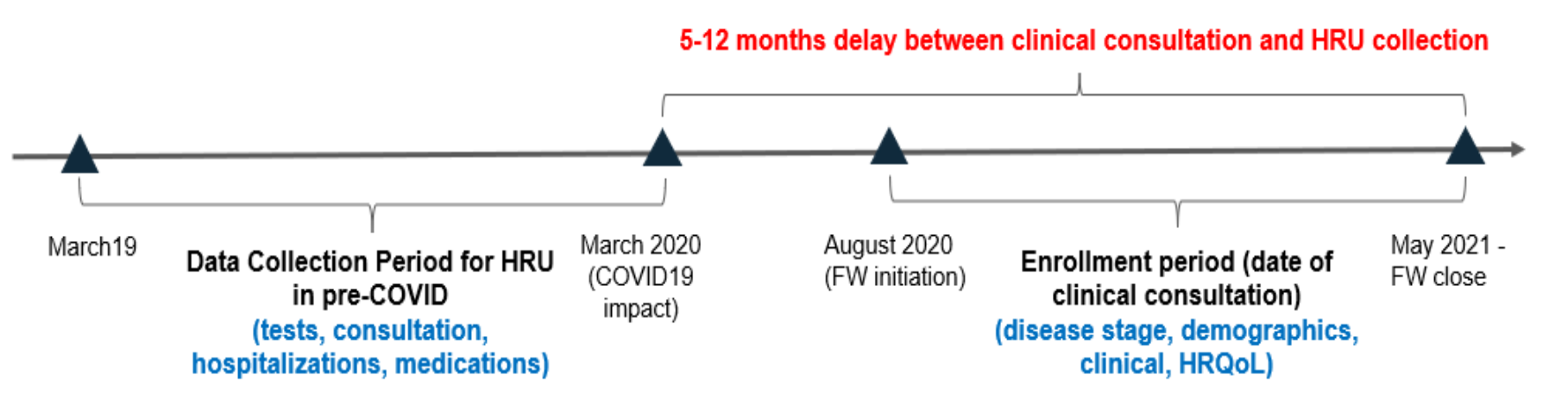
Methods continued

- The study was governed by an Expert Review Group (ERG), consisting of clinicians, allied health professionals, academics, and patient advocacy representatives, to provide expert input into the study.
- Ethical approval was granted by the Research Ethics Subcommittee at the University of Chester (RESCO420-1038).
- Data was collected from:
 - Physicians via the Case Report Form (CRF), collecting demographic, clinical, direct and indirect costs associated with HD.
 - PPIE questionnaires capturing information on demographics, health status, non-medical and indirect costs.
- This information was used to establish the clinical, economic, and humanistic burden associated with HD.

COVID-19 Fieldwork Risk Mitigation Strategy

- Data was collected between August 2020 and May 2021, with patients and caregivers reporting their HRQoL at the time of questionnaire completion.
- Physicians reported patient's HRU for the 12-month period between March 2019 and March 2020, to minimise underestimation due to limited access to healthcare as a result of COVID-19 public health measures, displayed in **Figure 2**.
- Other strategies taken to mitigate the effect of COVID-19 on the fieldwork (FW) process included:
 - Online questionnaires
 - Extending the time for FW – initially scheduled for four months, but subsequently extended to nine months
 - Questions monitoring the effect of the pandemic on patients in terms of their HRU, physical health, and mental health

Figure 2. HRU and clinical consultation data collection timeframe, as amended due to COVID-19



Results

- The HDBOI sample consisted of 2,094 HD patients, of which 40.4% were early stage (ES), 33.5% were mid stage (MS) and 26.1% were advanced stage (AS), assessed by the treating physician and based on disease progression.
- Patient representation across countries was similar, with a minimum of 220 patients from France and a maximum of 492 from the US and Italy, displayed in **Table 1**.
- For a subsample (N=718) the Shoulson and Fahn stages were reported by the treating physician: stage I (14.6%), II (24.4%), III (31.6%), IV (28.1%) and V (1.1%).
- A lower proportion of Stage V patients was anticipated by the ERG, as many of these patients reside in long term residential care homes.
- 482 patients completed questionnaires (PPIE-Patient), of which 42% were ES, 34% were MD, and 24% were AS.
- In addition, 503 caregivers completed optional questionnaires (PPIE-Caregiver), of which 35% were ES, 36% were MD, and 29% were AS.

Table 1. CRF, PPIE-Patient and PPIE-Caregiver by country: total and by disease stage

CRF	All Sample	Early	Mid	Advance/Late
Country	Freq (%)	Freq (%)	Freq (%)	Freq (%)
Germany	264 (12.6)	96 (11.4)	85 (12.1)	83 (15.2)
Spain	354 (16.9)	152 (18)	107 (15.3)	95 (17.4)
France	220 (10.5)	104 (12.3)	62 (8.8)	54 (9.9)
UK	272 (13)	91 (10.7)	111 (15.8)	70 (12.8)
Italy	492 (23.5)	190 (22.4)	182 (26)	120 (21.9)
US	492 (23.5)	213 (25.2)	154 (22)	125 (22.8)
Total	2094 (100)	846 (40.4)	701 (33.5)	547 (26.1)

PPIE-P	All Sample	Early	Mid	Advance/Late
Country	Freq (%)	Freq (%)	Freq (%)	Freq (%)
Germany	13 (2.7)	5 (2.4)	5 (3.1)	3 (2.6)
Spain	207 (43)	103 (50.5)	58 (35.4)	46 (40.4)
France	43 (8.9)	20 (9.8)	14 (8.5)	9 (7.9)
UK	56 (11.6)	6 (2.9)	26 (15.9)	24 (21)
Italy	126 (26.1)	55 (27)	49 (29.9)	22 (19.3)
US	37 (7.7)	15 (7.4)	12 (7.3)	10 (8.8)
Total	482	204 (42)	164 (34)	114 (24)

PPIE-C	All Sample	Early	Mid	Advance/Late
Country	Freq (%)	Freq (%)	Freq (%)	Freq (%)
Germany	7 (1.4)	1 (0.5)	2 (1.1)	4 (2.7)
Spain	199 (39.6)	93 (52.3)	54 (30.2)	52 (35.6)
France	42 (8.4)	17 (9.6)	15 (8.4)	10 (6.9)
UK	75 (14.9)	12 (6.7)	39 (21.8)	24 (16.4)
Italy	142 (28.2)	42 (23.6)	58 (32.4)	42 (28.8)
US	38 (7.5)	13 (7.3)	11 (6.2)	14 (9.6)
Total	503 (100)	178 (35)	179 (36)	146 (29)

Note: Early/Mid/Advanced stage is based on an assessment by treating physician. Total Functional Capacity (TFC) score based on the Shoulson and Fahn Staging System was reported for a subsample of patients.

Results continued

Table 2. Impact of COVID-19 pandemic reported by patient: total and by disease stage

	All patients	Early	Mid	Advance/Late
Impact on HRU	Freq (%)	Freq (%)	Freq (%)	Freq (%)
Yes	347 (72)	155 (76)	110 (67)	82 (71.9)
No	135 (28)	49 (24)	54 (33)	32 (28.1)
Total	482 (100)	204 (100)	164 (100)	114 (100)

	All patients	Early	Mid	Advance/Late
Impact on physical health	Freq (%)	Freq (%)	Freq (%)	Freq (%)
Yes	311 (64.5)	139 (68.1)	99 (60.4)	73 (64)
No	171 (35.5)	65 (31.9)	65 (39.6)	41 (36)
Total	482 (100)	204 (100)	164 (100)	114 (100)

	All patients	Early	Mid	Advance/Late
Impact on mental health	Freq (%)	Freq (%)	Freq (%)	Freq (%)
Yes	363 (75.3)	160 (78.4)	121 (73.8)	82 (71.9)
No	119 (24.7)	44 (21.6)	43 (26.2)	32 (28.1)
Total	482 (100)	204 (100)	164 (100)	114 (100)

- Approximately 75% of HD patients reported COVID-19 impacting on their mental health, with 72% reporting an impact on their HRU, and 64.5% reporting an impact on their physical health.
- Similarly, 74.8% of caregivers reported an impact on HRU, 71.8% reported an impact on their mental health, and 59.4% reported an impact on their physical health.

Conclusion

- The HDBOI study is a representative sample of the HD population across disease stages and studied countries.
- Although patients' clinical profile may not be reflected in HRU due to data collection lag, authors felt this bias is smaller than the bias that may be encountered if HRU was collected during the pandemic, with limited access to healthcare.
- The COVID-19 pandemic impacted patients and caregivers, particularly in terms of HRU and mental health, justifying our mitigation strategy.
- Finally, this study provides novel data to quantify HD health resource use by disease stage, increasing the evidence base for the HD community.

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