Health-related Quality of Life of Clostridium difficile infection: a methodological contribution to direct utility elicitation by TTO

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Background
Clindamycin Resistant bacteria is a medicine that thrives in the stomach and intestines and is associated with a high level of resistance. 3% of general population and 15-33% of in-patients are carriers of Clostridium difficile without showing any symptoms.

Diarrhoea is the most common manifestation of Clostridium difficile infection (CDI). Depending on severity, diarrhoea can lead to dehydration, electrolyte imbalance or other more severe complications that present surgical emergencies such as perforation.

The evidence of treatment being ineffective in 38-63% of patients with CDI provides room for more efficacious treatment.

Despite the relative high occurrence of health states associated with CDI-like diarrhoeas, there is paucity of high quality utility values in the literature to populate potential cost-effectiveness models to support the viability of new treatments.

Obtaining HRQL weights for CDI requires a flexible approach that takes into account both temporary and chronic health state nature associated with the disease.

Objectives
To evaluate the standard time trade-off (TTO) and Chain TTO techniques for eliciting utility of CDI-related chronic and temporary health states.

To compare TTO values with those from Healthcare Professionals (HCP) EQ-5D valuation.

To evaluate methods of calculating utilities for health states worse than death (WTD).

Methods
Ten vignettes representing possible health states after an episode of CDI infection were created based on the literature and interviews with five Gastroenterologists and Infectious disease specialists.

Current health (self-state) was included to give participants experience of the TTO process. “Slightly unwell” was developed as the anchor health state for temporary health state valuation.

HCPs provided the most likely level for each dimension that the average patient is likely to experience for health states according to the EQ-5D instrument.

Utility values were calculated from HCP valuations using the scoring function by Dolan in deriving the UK EQ-5D social tariffs.

A representative sample of the UK population were invited to value the health states - 50 participants were recruited for the pilot and 100 for the main study.

Each participant provided socio-demographic information, ranking of health states by preference and responses to a Computer-Assisted Personal Interview (CAPI) TTO protocol for all states considered - Chronic and Temporary.

The CAPI incorporated the conventional TTO protocol for chronic health states and the chained TTO protocol for the temporary health state.

Translation and monotonic transformation as methods to restrain the impact of extreme negative utilities were appraised.

Table 1. Characteristics of study population (n=100)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Gender</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>18-24</td>
<td>15%</td>
<td>51%</td>
</tr>
<tr>
<td>25-44</td>
<td>34%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>45-64</td>
<td>32%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 75,000</td>
<td>2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refused to say</td>
<td>30%</td>
<td></td>
<td></td>
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</tbody>
</table>

Results
54% of participants judged “moderate diarrhoea” as WTD in the pilot. Consequently slightly unwell was used as the anchor in temporary health state valuation.

100 participants took part in the main study. 10% did not trade any time for any of the HS and were excluded in the analysis. A further participant was excluded from the temporary HS analyses because he allocated all the time in the temporary HS to value and no time in the anchor health state and consequently it was not possible to calculate the utility.

The participants valued their current health (Self-state) as better than death. Mean HRQoL (Median 1.3).

Both chronic and temporary health states were valued by WTD participants.

78% of the participants ranked their chronic health states by utilities identically to the ranking by the average values. 46% achieved the same with the temporary health states.

Utility values for all health states are listed in Table 2.

Participant characteristics had no significant influence on how they valued the health states (p>0.05).

The interview had an impact on the participants that valued collectivity with iliac aneur (p=0.03) and recovery after moderate/severe diarrhoea (p=0.03).

Key Findings
A high proportion of the participants judged the health states as WTD, even for the relatively mild health states (24% valued AS Diarrhoea as WTD).

A few extreme negative values had a disproportionately high impact on the crude utility means. There were considerable differences in mean utilities depending on the transformation methods.

In general, TTO values by any method were lower than EQ-5D utilities from the same study based on expert opinion.

Discussion
Archiving and Adjusting had a potential to incorporate bias in the chain TTO protocol for valuing temporary health states.

The lack of patient input into the vignette construction and the non-random order during their valuation may have affected the results.

Lamers et al argue that methods to transform negative values were theoretically unsound.

A lead-time trade-off (LTTD) approach would avoid some of the nuances of dealing with negative utilities, but may not in the case where a large proportion of the population judge health states as WTD.

A person trade-off exercise would avoid the problem of negative utilities, however the participants would not value HS for themselves. Consequently, the values may not be considered as ‘utilities’.

The face-to-face approach may be unsuitable for the HS of an embarrassing nature such as HS associated with CDI-related disease.

A discrete choice experiment (DCE) could be a better method as they would have to trade-off between different dimensions, not just against time. In addition, DCE can be conducted online which would avoid biases relating to interviewer effects.

CONCLUSIONS
This study casts doubt about the suitability of face-to-face TTO protocol for eliciting utility values for CDI health states. Elicited values appear to be unrealistically low. We would recommend the utilisation of DCE (Discrete Choice Experiments) for future studies aiming to elicit utilities for CDI health states.

Acknowledgement
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Table 2. TTO HRQL Weights by Calculation method and HCP EQ-5D Valuation: Study population (n=89)

<table>
<thead>
<tr>
<th>Chonic health states</th>
<th>Temporary health states</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health states</td>
<td>0.060 (0.004)</td>
</tr>
<tr>
<td>EQ-5D Health states</td>
<td>0.056 (0.004)</td>
</tr>
<tr>
<td>Cardiac</td>
<td>0.050 (0.004)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>0.045 (0.004)</td>
</tr>
<tr>
<td>Emotional</td>
<td>0.042 (0.004)</td>
</tr>
<tr>
<td>Physical</td>
<td>0.037 (0.004)</td>
</tr>
<tr>
<td>Pain</td>
<td>0.035 (0.004)</td>
</tr>
<tr>
<td>Social</td>
<td>0.033 (0.004)</td>
</tr>
<tr>
<td>Vision</td>
<td>0.031 (0.004)</td>
</tr>
</tbody>
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List of abbreviations
BTD – Better than dead
CDI – Clostridium difficile infection
EQ-5D – Euroqol 5-dimension
HCP – Healthcare Professional
LTTD – Lead-time time trade-off
WTD – Worse than dead

CAPI – Computer- assisted Personal Interview