How to Mitigate "Carer QALY Trap" when Including Caregiver QOL in Cost-Effectiveness Analysis: A Model Simulation Using Lecanemab in Japanese Patients with Alzheimer's Disease

EE221

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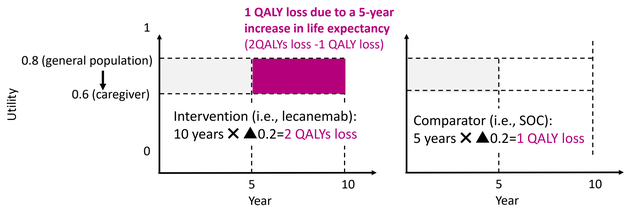
BACKGROUND

- Alzheimer's disease (AD) and other forms of dementia particularly burden caregivers with the long-term and all-encompassing nature of the care.
- In recent years, there has been growing interest in incorporating the spillover effects on family and informal caregivers, such as quality of life (QoL), into cost-effectiveness analyses.
- Caregiver disutility is commonly used to include caregivers' QoL in cost-effectiveness analyses. However, in the disutility approach, increasing in patient life expectancy would affect the caregiving burden, resulting in loss of quality adjusted life years (QALYs) for caregivers. This phenomenon is known as the "carer QALY trap" [1].

Figure 1. Caregiver QALY loss



OBJECTIVE

- To address methodological issues of the "Carer QALY trap", which arises from reflecting caregivers' QOL as disutility in a cost-effectiveness analysis.
- Through a model simulation of the lecanemab economic evaluation, we will estimate the impact on QALYs and compare these methods used to reflect caregiver QOL and elucidate the mechanism behind it.

METHODS

Overview

- This study used a disease progression model of AD to assess differences in estimates of health outcomes between approaches that reflect caregiver QOL.

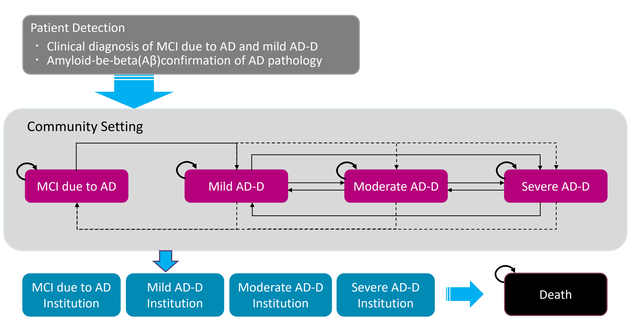
Table 1. Summary of the Study Design

Population	Patients with early AD (MCI due to AD or mild AD-D) with a confirmed Aβ pathology
Intervention	Lecanemab administered every 2 weeks (10 mg/kg) + SOC
Comparator	SOC
Time horizon	Lifetime (up to 30 years)
Outcomes	QALY • To reflect caregiver QOL, three approaches were compared: 1. no inclusion of caregiver QOL 2. inclusion using a decrement approach, which applied disutility 3. inclusion using an additive approach, which using caregiver utilities using absolute values.
Discount rate	2% per year[2]

Model structure

- A Markov state transition model with health states based on disease severity, institutionalization, and death was developed.

Figure 2. Model structure



Model Input

- The efficacy for lecanemab was derived from transitions between health states for 0-18 months in the Clarity AD and beyond 18 months, the hazard ratio (HR) for time-to-worsening of Clinical Dementia Rating-Sum of Boxes (CDR-SB) estimated from the 36-month open-label extension of Clarity AD was used[3,4].
- Patient characteristics and the discontinuation of lecanemab were also sourced from the Clarity AD [3].
- Other clinical model inputs were derived from published literatures.
- Patient and caregiver (dis-)utilities were obtained from published literatures.

Table 2. Clinical model inputs

Variable			Value	Sensitivity analysis: Distribution	Sensitivity analysis: confidence intervals	Ref
Characteristics						
Starting age (years)			71.5	Gamma	70.0 , 73.0	[3]
% female			52.4%	Beta	43.3%, 61.5%	
% MCI due to AD			62.3%	Beta	60.0%, 64.6%	
% Mild AD-D			37.7%	-	-	
Clarity-AD transition distribution at 0-18 months（monthly transition rates）						
Lecanemab	MCI due to AD to	Mid AD-D	1.62%	Dirichlet	-	[3]
		Moderate AD-D	0.14%			
		Severe AD-D	0%			
	Mild AD-D to	MCI due to AD	1.06%	Dirichlet	-	
		Moderate AD-D	0.81%			
		Severe AD-D	0.03%			
SoC	MCI due to AD to	Mid AD-D	2.26%	Dirichlet	-	
		Moderate AD-D	0.18%			
		Severe AD-D	0.02%			
	Mild AD-D to	MCI due to AD	0.68%	Dirichlet	-	
		Moderate AD-D	1.05%			
		Severe AD-D	0.09%			
Treatment effect of Lecanemab after 18 months（Time to worsening HR vs SoC）						
MCI due to AD			0.704	Log-normal	0.590, 0.840	[4]
Mild AD-D			0.704	Log-normal	0.590, 0.840	
Moderate AD-D			0.704	Log-normal	0.590, 0.840	
Transition probabilities of natural history（monthly transition rates）						
MCI due to AD to		Mild AD-D	1.52%	Beta	1.19%, 1.86%*2	[5]
		Moderate AD-D	0.51%	Beta	0.41%, 0.62%*2	
		Severe AD-D	0.02%	Beta	0.01%, 0.02%*2	
Mild AD-D to		MCI due to AD	0.28%	Beta	0.22%, 0.34%*2	
		Moderate AD-D	3.57%	Beta	2.72%, 4.51%*2	
		Severe AD-D	0.40%	Beta	0.32%, 0.49%*2	
Moderate AD-D to		MCI due to AD	0%	-	-	
		Mild AD-D	0.22%	Beta	0.18%, 0.27%*2	
		Severe AD-D	4.48%	Beta	3.37%, 5.76%*2	
Severe AD-D to		MCI due to AD	0%	-	-	
		Mild AD-D	0%	-	-	
		Moderate AD-D	0.21%	Beta	0.16%, 0.25%*2	
AD specific mortality (HR, vs General population mortality)						
MCI due to AD			1.14	Log-normal	0.91, 1.37*1	[6]
Mild AD-D			1.55	Log-normal	1.24, 1.86*1	
Moderate AD-D			2.80	Log-normal	2.24, 3.36*1	
Severe AD-D			5.48	Log-normal	4.38, 6.58*1	
General population mortality						
General population mortality			Life table	-	-	[7]
Monthly discontinuation rate after 36 month						
Lecanemab	MCI due to AD		0.9%	Beta	0.7%, 1.0%*1	[3]
	Mild AD-D		1.4%	Beta	1.1%, 1.7%*1	
Transition rate to institutionalization（/18 months）						
MCI due to AD			0.00%	-	-	[8]
Mild AD-D			3.20%	Beta	0.44%, 5.96%	
Moderate AD-D			9.10%	Beta	5.20%, 13.00%	
Severe AD-D			8.50%	Beta	4.51%, 12.49%	

*1 ±20% of the value for base case analysis
*2 ±20% of the annual value for base case analysis

Table 3. Utilities

Variable	Value	Sensitivity analysis: Distribution	Sensitivity analysis: confidence intervals	Ref
Patient health state utilities				
MCI due to AD	0.882	-	-	[9]
Mild AD-D	0.816	Beta	0.724, 0.904	[10]
Moderate AD-D	0.715	Beta	0.672, 0.754	
Severe AD-D	0.489	Beta	0.447, 0.528	
Utility decrement due to institutionalization				
MCI due to AD	0	Normal	-0.11, 0.12	[11]
Mild AD-D	0	Normal	-0.11, 0.12	
Moderate AD-D	-0.13	Normal	0.03, 0.23	
Severe AD-D	-0.13	Normal	0.03, 0.23	
Caregiver utilities (additive approach)				
MCI due to AD	0.929	-	-	[9]
Mild AD-D	0.911	Beta	0.865, 0.956	[12]
Moderate AD-D	0.878	Beta	0.808, 0.965	
Severe AD-D	0.858	Beta	0.746, 0.987	
Caregiver utilities (decrement approach)				
MCI due to AD	0			[12]
Mild AD-D	-0.018	*	*	
Moderate AD-D	-0.051	*	*	
Severe AD-D	-0.071	*	*	
Caregiver utility decrement due to institutionalization				
Institutionalization (all severities)	0.05	Beta	-0.03, 0.13	[11]

* Since the caregiver disutility is calculated based on the values of the additive approach, it is linked to the settings of the additive approach.

RESULTS

Disease progression and transition of care settings

- Patients treated with lecanemab spent a further 1.38 years in early AD and 0.58 years less in moderate and severe.
- Overall survival was 10.30 years for lecanemab and 9.50 years for SOC, with a survival benefit of 0.79 years with lecanemab.
- Lecanemab increased the time patients spent in community care by 0.87 years and reduced the time spent in institutional care by 0.08 years.

Table 4. Results of patient transition

	SoC	Lecanemab	Incremental vs. SoC
Mean time in MCI due to AD (years)	2.45	3.42	0.97
Mean time in mild AD-D (years)	2.02	2.43	0.41
Mean time in moderate AD-D (years)	1.34	1.59	0.25
Mean time in severe AD-D (years)	3.69	2.85	-0.84
Mean time in community (years)	8.19	9.07	0.87
Mean time in institution (years)	1.31	1.23	-0.08
Total life years	9.50	10.30	0.79

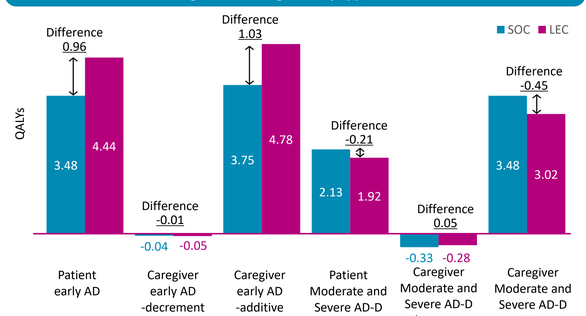
QALY estimation

- Lifetime QALYs gained by patients were 5.61 QALYs for SOC and 6.37 QALYs for lecanemab, with the incremental effect of lecanemab being 0.75 QALYs.
- In the decrement approach, QALYs lost by caregivers were 0.37 QALYs for SOC and 0.33 QALYs for lecanemab, and the incremental effect of lecanemab on caregivers' QALYs was 0.04 QALYs.
- In the additive approach, QALYs gained by caregivers were 7.23 QALYs for SOC and 7.80 QALYs for lecanemab, with an incremental effect of 0.57 QALYs for lecanemab.
- The incremental QALYs for lecanemab were as follows: 0.75 QALYs in the analysis excluding caregiver utilities, 0.79 QALYs in the decrement approach, and 1.32 QALYs in the additive approach, with the greatest incremental benefit in the additive approach.
- Although lecanemab prolonged the time that patients remained in early AD and life expectancy, there were only small additional QALYs for caregivers in the decrement approach.

Table 5. Disaggregated QALYs

	SoC	Lecanemab	Incremental vs. SoC
Patient			
in MCI due to AD	1.97	2.68	0.71
in mild AD-D	1.51	1.76	0.25
in moderate AD-D	0.81	0.92	0.12
in severe AD-D	1.33	1.00	-0.33
Total QALYs	5.61	6.37	0.75
Caregiver <Decrement approach>			
in MCI due to AD	0.00	0.00	0.00
in mild AD-D	-0.04	-0.05	-0.01
in moderate AD-D	-0.07	-0.08	-0.01
in severe AD-D	-0.26	-0.20	0.06
Total QALYs	-0.37	-0.33	0.04
Caregiver <Additive approach>			
in MCI due to AD	2.07	2.82	0.75
in mild AD-D	1.68	1.96	0.28
in moderate AD-D	1.00	1.15	0.15
in severe AD-D	2.47	1.87	-0.60
Total QALYs	7.23	7.80	0.57

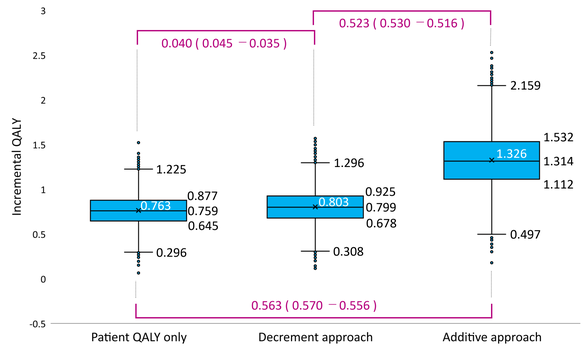
Figure 3. QALYs gained by approaches



Sensitivity analysis

- Parameters were set probabilistically based on confidence intervals and distributions for each parameter. It followed a standard Monte Carlo approach consisting of 10,000 randomly drawn simulations of the parameter values.
- The mean incremental QALYs for lecanemab of sensitivity analysis were similar to those of the base analysis.
- In the additive approach, the incremental effects tended to be higher than in the other approaches.

Figure 4. Results of 10,000 simulations in the sensitivity analysis



CONCLUSIONS

- Using a Markov model approach to predicting health outcomes patients with early AD who received either lecanemab treatment or SOC, lecanemab treatment was estimated to extend the time spent in early AD stage by delaying disease progressions.
- This would be beneficial for patients as well as family caregivers, however, when expressing outcomes in terms of QALYs under the decrement approach, the longer a patient remains in the early stage of AD, the more family caregivers are perceived to incur a continuing burden. In contrast, the additive approach does not lead to a Carer QALY trap because it assesses caregivers' whole QOL.
- No health technology assessment (HTA) guidelines or other documents have provided guidance on how to address caregivers' QOL. In recent years, studies have begun to consider the additive approaches or the impact of bereavement[13,14].
- Future HTA evaluations and research should refer to already reported case studies, address the challenges of the decrement approach, and consider adopting an approach that takes into account caregiver QOL.

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Declaration

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