Development of a Patient-Reported Outcome Measure in Wilson Disease

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BACKGROUND

- Wilson disease is a rare and sometimes fatal disorder in which a mutation of the gene *ATP7B* causes copper to accumulate in the blood. This toxic accumulation of copper can result in a range of disease presentations, including liver disease, psychological problems, and neurological issues
- The symptoms and impacts of Wilson disease can result in an enormous humanistic burden and can decrease health-related quality of life for patients
- Given the lack of validated patient-reported clinical outcome assessments (COAs) appropriate for use in Wilson disease, the Wilson Disease Functional Rating Scale – Patient Report (WDFRS-PR) was developed to assess the signs, symptoms, and impacts of Wilson disease
- The WDFRS-PR was developed using results from an online survey[1] and input from clinicians experienced in treating Wilson disease and is intended to assess the symptoms and impacts of Wilson disease. Concepts were used to develop a preliminary conceptual framework

OBJECTIVES

- The objective of this research was to confirm the content validity of the Wilson Disease Functional Rating Scale – Patient Report (WDFRS-PR) for use in the Wilson disease patient population

METHODS

- Institutional review board/ethics approval was obtained
- Participants completed the WDFRS-PR
- Mixed-concept elicitation and cognitive interviews were conducted to confirm the content, identify any missing concepts, and debrief the draft questionnaire

RESULTS

- A total of 29 adult and adolescent patient interviews were conducted, with 14 participants from an independent qualitative study participating in mixed-concept elicitation and cognitive debriefing interviews and 15 participants from a clinical survey study participating in cognitive debriefing interviews
- Results from the 14 concept elicitation interviews helped to further confirm the concepts in the WDFRS-PR along with spontaneous report of new concepts. A preliminary conceptual framework of signs, symptoms and impacts in Wilson disease is presented in **Figure 1**
  - During the concept elicitation portion of the Endpoint Outcomes study, patients reported a total of 34 unique signs and symptoms. The most frequently reported concepts included difficulty concentrating (n = 10 of 14, 71.4%), difficulty remembering things (n = 8 of 14, 57.1%), fatigue (n = 6 of 14, 42.9%) and joint pain (n = 6 of 14, 42.9%). Signs and symptoms of Wilson Disease reported both spontaneously and following probing by at least a third of participants are shown in **Figure 2**.
  - Additionally, patients reported a total of 40 unique disease impacts across 12 domains (i.e. activities of daily living, appearance, diet and medication, emotional, physical, financial, free time, organ-related, sleep, social life, disease management, work or school). The most frequently reported impacts included difficulty scheduling meals around medication (n = 10 of 14, 71.4%), restricted diet (low-copper diet) (n = 9 of 14, 64.3%), limits social activities (n = 8 of 14, 57.1%), difficulty performing at work/school (n = 6 of 14, 42.9%) and difficulty managing medication regimen (n = 6 of 14, 42.9%). Impacts of Wilson Disease reported both spontaneously and following probing by at least a third of participants are shown in **Figure 2**.
- N = 29 participants completed a cognitive debriefing of the WDFRS-PR. Overall, the WDFRS-PR instructions, items, and response options were interpreted as intended and reported to be clear
- Furthermore, a readability assessment was conducted for the WDFRS-PR, and the reading level was found to be appropriate for use in the intended population. Changes recommended to the WDFRS-PR included revising the concept of "saliva production" to "drooling" to improve clarity
- Participants reported varying levels of experience with concepts in the WDFRS-PR, with anywhere from 27.6% to 65.5% participants reporting that certain concepts (27.6% = more aggression than normal; 65.5% = fatigue) were relevant to them
  - The most relevant concepts were fatigue (n = 19 of 29, 65.5%), difficulty exercising or performing physical activity (n = 17 of 29, 58.6%) and difficulty concentrating (n = 17 of 29, 58.6%)

REFERENCES

1. Dress A, et al. *Future Rare Disease*. 2021; 1(3). Available at: https://doi.org/10.2217/frd-2021-0003

RESULTS, continued

Figure 1: Preliminary conceptual framework of signs, symptoms, and impacts of Wilson disease

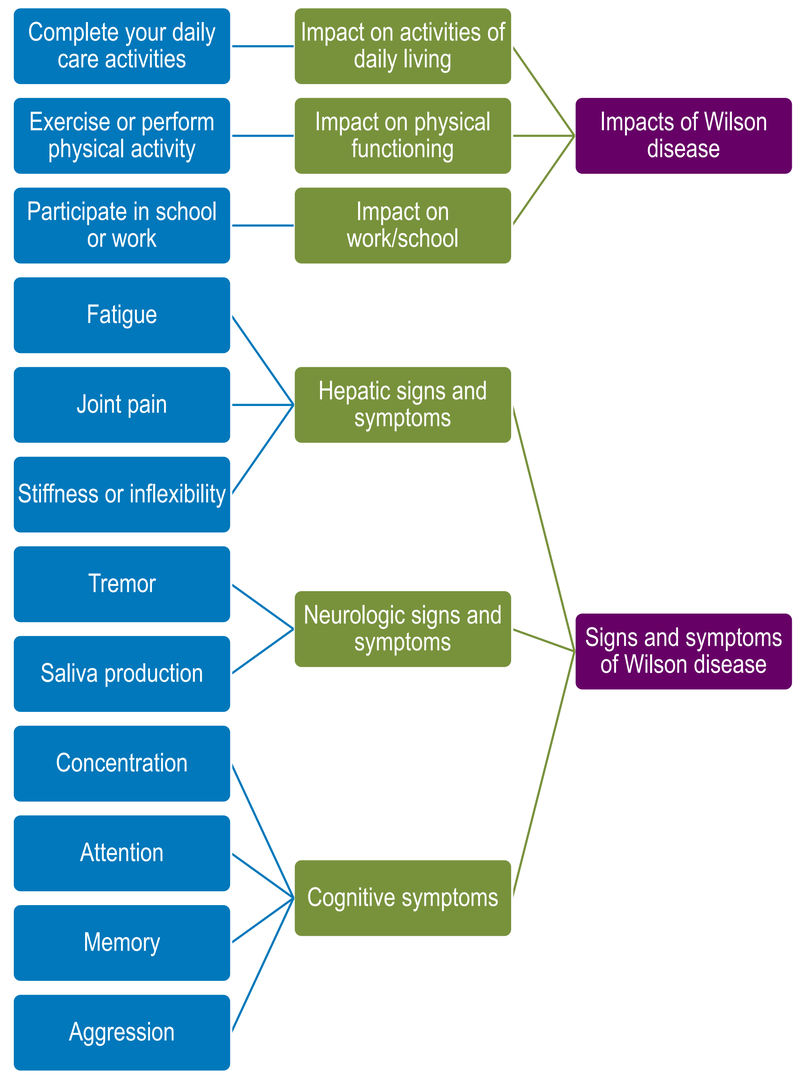


Figure 2: Signs and symptoms of Wilson disease reported both spontaneously and following probing by at least a third (≥ 35.7%) of participants

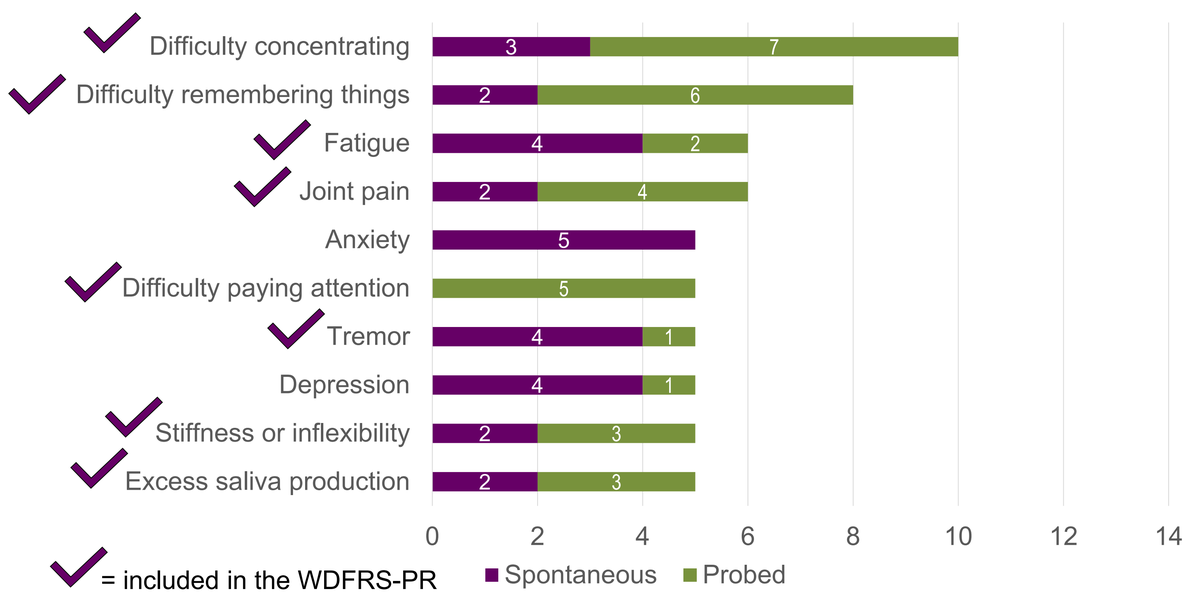
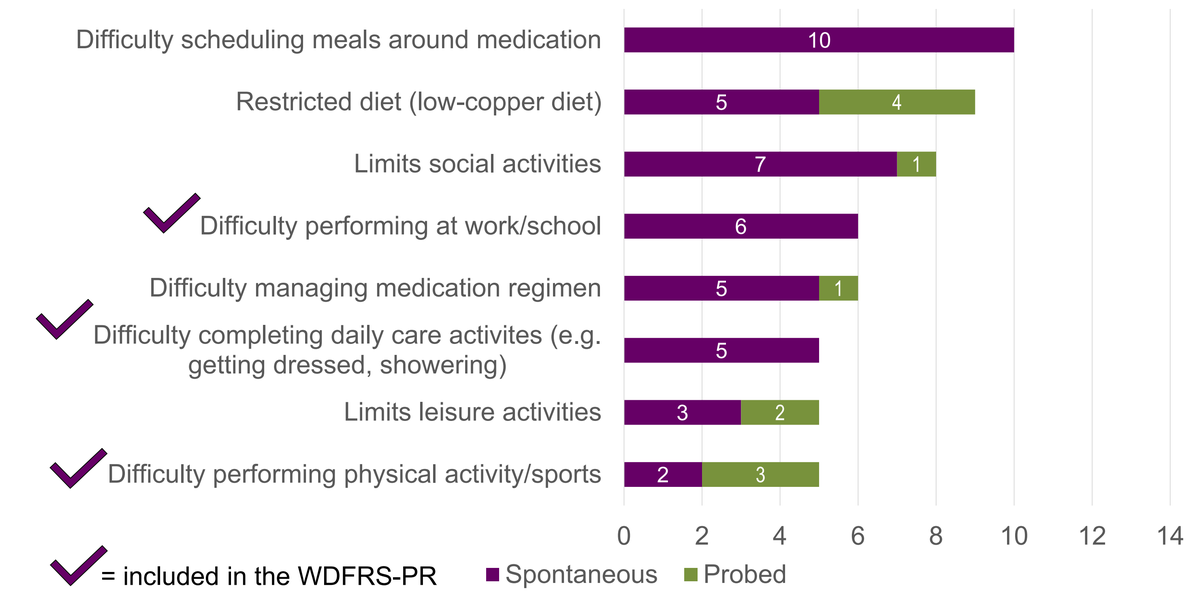


Figure 3: Impacts of Wilson disease reported both spontaneously and following probing by at least a third (≥_35.7%) of participants



CONCLUSIONS

- Given the rarity of Wilson disease, a rigorous yet pragmatic process was undertaken to develop and assess the content validity of the WDFRS-PR
- Relevance across the measures varied, although this is likely a result of the heterogeneous presentation of Wilson disease
- Future research includes comparison of the interview results to an existing conceptual model in Wilson disease and updates to the WDFRS-PR to reflect patient input. There is also a clinician-administered component to the WDFRS currently in development

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