A Targeted Literature Review to Inform Future Economic Evaluations of Huntington's Disease

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Introduction

- Huntington's disease (HD) is a rare neurodegenerative disorder characterised by undesirable choreatic movements, behavioral and psychiatric disturbances [1].
- HD progression has a detrimental impact on all aspects of an individual's life, resulting in substantial burden from both an economic and a wider societal perspective [2].
- The introduction of gene therapy (GTx), which may be offered to HD patients in the future, raises questions related to its cost-effectiveness and affordability for HD patients. However, evidence to inform economic evaluations of GTx in HD is scarce.
- Future GTx has the potential to alleviate disease burden, requiring the generation of further evidence to inform cost-effectiveness analyses.

Rationale and Objective

- We sought to understand the current landscape of GTx and HD literature as a precursor to developing an early, conceptual cost-utility analysis (CUA) model of GTx for HD with consensus-driven input parameters.
- Our objective was to identify estimates of the economic burden of HD, including cost data and epidemiological information with respect to HD.

Methods

- We conducted a targeted literature review (TLR); the information captured from this review is to be subsequently utilised to inform the conceptual CUA model in terms of input parameters used, modelling methodology, and specification.
- A comprehensive search of studies assessing HD costs, health resource utilisation (HRU), and burden of illness (BOI) was conducted on varying databases (EMBASE, Medline via the PubMed interface and Web of Science).
- The search was limited to publications released in the past 10 years.
- Forward and backward citation searching was used to identify and retrieve additional key papers.
- We also performed a manual search of publications from recent congresses.
- The search strategy involved identifying studies that included words relating to 'Huntington's disease', 'cost', 'health resource utilisation', 'budget impact' and 'burden of disease'.
- Studies were screened against a pre-defined inclusion criteria e.g., grey literature (HD congress posters and abstracts).

Eligibility criteria

Inclusion criteria	Exclusion criteria
• HD studies • Published abstracts and conference posters (3-5 years) • Studies published within the last 10 years (January 2011 - June 2021)	Studies without any: • HD Resource utilisation • HD Cost data • HD BOI data • Non-HD studies • Published before 2011 • Not published in English • Non–relevant publication type or any other non-peer-reviewed literature) • Comments to published articles • QoL burden studies

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References

1. National haemophilia foundation (NHF). Hemophilia A and haemophilia B. 2019.
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Results

- BOI full-text study articles strictly pertaining to both cost and resource utilisation in HD were sparse.
- With the small number of cost studies identified (n=3), studies were not restricted to specific geographical locations, in efforts to gather as much relevant data as possible.
- We identified 20 international BOI studies in Australasia, Europe, North and Latin America.

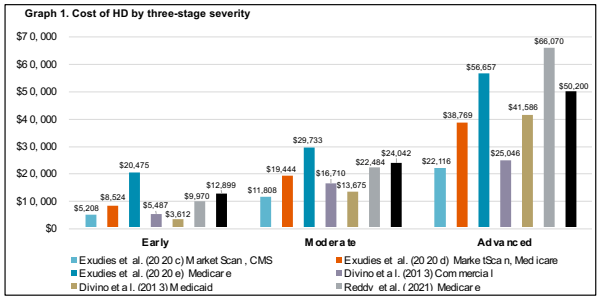
Table 1. Extraction of data in US and non-US based Burden of illness studies

Publication Type	Study	Data Source	Perspective	Outcomes (Direct Costs Highlighted)	Breakdown by HD State
US Based BOI studies					
Abstract	1. Anderson et al Neurology. (2018): P4. 044	MarketScan Commercial and Medicare Supplemental databases	Healthcare payer	Direct costs & Resource utilisation	NA (abstract only)
Posters	2. Exuzides et al (a) Academy of Managed Care Pharmacy 2020	HD cohorts: custom web-based survey in the US PD & general population: US National Health and Wellness Survey	Healthcare payer and societal	Resource utilisation	N
	3.Exuzides et al (b) Academy of Managed Care Pharmacy 2020	Medicare	Health care payer	Direct costs & Resource utilisation	N
	4.Exuzides et al (c) MDS 2020 24th International Congress of Parkingson's Disease and Movement Disorders	Claims data identified from IBM MarketScan Commercial, Medicaid and Medicare Supplemental databases.	Healthcare payer	Direct costs & Resource utilisation	Y (Early, Moderate, Advanced)
	5.Exuzides et al (d) Value in Health. 2020 1;23:S263-4.	Medicare	Healthcare payer	Direct costs & Resource utilisation	Y (Early, Moderate, Advanced)
	6.Exuzides et al (2020 e) medically.gene.com	Truven MarketScan Commercial and Medicare Supplemental Databases	Healthcare payer	Direct costs & Resource utilisation	Y (Early, Moderate, Advanced)
	7. Raimundo et al. 23rd International Congress of Parkinson's Disease and Movement Disorders (2019)	Private + Medicare + Medicaid	Healthcare payer	Resource utilisation	Y (Early, Moderate, Advanced)
	8. Reddy et al. MDS 2020 24th International Congress of Parkingson's Disease and Movement Disorders	Medicare*	Healthcare payer	Direct Palliative care costs & Resource utilisation	N
	9. Reddy et al. Academy of Managed Care Pharmacy .2021	Medicare*	Healthcare payer	Direct costs & Resource utilisation	Y (Early, Moderate, Advanced)
	10. Ta et al. Academy of Managed Care Pharmacy .2021	Medicare*	Healthcare payer	Direct costs & Resource utilisation	Y (Early, Moderate, Advanced)
Full-text articles	11. Divino et al. J. Med. Econ. 16. 2013, pg1043–1050	Medicaid MarketScan 2002–2009 databases	Health care payer	Direct costs	Y (Early, Moderate, Advanced)
	12. Sung et al. J. Health Econ. Outcomes Res. 6. 2018; pg15–24	Truven MarketScan® Commercial Claims and Encounters (Commercial) Database	Health care payer and societal	Direct costs & resource utilisation	N
International BOI Studies					
Abstract	13. Young & Quarrel. J Neurol Psychiatry (2018). pg F19	Interview and questionnaire	UK; Healthcare payer and societal perspective	Direct and indirect costs	NA (abstract only)
	14. Rodrigues et al. Value in Health (2020), pg S624	Multicentre retrospective and cross sectional data at the patient, caregiver, and physician level	EU 5; Healthcare payer and societal perspective	Direct and indirect costs & societal costs	NA (abstract only)
	15. Dorey et al. Value in Health. 2013: PND36	Cross-sectional survey across EU and US	Multinational; Healthcare payer and societal	Direct and indirect costs & Resource utilisation	NA (abstract only)
Posters	16. Dorey et al. World Congress on Huntington's Disease. 2011: P240	Primary data collection via survey	Multinational; Healthcare payer and societal	Direct and indirect costs & Resource utilisation	N
	17. Ko et al. MDS 2020 24th International Congress of Parkinson's disease and Movement disorder	HD patients used from Enroll-HD (NCT01574053) observational study used to conduct analysis	Multinational; Societal	Employment status	Y (Stage I-V TFC score)
Full-text articles	18. Jones C et al. European journal of Neurology. 2016 Oct;23(10):1589-96.	European Huntington's Disease Network REGISTRY	UK; Healthcare payer and societal	Direct costs & societal costs	Y (Stage I-V TFC score)
	19. Ohlmeier et al. BMC Neurology (2019) 19:316	Institute for Applied Health Research Berlin (InGef) Research Database	Germany; Health care payer	Resource utilisation	N
	20. Silva-Paredes et al. BMC Health Services Research (2019) 19:1017	NRC–INCN: Neurogenetics Research Center –Instituto Nacional de Ciencias Neurológicas; SIS: Integral Health Insurance	Peru; Societal	Direct and indirect costs	N

Results continued

- A majority of studies (11/20) focused on the healthcare payer (HP) perspective alone, 7/20 studies reported HP alongside societal costs (SC), and 2/20 studies reported SC alone.
- Of the 20 publications in the analysis, majority of the studies captured direct costs. One paper included direct, indirect and wider societal costs.
- HD disease severity stratification was presented in 9/20 studies, with 2/9 utilising the Total Functional Capacity (TFC) scoring measure, while the remaining 7/9 categorised HD stages "early, moderate and advanced" using HRU type (e.g., hospice care exemplified HD advanced stage).

Graph 1. Cost of HD by three-stage severity



- HD related costs vary by country; the annual cost for an HD patient was on average the highest in the US HD population. Using a standardised currency, HRU and annual costs per patient increased with HD stages.
- Annualised direct medical costs of HD ranged from $5,208 to $12,899 for early stage HD, from $11,808 to $29,733 for moderate stage HD, and from $22,116 to $66,070 for advanced stage HD.

Discussion & Conclusion

- Using the above TLR findings, a health-economic model is currently under development in collaboration with leading experts in the field.
- Our TLR results highlighted substantial HD economic costs alongside evidence gaps in the literature.
- Given the extensive societal HD burden, the 9/20 studies identified presented disparities in information of indirect cost such as productivity loss, and caregiver burden.
- A highly cited study by Jones et al (2016) captured high disparity in direct versus societal costs; across the lifespan of an HD patient, direct costs observed were $36,407 (early to advanced stage) compared to societal costs of $92,521.
- Moreover, validated HD disease progression measures such as TFC were rarely employed, instead HD progression was categorised by the type of HRU utilised.
- Such categorisation may not provide an accurate reflection of HD health state residency.
- Future BOI studies are needed to provide comprehensive evidence for HD cost-effectiveness analyses.
- Further research may also be needed after disease modifying treatment becomes available.