

Capturing the Impact of Grief and Bereavement on Caregivers in

National Institute for Health and Care Excellence

Highly Specialised Technology Appraisals

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BACKGROUND

The National Institute for Health and Care Excellence (NICE) Highly Specialised Technology (HST) programme evaluates medicines for very rare and often very severe diseases where patients experience progressive, rapidly deteriorating and life-limiting illness. The NICE reference case specifies that economic evaluations should include direct health effects on patients and caregivers where relevant(1). Although the impact of looking after a person with a rare disease is often considered, the impact of their death on caregivers and families is not well understood. Caregivers and families may experience anticipatory grief as a result of the impending loss of a patient after a terminal diagnosis. The emotional burden after a bereavement may also continue for a prolonged period after the acute stages of grief due to their loss.

We aimed to investigate if and how the impact of grief and bereavement on caregivers/ families has been captured in NICE HST appraisals.

METHODS

A targeted review of all completed and ongoing NICE HST appraisals to date with at least one committee meeting was conducted in April 2022. Both the company and patient organisation (PAG) submissions were reviewed. Details on the clinical area, methods of capturing the impact of grief and bereavement on caregivers, and the impact on the incremental cost-effectiveness ratio (ICER) were reviewed. The opinions of the external assessment groups (EAG) and NICE committees were also considered.

RESULTS

The study included 23 HST appraisals that were completed or on-going. Eight of 23 HST appraisals included considerations of bereavement. Three covered clinical areas associated with childhood mortality, three with adult mortality and two with both childhood and adult mortality (Table 1).

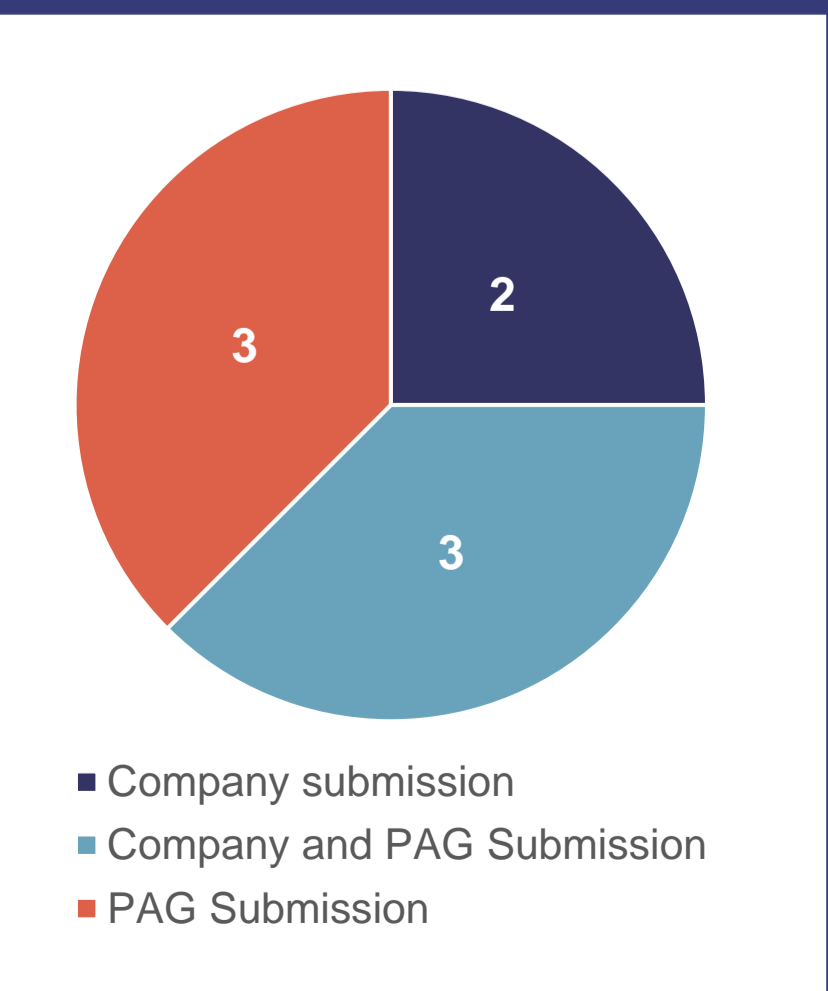
Table 1: Summary of included HST Appraisals

| Appraisal | Disease area | Age |
|-----------|---|------------|
| HST18 (2) | Metachromatic leukodystrophy (MLD) | Variable |
| HST15 (3) | Spinal muscular atrophy | Paediatric |
| HST12 (4) | Neuronal ceroid lipofuscinosis type 2 | Paediatric |
| HST11 (5) | Inherited retinal dystrophies caused by RPE65 gene mutations | Adult |
| HST10 (6) | Hereditary transthyretin amyloidosis (hATTR) | Adult |
| HST9 (7) | Hereditary transthyretin amyloidosis | Adult |
| HST7 (8) | Adenosine deaminase deficiency–severe combined immunodeficiency | Paediatric |
| ID800 (9) | Alpha mannosidosis | Variable |

Grief and bereavement was considered in either the company submission, patient advocacy group submissions or patient expert statements. (Figure 1)

In the remaining appraisals that did not include considerations of grief or bereavement eight covered clinical areas associated with children and five with both adults and children.

Figure 1: HST appraisals that include bereavement



HST appraisals that quantitatively included impact of grief and bereavement on caregivers:

Only two appraisals quantified the carer disutility due to bereavement in the economic model (Table 2). HST7 (8) modelled family quality adjusted life year (QALY) loss resulting in an ICER decrease by 9%. The carer disutility was based on an economic evaluation of a meningitis vaccine in which an additional QALY loss experienced by a bereaved family is assumed to be 9% of the child’s QALY loss. (10) Another, ID800 (9) included a carer utility decrement in the base case corresponding to the most severe patient health state. The company used the Extended Disability Status Scale(11) which illustrates that caregiver disutility increases as the disease becomes more severe. A patient was assumed to be in the most severe health state for four weeks, in the submission the utility decrement for the severe health state was applied for a full year to account for the bereavement process. The impact on the ICER for ID800 was not publicly available.

Table 2: Cost-effectiveness results after including the impact of bereavement on carers

| Appraisal | Included | QALY with carer HRQoL | QALY without carer HRQoL | ICER with carer HRQoL | ICER without carer HRQoL | Percentage change in ICER | Source |
|-----------|-------------------|-----------------------|--------------------------|-----------------------|--------------------------|---------------------------|------------------------|
| HST7 | Scenario Analysis | 14.9 | 13.6 | £33 201 | £36 360 | -9% | Christensen et al (10) |
| ID800 | Base Case | Not available | | | | | Gani et al 2008 (11) |

HRQoL, health related quality of life; QALY, quality adjusted life year

HST appraisals that included considerations of the impact of grief and bereavement on caregivers:

The impact of bereavement was discussed in three company submissions without formally including it in the economic model and in the patient group submissions or patient expert statements in six of eight appraisals. These highlighted the multiple losses experienced by families and the anticipatory grief surrounding the potential loss of a family member.

Table 3: Details of appraisals that include considerations of grief and bereavement

| Appraisal | Details |
|-----------|--|
| HST18 (2) | CS: includes caregiver quotes about managing feelings of grief both before and after the death of a patient. PAG submission: includes a caregiver survey to increase the understanding of MLD, the impact on patients and their families and the effects of gene therapy. The survey highlighted the mental health issues in MLD affected families which include intense grief. Patient expert statement: includes accounts of a cycle of grief and desperation. |
| HST15 (3) | CS: describes that caregivers often report feeling of anticipatory grief and enduring multiple losses. The CS also highlighted that the emotional burden of caregivers continues with bereavement (12). Although the CS did not quantify this burden it referenced TA588 which utilised a disutility of -0.04 due to bereavement (13). PAG submission: describes the impact on families including the chronic grief and potential looming loss of their child. |
| HST12 (4) | CS: includes a survey of 19 families in the UK and Germany which suggests that disease stage and severity impact caregiver burden. The survey indicates that family QoL in the severe stage of their child’s disease is significantly lower than in the bereaved stage (14). PAG submission: includes that the emotional wellbeing of parents is severely affected and describes how the grieving process begins long before the death of a child. Patient expert statement: includes accounts of parental grief which starts after receiving a terminal diagnosis. |
| HST11 (5) | PAG submission: conducted a large organisational survey which highlights that the progressive nature of sight loss conditions leads to a continual series of losses with associated grief, and the need to continually adapt to increasing disability is stressful. The submission also described that parents often fear for their child’s future. |
| HST10 (6) | PAG submission: a summary report from research to understand the burden of disease and perspectives on treatment includes that hATTR considerably impacts carers and highlights the emotional burden of impending loss. |
| HST9 (7) | PAG submission: a summary report from research to understand the burden of disease and perspectives on treatment includes that hATTR considerably impacts carers and highlights the emotional burden of impending loss. |

CS, company submission; PAG submission, patient advocacy group submission.

Comments made by the NICE committee or EAG

No comments on the approaches used in ID800(9) or HST7(8) were reported by the EAG. However, in ID800 the EAG ran a scenario analysis without caregiver disutilities. The NICE committee did not agree with the approach in HST7 and considered that this would not fully capture the quality of life benefit to carers after successful treatment. In HST15(3) the EAG noted that the company highlighted the impact of bereavement on caregivers, however did not attempt to quantify this due to insufficient methodology.

LIMITATIONS

This targeted review only looked at HST appraisals. NICE conducts appraisals on other technologies under the Single Technology Appraisal process where the impact of bereavement may also be included. Some committee discussions around the impact of bereavement on caregivers may not be captured in publicly available documents where some information is redacted.

REFERENCES

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CONCLUSIONS

The importance of bereavement in rare diseases was reflected by its inclusion in over 30% of HST appraisals. However, methodological challenges exist for capturing the impact of bereavement and anticipatory grief on caregivers. Not including that the substantial impact of grief on QoL likely significantly undervalues treatments for life-limiting diseases. A NICE task and finish report stated that the effect of bereavement should not be included in economic models because the methods are not well developed (15). As such, further research is required to enable full consideration of the impact of premature death of patients with rare conditions on caregivers.

DISCLOSURES

This study was sponsored by Sanofi. KM, and HW are Sanofi employees.

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