

A vignette study to derive health-related quality of life weights for patients with steroid refractory chronic graft-versus-host disease receiving third line therapy in the United Kingdom

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INTRODUCTION

- Several haematologic diseases can be cured following allogeneic haematopoietic stem cell transplantation (alloHSCT).
- A significant cause of morbidity and mortality after alloHSCT is chronic graft-versus-host disease (cGVHD)¹ which occurs in 30-70% of patients².
- cGVHD can have a negative impact on health-related quality of life (HRQL) due to the involvement of multiple organs^{3,4}.
- Accurate characterisation of HRQL is important as patients often receive multiple lines of therapy and experience increasing burden and/or iatrogenic side effects as the disease progresses.

OBJECTIVE

- **To estimate HRQL weights (utilities) associated with third line cGVHD using vignette methodology.**
- Utilities for health states related to late stage cGVHD are not well documented. This is the first study of its kind in cGVHD.

METHODS

Vignette development:

- Four previously published vignette studies⁵⁻⁸ in comparable haematological conditions which included GVHD states were identified from a literature search.
- Using this as a starting point, four draft vignettes were developed to encompass different levels of treatment response at third line characterised by increasing disease severity (complete response, partial response, lack of response, recurrent cGVHD).
- Semi-structured interviews were conducted with clinical experts (N=5) to refine and validate the content of the draft vignettes.
- The draft vignettes were revised following feedback. After five interviews, a high degree of consensus was achieved, and the vignettes were considered finalised. An example vignette is presented in Figure 1.

Vignette valuation:

- United Kingdom (UK) general public (N=300) were recruited via an online recruitment platform and completed an online survey in which they valued the four vignettes using the EQ-5D-5L⁹ and EQ-5D-VAS.

Figure 1: Example vignette – Partial response

- You have had a transplant to treat a life-threatening illness, which is currently successful.
 - You experience difficulty in walking any distance due to fatigue. You have experienced some unwanted effects of the transplant:
 - You have chronic diarrhoea. You experience abdominal pain and often need to go to the toilet urgently.
 - You are malnourished and experience unintentional weight loss due to your high nutritional requirements and chronic diarrhoea.
 - You have dry mouth and dry eyes. This is uncomfortable and requires frequent use of eye drops and the avoidance of certain foods.
 - You have been prescribed medication and have to return to hospital at least every four weeks for blood tests and to manage your symptoms. Currently, you are allowed to be at home, but there is a chance of hospitalisation if you catch an infection, or your symptoms worsen.
 - You are able to wash and do jobs around the home. You find dressing difficult due to joint stiffness you experience. You find it difficult to go shopping and are not able to complete daily activities or work because you become tired more easily and worry about catching an infection.
 - Your ability to socialise with friends and family is limited due to the symptoms you are experiencing and concerns about catching an infection.
 - You experience anxiety because of the unpredictable symptoms you are experiencing. You sometimes worry about your illness reoccurring in the future.

RESULTS: UTILITY ESTIMATES

- A total of 300 participants completed the online survey. Full sample characteristics are presented in Table 1.
- Utility estimates are presented in Figure 2. Utility estimates varied from 0.577 (complete response) to 0.061 (recurrent cGVHD).
- VAS scores are presented in Figure 3. VAS scores varied from 46.8 (complete response) to 25.6 (recurrent cGVHD).

Table 1: Sample characteristics

Characteristic		N=300
Age	Mean (SD)	47.2 (15.8)
	Range	18-81
	Male n (%)	153 (51.0%)
Gender	Female	146 (48.7%)
	Other	1 (0.3%)
Location	England	261 (87.0%)
	Scotland	26 (8.7%)
	Wales	10 (3.3%)
	Northern Ireland	3 (1.0%)
Living situation	Living with partner/spouse	192 (64.0%)
	Living alone	61 (20.3%)
	Living with relatives	35 (11.7%)
Employment status	Employed, full-time	136 (45.3%)
	Employed, part-time	54 (18.0%)
	Retired	54 (18.0%)
	Unemployed	26 (8.7%)
Diagnosis of chronic illness	Student	19 (6.3%)
	No	193 (64.3%)
	Yes	102 (34.0%)
	Prefer not to say	5 (1.7%)

Figure 2: EQ-5D-5L utility estimates in cGVHD

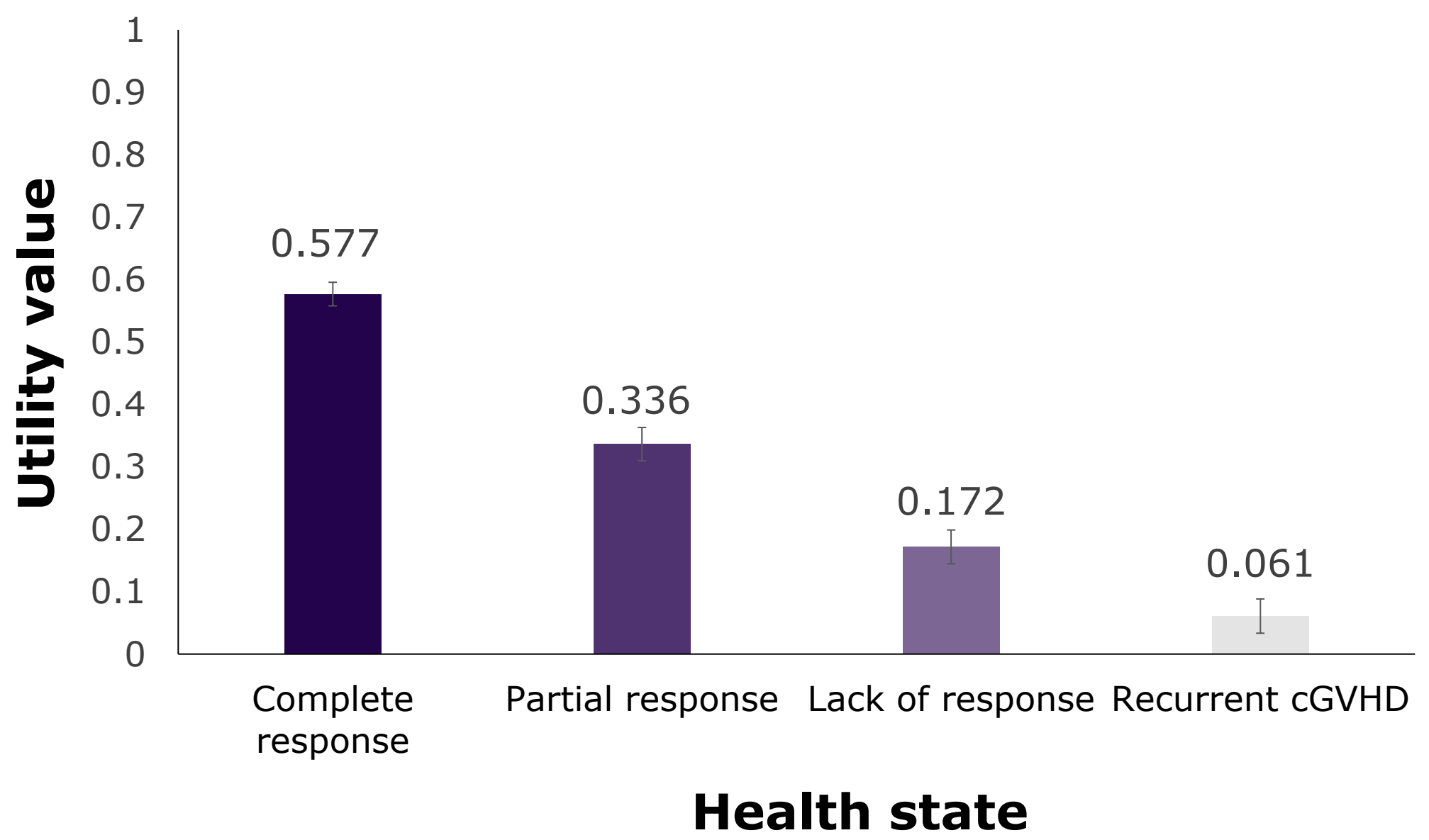
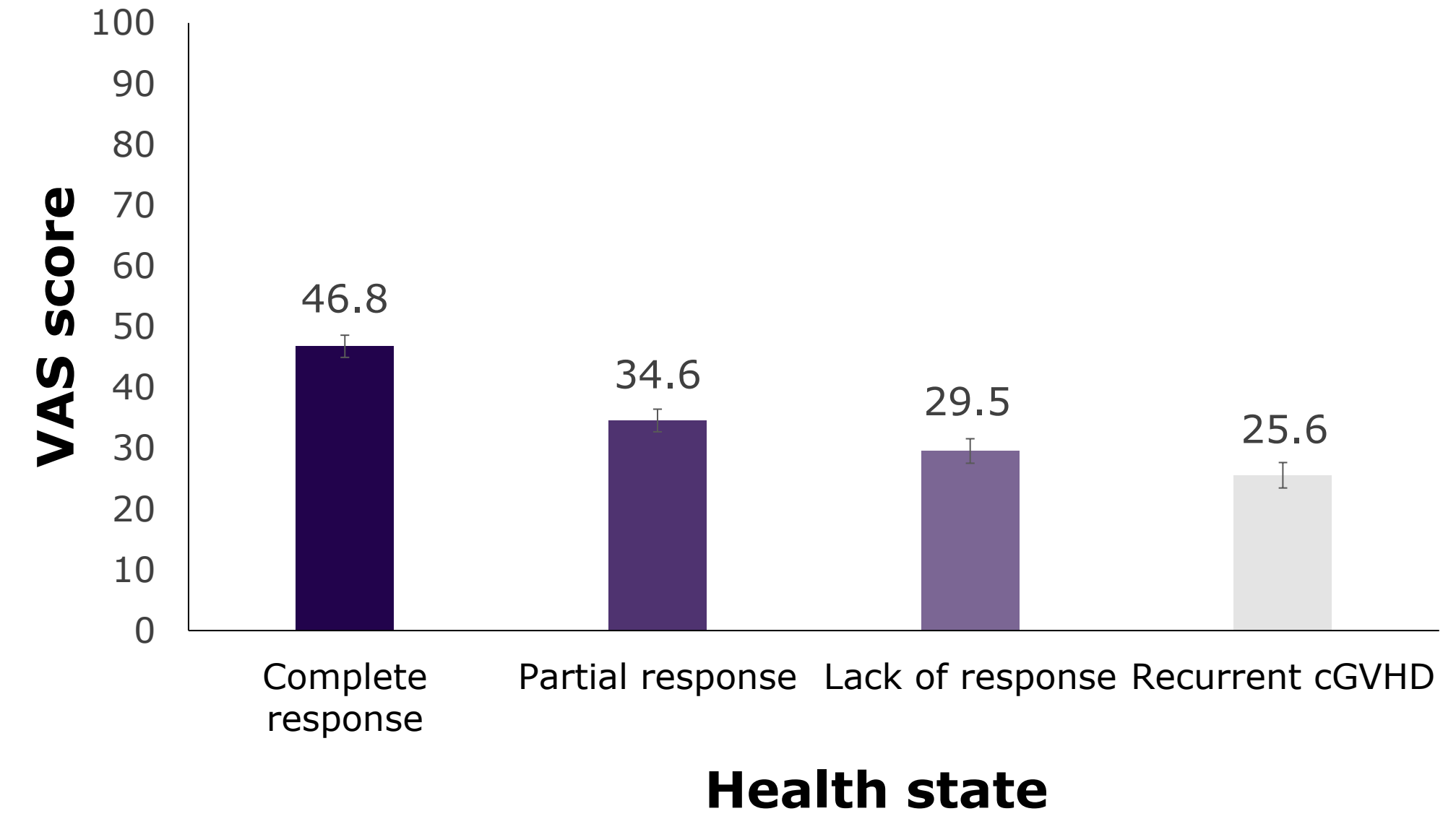


Figure 3: EQ-5D-VAS scores in cGVHD



RESULTS: QUALITATIVE INTERVIEWS

- Interviews with clinical experts provided a detailed summary of the numerous aspects of daily life that are affected by cGVHD.
- Impacts included changes to physical function and appearance such as skin rash resulting in visible scarring and reduced mobility; high levels of fatigue and increased risk of infection leading to activity disruption and reduced ability to socialise; high volumes of medication and frequent hospital appointments to manage symptoms; and emotional impacts due to the nature of symptoms experienced and necessity of treatment.

"They have anxiety, they socialise less, they're not able to [live] their life normally" – KOL02, Consultant Haematologist

"They tend to get so fatigued they struggle to maintain a conversation" – KOL04, Specialist Pharmacist

"They'll probably be on a lot of different medications...sometimes they are seeing multiple specialists...and some of our patients feel that just going to their hospital appointments is like a full-time job" – KOL5, Consultant Haematologist

- The qualitative data that informed the vignettes supports the face validity of the utility findings and demonstrates a severe HRQL burden at this stage of cGVHD.

DISCUSSION

- This study generated utility estimates for vignettes describing different levels of treatment response in patients with cGVHD receiving a third line therapy.
- The utilities demonstrate a substantial burden associated with cGVHD, even in patients with a complete response to treatment.
- The utility estimate for the complete response health state is similar to previous estimates:
 - Castejón et al. (2018) GVHD state: 0.43⁶
 - Matza et al. (2020) cGVHD state: 0.51⁸
- The utility estimate for the recurrent cGVHD health state is comparable to a health state describing death. Although this value is very low, similar estimates have been reported in the literature:
 - Nafees et al. (2021) GVHD state: 0.07⁷
- The low utility estimates are partly a reflection of the public's perception of disease severity. Patients themselves may learn to cope and adjust over time.

CONCLUSIONS

- **There is a substantial HRQL burden associated with cGVHD, and large differentiation according to treatment response.**

LIMITATIONS

- It was not possible to conduct qualitative interviews with patients currently experiencing cGVHD so the vignettes were developed without this input. However, the studies that were used to develop the vignettes did include patients.
- cGVHD is highly heterogenous. Vignettes were developed to describe a 'typical' patient in each health state however it is acknowledged that HRQL impacts would depend heavily on organ involvement.

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DISCLOSURES

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