CDAD-DaySymSTM: A new patient-reported outcome tool for Clostridium difficile-associated diarrhoea

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INTRODUCTION

Background

- Clostridium difficile infection (CDI) is a growing global public health challenge, with dramatic increases in incidence, severity, mortality, and healthcare burden in recent years. 1
- The incidence of cases of new-onset CDI following initial treatment is also rising. 2

Clinical manifestation

- Symptoms of C. difficile infection range from diarrhoea of varying degrees of severity to colitis, systemic toxic shock, and even death. 3

Symptoms of C. difficile-associated diarrhoea (CDAD)

- Important because they impair patient functioning and quality of life 4
- Since the patient voice in the drug approval process is important because they impair patient functioning and quality of life, 5 clinical studies of new agents for CDAD should evaluate symptoms in addition to objective clinical assessments; however, no patient-reported outcome (PRO) questionnaire measuring symptoms is currently available. 6

The 2009 Food and Drug Administration (FDA) PRO Guidance for Industry emphasizes the importance of documenting consent validity, including evidence that the questionnaire is conceptually comprehensive, relevant, and understandable to patients with the disease. 7

Objective

- To develop a symptom PRO for CDAD in accordance with the FDA Guidance.

METHODS

Study design

- A cross-sectional, qualitative research study was undertaken consisting of 2 main phases (Figure 1):
  - Concept elicitation interviews of CDAD patients and nurses to better understand the patients’ experience of their disease, and inform the development of the new PRO.
  - Cognitive interviews with 5 clinical experts from Europe and the US informed the development of the study protocol and a semi-structured interview guide.

Participants

- Patients with CDAD meeting study eligibility criteria (Table 1) were recruited at 5 participating study sites in the US.
- All patients provided written informed consent.
- Nurses from the 5 participating sites who treated CDAD patients on a regular basis were recruited to participate in supplemental interviews in Phase 1.

Phase 1: Concept elicitation interviews

- Patients’ spontaneously reported experiences with CDAD symptoms were gathered from patient interviews as well as supplemental interviews with nurses, who were asked about symptoms reported by patients.
- Once concept saturation was reached, the draft PRO, named the CDAD-DaySym™, was developed with input from the panel of clinical experts.

RESULTS

Participant sample

- A total of 34 patients and 6 nurses were recruited across both study phases.

Patient characteristics are shown in Table 2. Recruitment targets were generally met, though there were fewer patients than anticipated with first recurrence and second recurrence.

Phase 1 interviews

- Clinical experts provided feedback on the draft PRO by answering questionnaires and scoring its comprehensiveness of the questionnaire items.

Phase 2 interviews

- The final PRO was tested with the CDAD patients and nurses to determine flexibility (grade level and readability).

The draft PRO was reviewed by a translation expert to assess the ease of future translation to other languages and to determine feasibility (grade level and modifiability).

Phase 2: Cognitive interviews

- Patients with CDAD were interviewed by telephone in 2 iterative rounds, and asked to complete the PRO.
- Interviewers used a semi-structured interview guide to obtain feedback on:
  - Relevance, comprehensibility, acceptability, and comparability/relevance of the questionnaire items;
  - Interpretablity and appropriateness of the instructions, response options, and recall period.

The revised PRO incorporated 5 hypothesised symptom sub-concepts (subdomains) comprising 13 items (Figure 2).

The formatting and phrasing of the PRO including the instructions, items and response options were clear and easy to understand, and patients were able to use the questionnaire as intended.

Minor changes were made to the PRO following the first and second rounds of cognitive interviewing, as follows:
- Revisions to the instructions to improve translatability
- Rewording of 2 items for clarity
- Reordering of the 2 items for logical flow
- Separation of an item into 2 due to patients perceiving the 2 items differently and clinical experts noting different underlying physiological mechanisms

The revised PRO incorporates 5 hypothesised symptom sub-concepts (subdomains) comprising 13 items.

CONCLUSIONS

- The patient perspective in CDAD is important.
- The CDAD-DaySym™ was demonstrated to capture the patient voice as a comprehensive measure of CDAD symptoms, with data from initial qualitative research supporting its content validity in patients with varying severity of CDAD.

The psychometric properties of the PRO must be evaluated before the questionnaire can be used in clinical practice or clinical studies; validation will be performed in two clinical trials.

DISCUSSION

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References

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