The inclusion of caregiver burden in the NICE HTAs of treatments for mental health disorders

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Introduction

It is estimated that 1 in every 8 people are living with a mental health disorder (1), corresponding to around 970 million people across the world experiencing mental or behavioural disorders (1,2). Currently, more patients are treated at home than in hospital, which may consequently increase the burden of caregivers.

The National Institute for Health and Care Excellence (NICE) specifies all direct health effects, whether for patients or other people (where relevant, carers) be included in their reference case (3), to maximise the health of a population; however, few health technology appraisals (HTAs) include caregiver burden in their base case and scenario analysis.

Objectives

There is a significant caregiver burden associated with mental health disorders due to their intensity, duration, and age of onset. Mental health disorders can have a profound and far-reaching impact on caregivers, both financially and on their quality of life (QoL). Therefore, it is important to include caregiver burden in HTAs to assess the true benefit of treatment on the total population, as the benefit goes beyond the patient.

Therefore, this analysis aimed to assess:

1 How often caregiver burden is included within NICE HTAs for treatments for mental health disorders (in the base case and scenario analysis)

2 To assess the methods used for including caregiver burden

3 To explore challenges and potential solutions for its inclusion in future submissions
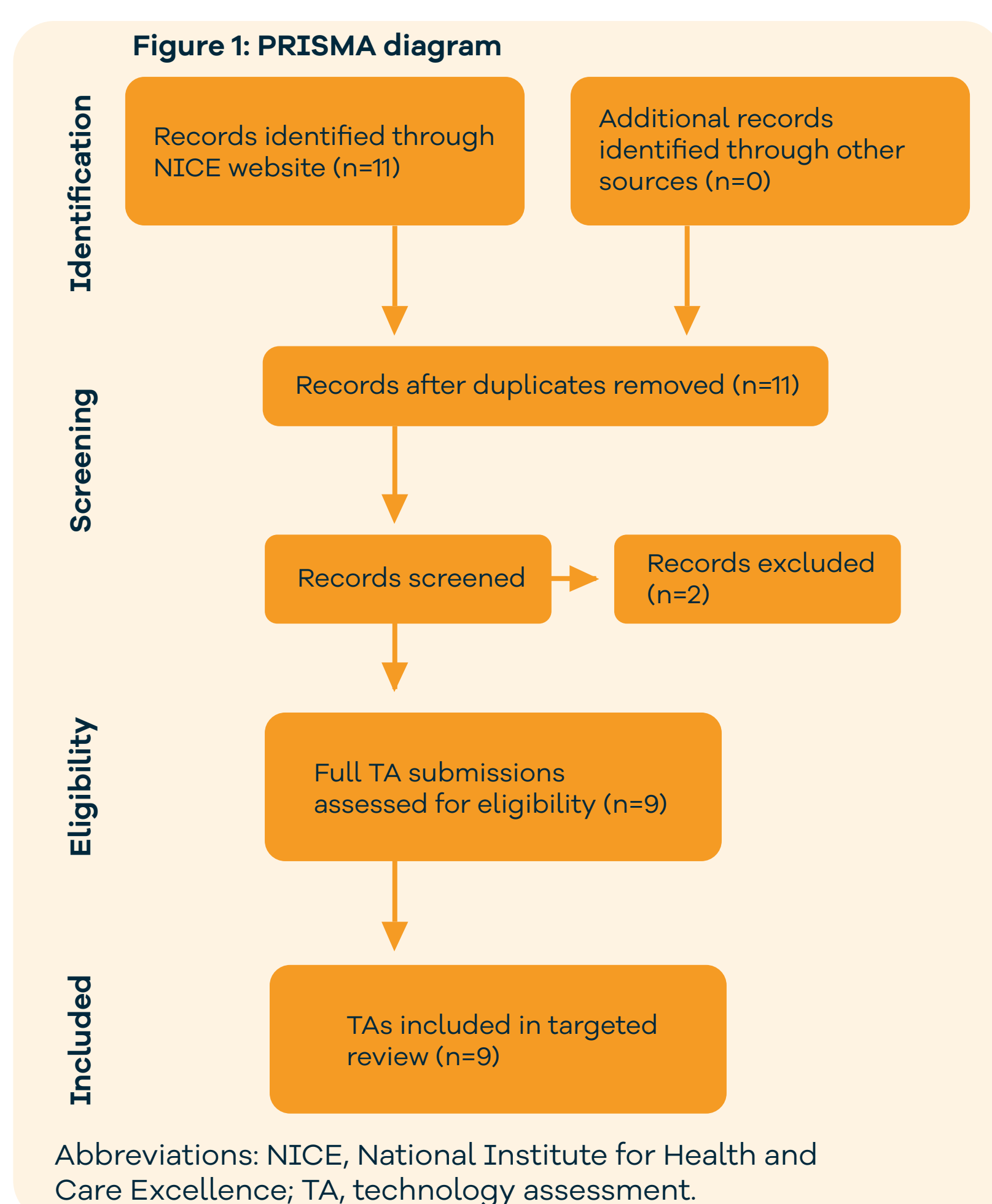
Methodology

A targeted review of UK HTAs was conducted to identify the extent to which caregiver burden is included in technology appraisals (TAs) in the assessment of patients with mental health disorders (Figure 1). TAs for treatments that fell under the category for "mental health, behavioural, and neurodevelopmental conditions" were identified from NICE's website (4). A data extraction form was created to capture whether caregiver burden was considered in each appraisal, and report the methods used to capture burden. The critiques from the evidence assessment group and NICE were also captured.

The following documents were reviewed:
• Manufacturers' submissions
• Evidence assessment group reports
• Final appraisal documents

The key focus area of this research was whether caregiver burden was included within NICE's HTA submissions in mental health, behavioural, and neurodevelopmental conditions, in either the base case or scenario analysis, and whether it impacted the decision. Each document was searched for the following terms: 'caregiver', 'carer', and 'burden' to assess how caregiver burden was reported. The methods used to consider caregiver burden in terms of costs or QoL were summarised, and a review of how caregiver QoL was included in the models were assessed. The type of data used to inform caregiver burden was also reviewed.

Figure 1: PRISMA diagram

Identification
- Records identified through NICE website (n=11)
- Additional records identified through other sources (n=0)

Screening
- Records after duplicates removed (n=11)
- Records screened → Records excluded (n=2)

Eligibility
- Full TA submissions assessed for eligibility (n=9)

Included
- TAs included in targeted review (n=9)

Abbreviations: NICE, National Institute for Health and Care Excellence; TA, technology assessment.

Results

The HTA search identified 11 appraisals, of which two were terminated, leaving nine for evaluation. Of the nine that were relevant for review (Table 1), five held sufficient details regarding caregiver burden (Table 2).

Table 1: HTAs identified in targeted search

TA	Disease state	Recommendation	Inclusion of caregiver burden
TA114 (5)	Drug misuse	Recommended as options for maintenance therapy	N
TA115 (6)	Drug misuse	Recommended on condition	N
TA213 (7)	Psychosis and schizophrenia	Recommended on condition	N
TA217 (8)	Dementia, AZ	Recommended as monotherapies	Y
TA292 (9)	Bipolar disorder	Recommended within MA	N
TA325 (10)	Alcohol-use disorders	Recommended within MA	N
TA337 (11)	Alcohol-use disorders	Recommended within MA	N
TA367 (12)	Depression, major depressive episodes	Recommended within MA	N
TA854 (13)	Depression, TR	Not recommended according to company's positioning	Y

Abbreviations: AZ, Alzheimer's; MA, marketing authorisation; N, no; TA, technology assessment; TR, treatment-resistant; Y, yes.

Of the five relevant TAs identified (Table 2), three appraisals mentioned that caregiver burden had not been documented and acknowledged that by excluding the impact on caregivers, the QALY would be underestimated in these analyses. The remaining two included caregiver QoL in a scenario analysis. These appraisals were in depression and dementia.

Table 2: Caregiver burden reported in TAs

TA, year	Disease state	Intervention, time horizon	Model type	Key findings
TA217, 2011 (8)	Dementia	AChEI, 20 years	Markov	A scenario analysis was conducted where the impact on family and/or carers was considered. The analysis assumed that there would be a negative impact on QoL to caregivers while the patient was in the MDE health state.
TA292, 2013 (9)	Bipolar disorder	Aripiprazole, 3 years	Markov	The clinical advisors noted that the impact of acute manic and mixed episodes on caregivers is not addressed in the submission. Advisors to the ERG also highlighted that the manufacturer had not discussed the role of the caregiver in the patient's management of their illness, including medication adherence as well as identifying prodromal symptoms prior to acute episodes in its submission.
TA325, 2014 (10)	Alcohol-use disorders	Nelmefene, 5 years	Markov	No caregiver views had been documented. The committee stated that the utility values in the model may have underestimated the true benefit as it did not consider the QoL of family and carers.
TA337, 2015 (11)	Alcohol-use disorders	Rifaximin, lifetime	Markov	The manufacturer indicated that reducing the recurrence of hepatic encephalopathy symptoms would have an impact of QoL of caregivers as shown in a study by Bajaj et al 2011 (14). The Committee agreed that the costs associated with constant care from caregivers could not be built into the model and factoring them in would reduce the ICER.
TA854, 2022 (13)	Depression	Esketamine, 5 years	Markov	The company submission included a disutility value for the effect of treatment-resistant depression on caregivers. This was done by applying a disutility to the MDE health state. This was the difference in utility between caregivers of people with symptomatic treatment-resistant depression and caregivers of people with treatment-resistant depression that was in remission. The ERG commented that it is better to subtract that state from the utility of full health, to estimate disutility for a specific state. Consequentially, the ERG used this methodology and applied a lower value of disutility. The ERG scenario was considered to be the most appropriate. However, there were discussions about how appropriate it was to include caregiver disutility due to the lack of data on the direct effect treatment-resistant depression had on caregivers QoL.

Within TA217, the analysis assumed a negative impact on caregiver QoL, depending on patient's health state occupancy. Modelling caregiver QoL by patient disease state is consistent with the approach taken to model patient QoL. Caregiver utilities were estimated using SF-36 scores and the Brazier algorithm from three clinical trials. (15)

Caregiver burden accounted for 10% of the incremental QALYs. Caregiver burden did not impact the conclusion of the committee, however further research was recommended to assess the relationship between disease progression and carer QoL.

Within TA854 base case, the manufacturer increased the cost and utility decrement of the major depressive episode (MDE) state to account for lost productivity and caregiver burden. Caregiver QoL was informed by a study with a sample of carers of those with the disease. The committee concluded the evidence provided was of good quality but highlighted there is a lack of data on the direct effect treatment on caregivers' burden. Thus, the evidence review group concluded that it was appropriate to consider a scenario with caregiver disutility and no caregiver disutility, as the impact was uncertain. However, despite the scenarios, the treatment was not recommended.

Conclusion

Omitting caregiver burden from models is inconsistent with the goal of maximising health from a general population, with a fixed budget, and risks decisions that reduce overall health. A challenge with including caregiver burden in cost-effectiveness models is the lack of data on the true costs associated with care and the direct effect treatment has on caregiver QoL.

The NICE committees in TA217 and TA854 appear willing to consider the impact on caregivers, but the quality of evidence is lacking. Implementing methods aligned with those used to assess the QoL of patients would be the gold standard solution (captured during RCTs and, systematic literature reviews). However, it appears that little robust evidence exists to be identified and therefore manufacturers should look to improve the evidence base in this area. Without RCT data to inform utility values, systematic reviews and anecdotal evidence from clinical practice regarding the benefits to patients and carers should be sought.

Potential solutions include capturing caregiver impact in the associated treatments RCTs or use of real-world evidence. Given the significant caregiver burden associated with mental health disorders, it is important to overcome the challenges associated with the lack of data, so that NICE can consider the impact on the wider population in its decision-making process.

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