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Incorporation of utility estimates for caregivers an/or family members in economic evaluations

The power of knowledge.
The value of understanding.

Incorporation of caregiver/family spillover utility in economic evaluations

- Controversy remains over whether spillover utility should be routinely incorporated in economic evaluations
  - E.g., Brouwer 2019, McCabe 2019 [Pharmacoeconomics themed issue; Apr 2019:37(4)]
  - The NICE DSU has called for further research and guidance (Pennington and Wong 2019)
- Current economic modelling guidelines vary, but many recognise that caregiver and/or family effects should be included, where relevant (Basarir et al., 2019)

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Poll: What percentage of economic evaluations include caregiver / family QALYs?

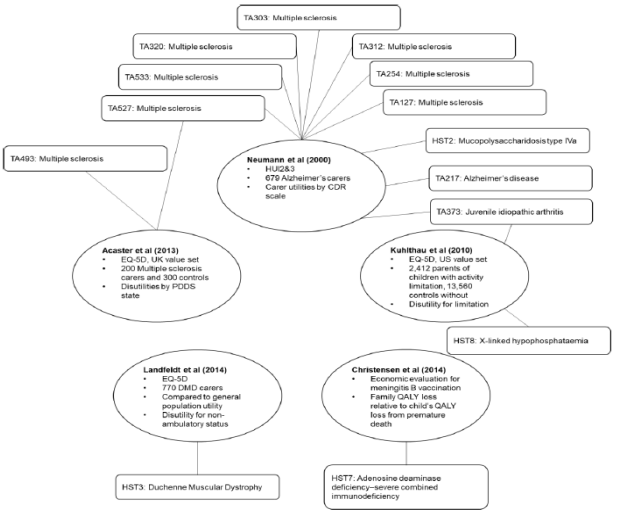
Incorporation of caregiver/family spillover utility in economic evaluations

RTI (h)(s) Health Solutions

- Currently, very few economic evaluations include caregiver/family utility effects
  - Of 422 NICE appraisals, only 4% (12 TAs and 4 HSTs) included carer QALYs in the economic evaluation (Pennington and Wong 2019)
  - This may be due, at least in part, to issues with the availability of utility estimates for caregivers

~ 4%

Data for other health conditions have often been used… due to lack of available caregiver utility data



Source: Pennington and Wong, 2019

Approaches to incorporating carer utility in cost-effectiveness models

- Carer disutility varies according to patient's health state
- Carer utility varies according to patient's health state
- Carer disutility varies according to patient's treatment (on/off treatment)

→ Carer disutility or utility was included until the patient died → implicit assumption of no carer utility loss after patient's death

- QALY loss due to death of the patient

→ Family utility loss after patient's death is explicitly modelled

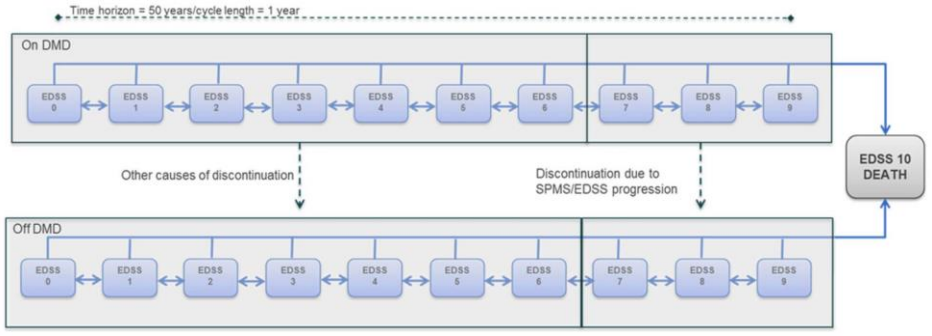
- Displacement multiplier[a]

→ To account for forgone spillovers from displaced health spending

[a] E.g. Al-Janabi et al., 2016

Carer Disutility Varies by Patient Health State

Cladribine for the treatment of relapsing-remitting multiple sclerosis (TA493)



EDSS = Expanded Disability Status Scale

Carer Disutility Varies by Patient Health State

Cladribine for the treatment of relapsing-remitting multiple sclerosis (TA493)

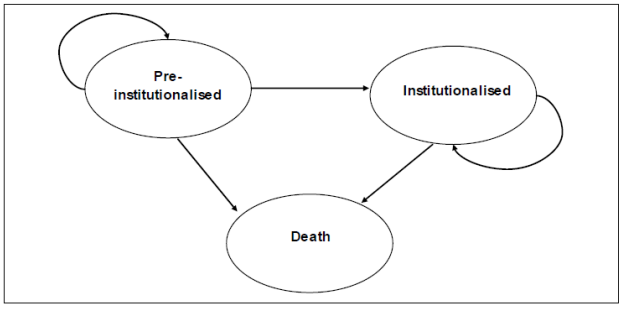
Model Health State	Matched PDSS score	Difference in mean caregiver EQ-5D vs matched controls by PDDS score (Acaster et al., 2013)
EDSS 0-2	PDDS 0-1	-0.002
EDSS 3	PDDS 2-3	-0.045
EDSS 4	PDDS 4	-0.142
EDSS 5	PDDS 5	-0.160
EDSS 6	PDDS 6	-0.173
EDSS 7	PDDS 7	-0.030
EDSS 8-9	PDDS 8	-0.095

Caregiver utility decreases with worsening health state up to PDDS 7 and 8 (wheel chair use and bedridden), where the loss in HSU declines versus PDDS 6

EDSS = Expanded Disability Status Scale; PDDS = patient-determined disease steps

Carer Utility Varies by Patient Health State

Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease (TA217 Assessment Group model)



Pre-institutionalised utility is dependent upon time to institutionalization and determined by MMSE category.

MMSE = Mini-mental state examination

Carer Utility Varies by Patient Health State

Donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease (TA217 Assessment Group model)

MMSE category	Matched CDR score	Caregiver HUI2 (Neumann et al., 2000)
26-29	0.5 (questionable)	0.88
21-25	1 (mild)	0.87
11-20	2 (moderate)	0.87
0-10	3 (severe)	0.86

CDR = Clinical Dementia Rating Scale; MMSE = Mini-mental state examination

Carer Disutility Varies by Treatment

Abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis (TA373)

- Caregiver utility was included in the Assessment Group scenario analyses

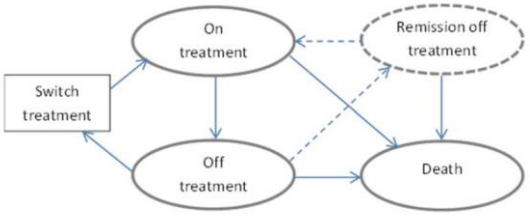


Figure 8 Schematic of the SHTAC JIA model structure

x

Carer Disutility Varies by Treatment

Abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis (TA373)

	On biologic treatment	Off biologic treatment	Source for the "Off biologic treatment" estimate
Base case	0	0	Assumption
Higher estimate	-0.035	-0.070	Kuhlthau et al., 2010 Comparison parents of children with and without activity limitations (limitations due to e.g., paraplegia, blindness, ADHD, and asthma) using EQ-5D
Lower estimate	-0.010	-0.020	Gani et al., 2008 (multiple sclerosis economic evaluation) referenced to Neumann et al., (2000); estimate for Alzheimer's disease (HUI2&3)

The "On biologic treatment" estimate was derived from the "Off biologic treatment estimate", assuming 50% of the "Off biologic treatment" utility decrement

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QALY Loss After Patient's Death

Strimvelis for treating adenosine deaminase deficiency–severe combined immunodeficiency (HST7)

- QALY loss due to death of a child was included in a scenario analysis
- Assumed to be 9% of the child's QALY loss on death (after Christensen et al, 2014)
- Discounted QALY loss of the child on death was calculated as the difference between the general population survival and the HSCT survival, integrated from Year 1 to Year 100 (20-23 QALYS)
- The additional QALY loss experienced by the bereaved family (9% of the child's loss) was 1.8 – 2.1 QALYs
- Applied as a one-off QALY loss
- The NICE Appraisal Committee considered that this would not fully reflect the quality-of-life benefit to carers after successful treatment, expected to occur immediately after successful treatment but could not be accounted for due to lack of data; benefits for carers were qualitatively taken into consideration

HSCT = hematopoietic stem cell transplantation

How many caregivers/family members?

- Empirical research has suggested that several individuals are affected
  - Hierarchical mapping has suggested a median of 3 close people and 8 in total are affected by illness/treatment at end-of-life (Canaway et al., 2019)
- Most models including caregiver utility have considered the impact on 1 carer
- Some exceptions:
  - Duchenne muscular dystrophy (HST3): between 2 and 4 carers
  - Myelofibrosis (TA386): 1.76 carers for 57.48% of patients (based on a burden of illness study)
  - Adenosine deaminase deficiency–severe combined immunodeficiency (HST7): QALY loss on patient death for a family with an unspecified number of members

In conclusion - some pragmatic suggestions for consideration

- Consider whether the relevant guideline(s) for economic evaluation state that caregiver/family utility may / should be included
- Consider whether caregiver/family utility effects are relevant[a]
- Identify best available utility estimates
  - Published systematic reviews may be helpful (Wittenberg and Prosser, 2019)
  - An online, open-access repository is planned (Wittenberg and Prosser, 2019)
- If more than one caregiver/family member may be affected, identify any data describing the extent of the family network affected[a]
- If data are poor or not available, plan additional research [noting John's comments on measures]
- In selecting the modelling approach, consider whether the HRQL benefit to carers is expected to be dependent on:
  - The patient's disease status (effect of treatment on carer HRQL is mediated through improvement in the patient's disease status)
  - Whether the patient is on treatment (direct effect of treatment on carer HRQL, not mediated through improvement in the patient's disease status)
- Provide separate analyses including and excluding spillover utility
- Be prepared to justify the approach

[a] Ideally based on quantitative and/or qualitative evidence for utility and/or HRQL impact

Questions? Experience to share?

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Poll: In future, I will consider including caregiver / family quality of life in economic evaluations

Acknowledgements

- Many thanks to:
  - Helen Knight, Programme Director, National Institute for Health and Care Excellence
  - Dr. Hareth Al-Janabi, NIHR Career Development Fellow and Senior Lecturer, Institute of Applied Health Research, University of Birmingham

For their contribution to the development of this workshop

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