New therapies in Huntington's Disease (HD): Challenges in modelling for health economic evaluations

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BACKGROUND

- Huntington's disease (HD) is a rare genetic, neurodegenerative disease characterised by cognitive, behavioural and motor symptoms (Figure 1).
- Most individuals with HD experience increasing disability, loss of independence and profound behavioural and cognitive changes, resulting in a heavy impact on heavy quality of life (QoL) and economic burden to the patients and their families.
- There is a lack of existing knowledge related to the socioeconomic and quality of life (QoL) burden of HD on individuals and their family members, particularly in late stage disease.
- To our knowledge, there are very limited existing published cost-effectiveness models for HD.

We aim to explore the challenges surrounding decision modelling for economic evaluation of interventions for HD to develop a conceptual disease model for HD.

METHODS

- A literature review was conducted to characterise the current understanding of the disease progression, the quality of life and economic impact of HD.
- Advice from clinical and health economic experts was sought to address the challenges on the selection of the health states, disease progression measures and the approach to model mortality.
- Qualitative synthesis was performed to summarise the challenges in conceptualizing the model for economic evaluation in HD.

RESULTS

Measures of Disease Progression

- The majority of the studies identified are modeling the HD course based on the TFC score.
- Examples of assessments used in clinical and research settings to measure HD are: 1) motor functioning measure (UHDRS Motor Exam), cognitive measures (Verbal Fluency, Stroop, SDMT), Functional Assessment measures (UHDRS TFC, UHDRS Functional Assessment Scale and UHDRS Independence Scale).

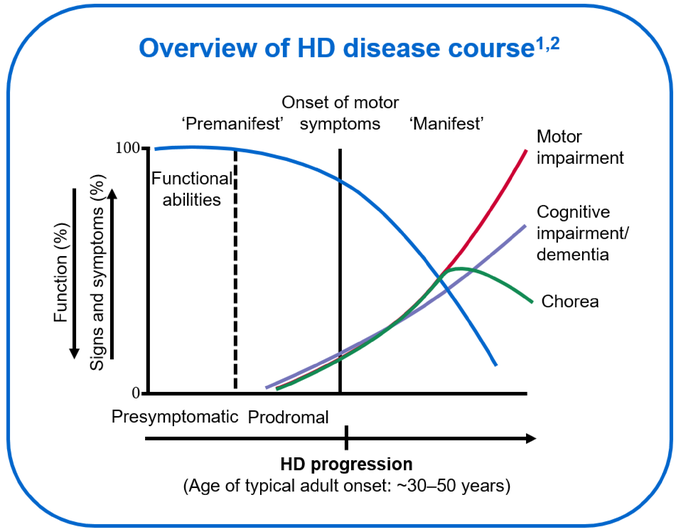
Mortality

- Although not specifically the focus of the literature review, we have identified natural history registry data (Enroll-HD) (3) which contains relevant mortality data. Several other studies were identified related to mortality. (5,6).

Costs and QoL Data:

- Only one cost-effectiveness (CE) analysis for HD was found in published literature (4).

Figure 1



DISCUSSION

Natural history/ Disease progression: Careful consideration needs to be taken with the choice of progression measure because models generally simplify the conceptualization of the disease course, limiting the number of disease states and the type of data that can be used to inform the progression of the disease.

Based upon natural history, the likely cycle length is 6 months to 1 year, as change in disease is particularly slow.

Mortality: There is uncertainty surrounding the type of data used to model mortality in HD. Although there is evidence of reduced survival in people with HD, it is very challenging to assess how a potential disease-modifying treatment for HD can affect mortality rates. Hence, it is hypothesized that a treatment which slows progression could carry a mortality benefit. Natural history data from registries should be carefully evaluated in order to be used to show mortality rates according to disease state.

QoL: Whilst there are some QoL data in the published literature, especially for early manifest HD, there is lack of data on QoL of later stages of HD. These various gaps in the literature will need to be addressed for future modeling efforts. QoL data by disease stage for the patients is required, as well as generation of data on disutilities for caregivers.

Costs: There are various gaps in the literature that will need to be addressed for future modeling efforts. A full costing study for health state costs by disease stage is required, as well as generation of cost impacts for caregivers. If possible, data on non-health costs such as lost productivity (due to absenteeism and unemployment) should be captured.

Caregivers: There is much burden to caregivers in terms of costs and QoL, and this should be incorporated into the model. However, the most appropriate method(s) to incorporate caregiver effects of a treatment is a subject of debate.

Apathy: We consider that the symptom/sign of apathy could directly be modelled by adjusting utility values – because as disease progresses, apathy worsens, reducing the patient's insight into their diminishing level of QoL.

CONCLUSION

- The choice of measure must be sensitive enough to distinguish any changes in disease progression at all stages of the HD spectrum to prevent underestimating the rate progression and treatment effects at other stages of disease.
- Filling data gaps between outcomes used across clinical trial settings and real-world settings in a standardized way is a starting point.
- Due to a lack of disease-modifying therapies currently available for the treatment of Huntington's disease, defining model comparators (e.g. best supportive care, competing gene therapy, etc.) will require careful attention to the comparator landscape.
- We describe here components towards generation of a CE model in HD.

The complex nature of HD, along with the likely requirement to assess the economic impact of interventions from the pre-symptomatic stages across the full disease continuum, has emerged as one of the main challenges in modeling HD.

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