Preference weights for quality-adjusted life-years estimation of treatments for paroxysmal nocturnal hemoglobinuria in the UK

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BACKGROUND

- Paroxysmal nocturnal hemoglobinuria (PNH) is a rare hematologic disorder caused by uncontrolled activation of the terminal complement pathway that manifests with intravascular hemolysis, hemolytic anemia, and thrombosis.[1]
- Eculizumab (Soliris®) and ravulizumab (Ultomiris®) are the only approved treatments for PNH.[2,3]
- Ravulizumab is administered every 8 weeks and has been shown to be clinically non-inferior to eculizumab, which is administered every 2 weeks.[4,5]
- Therefore, the decision maker is faced with two treatments that may be equally effective but vary in terms of their burden to patients.
- Stated preference research can be used to understand the value that people place on differences in treatment administration and provide preference weights for quality-adjusted life-years estimation in cost-effectiveness analyses.

OBJECTIVES

- In cost-effectiveness analyses for health technology assessment, there is a normative view that outcomes such as quality of life should be weighted by the preferences of the general public.
- As such, this study aimed to evaluate the value that the UK general public places on dosing frequency and other treatment attributes for PNH and to estimate disutilities for use in cost-effectiveness analyses.

METHODS

Participant recruitment

- The survey was administered to UK general public participants (age ≥ 18 years) recruited through specialist recruitment panels (online panels consisting of members of the public with an interest in participating in research studies).
- The survey included background details regarding PNH without naming the condition, including symptoms and how it affects people. The actual disease was undisclosed so that participants did not look up the disease to obtain more information.

Discrete choice experiment

- A discrete choice experiment (DCE) presents participants with pairs of hypothetical choices and they are asked to select one pair based on their preference.
  - Each choice is defined in terms of its specific attributes, which are in turn characterized by distinct levels.
- The aim of the DCE was to evaluate the relative importance of PNH treatment attributes to the respondents and to establish their willingness to trade attributes after weighing them against each other.
- The attributes for inclusion in the DCE survey were identified from a review of the regulatory approvals for eculizumab and based on discussion between clinical experts.
- Attributes and defined levels were combined into choice sets using a published method for optimally combining a range of factors in an experimental setting.
- The survey consisted of 16 pairs of choice sets.
  - As a test that participants understood the survey, in one of the choice sets, one treatment option was logically preferable to the other.
  - An example of a choice set is shown in **Figure 1**.
- Discrete choice data were analyzed using the mixed effects logit regression model, which accounts for preference heterogeneity between respondents.
- Marginal rates of substitution (MRS) indicate the extent to which participants are willing to forego a unit of one attribute in order to gain a unit in a different attribute.
  - We hypothesized that the MRS indicate the extent to which people are willing to trade a year of life in order to avoid episodes of hemolysis or the need for a blood transfusion.
  - Thus, MRS were estimated between survival and other treatment attributes in order to estimate disutilities weighted against average life expectancy.
  - Average life expectancy was estimated based on the mean age of the study population.

Participants were presented with a DCE survey to evaluate the following PNH treatment attributes:

Figure 1. Sample choice set included in the discrete choice experiment survey

Please imagine that you have been told that you have PXH disease and you need to start a treatment. For each choice below please indicate whether you prefer treatment A or B.

	Treatment A	Treatment B
Treating PXH disease *On average how much is life expectancy reduced by PXH disease with treatment?*	Life expectancy reduced by 8 years	Life expectancy reduced by 4 years
Administering treatment *Treatment is via an intravenous infusion into your arm*	Treatment is every 8 weeks (6–7 times a year) It is delivered at home Treatment takes about 3 hours	Treatment is every 2 weeks (26 times a year) It is delivered at home Treatment takes about 1 hour
Risk of meningitis-type infection	One additional person per thousand will develop meningitis a year	One additional person per thousand will develop meningitis in 2 years
Return of symptoms *Red blood cell destruction* Causes abdominal pain, dark urine, swallowing difficulties	Patients **never** experience destruction of red blood cells	**Severe** red blood cell destruction Requires treatment in hospital
Need for a blood transfusion	**Never** need a transfusion	Need a blood transfusion **once a year**

Which treatment is best? Please tick A or B **A** ☐ **B** ☐

PXH, paroxysmal nocturnal hemoglobinuria (undisclosed to participants).

RESULTS

Demographics

- Of 507 respondents, response checks showed that 122 failed the dominant choice test; these respondents were excluded from the analyses.
- Of the 385 participants included in the analysis, 56.1% were female, 89.1% were white (Caucasian) and 50.4% were in paid employment.
- The sample of participants reflected the UK population demographics in terms of gender, age and ethnicity and were based in all main regions of the UK.

Discrete choice experiment

- The results of the DCE are presented in **Figure 2**.

Life expectancy

- Potential reduction in life expectancy was a significant predictor of choice, with a significant aversion to a reduction in life expectancy.

Treatment administration

- Participants preferred six or seven treatments a year (reference) to 26 treatments a year.

Risk of meningitis-type infection

- Participants preferred no risk of infection to a low (1 in 1000) risk of infection every year.
- However, low risk of infection every 2 or 5 years was not preferred by participants over no risk of infection.

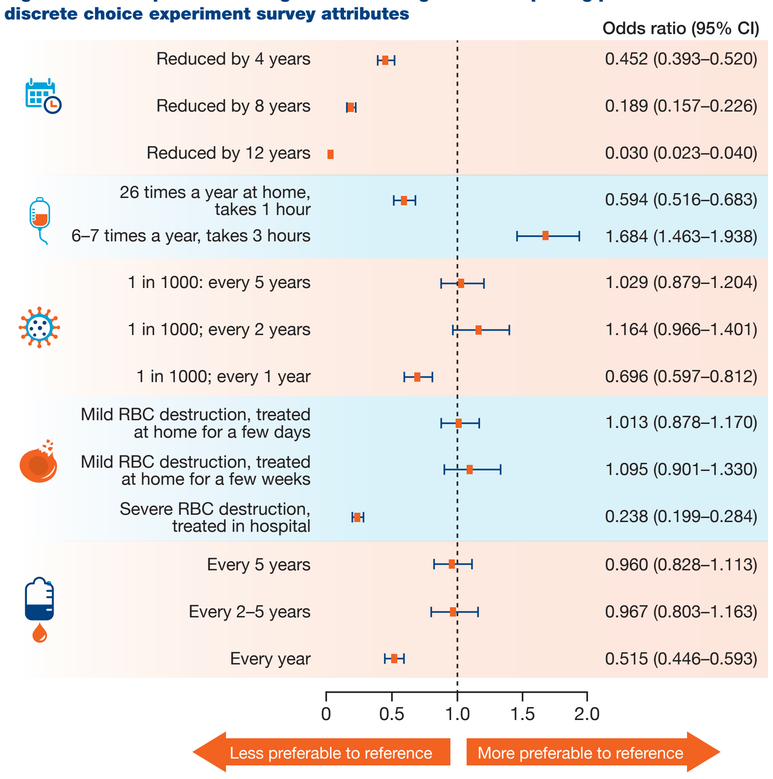
Burden of hemolysis

- Participants preferred to avoid severe hemolysis requiring admission to hospital.
- Mild hemolysis treatment or management at home was not preferred by participants over no hemolysis.

Blood transfusions

- Participants preferred to avoid the need for transfusions every year but showed no preference for avoiding blood transfusions every 2–5 years.

Figure 2. Forest plot illustrating conditional logit model depicting preferences for discrete choice experiment survey attributes

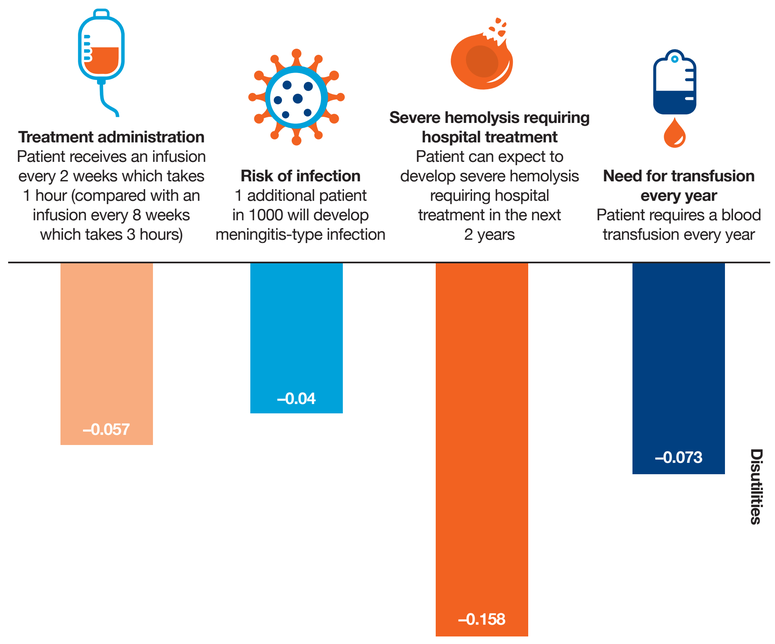


CI, confidence interval; RBC, red blood cell.

Estimated disutilities

- The results of the MRS are presented in **Figure 3**.
- The estimated life expectancy of the participants in the sample was 31.17 years.
- Participants were willing to trade 4.93 years of life for avoidance of severe hemolysis requiring hospitalization (thus, disutility = –4.93/31.17 = –0.158).

Figure 3 Estimate marginal utilities (expressed as a disutility) for differences in attribute levels



CONCLUSIONS

- This study estimated disutilities for events that would be difficult to measure in a clinical study.
- In this rare disease context, this study showed the value that the general public places on attributes of treatment for PNH.
  - Participants placed significant value on treatment choices that maximized life expectancy.
- The main limitation of the study is that it is impossible to confirm that participants had read and fully understood all information received.
- However, we believe that this is a useful method for estimating disutilities for economic modeling where data from the EQ-5D are not available.

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DISCLOSURES

KJM, RS, KA and IT are employees of and hold stock in Alexion Pharmaceuticals. AL holds stock in Acaster Lloyd Consulting Ltd. Acaster Lloyd Consulting Ltd received a fixed fee for their work on this project. CJP and AH received honoraria from Alexion Pharmaceuticals for their work on this project.

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