Adjusting Utilities Using Age and Time-to-Death Decrements in Cost-Effectiveness Analyses: A Case Study in Relapsed and/or Refractory Multiple Myeloma

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Abstract HTA82

INTRODUCTION

- **Age-based utility norms** are often used to adjust health state utility values in cost-utility analyses (CUAs) with lifetime horizons to account for the declining quality-of-life (QoL) of individuals as they age[1]. However, **time-to-death (TTD)** was found as a significant driver of QoL decline in previous researches as well[2].
- Versteegh et al (2022)[3] reported that **TTD significantly impacts QALY gains**, especially in the longer-term survival period. And TTD is more associated with QALY gains than age.

OBJECTIVES

To compare the effect on QALYs when **adjusting health state utilities based using TTD and age-based norms** in a CUA for relapsed and/or refractory multiple myeloma (RRMM).

METHODS

Targeted literature review to inform the model specifications

- Among the indications assessed in Versteegh et al. (2022)[3], RRMM was selected for the case study.
- NICE TA897[4] was chosen to replicate since its clinical and cost parameters, as well as results, were transparently reported.
- TA897 assessed the clinical and cost-effectiveness of **daratumumab combined with bortezomib and dexamethasone** (DBd) compared to bortezomib plus dexamethasone (Bd) in adult RRMM patients.

Cost utility analysis development

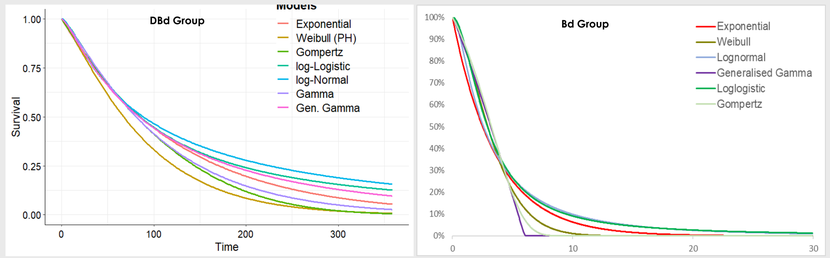
Time horizon	Model structure	AE & Cost & Utility parameters
Life-time (30 years)	**Partitioned survival model**	**TA897[4]**

- **Sensitivity and scenario analyses** were performed to identify when utility adjustment method had the **largest impact**.

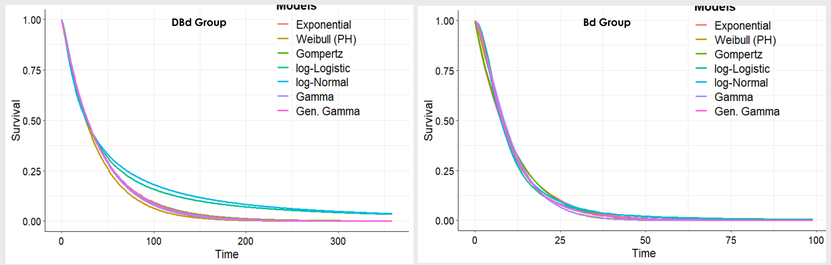
Survival analysis

- Parametric survival functions were generated from **digitized KM curves of the CASTOR trial[5]** to fit and extrapolate survival curve.

✓ **Log-logistic** distribution was selected as base case for **OS**



✓ **Exponential** distribution was chosen as the base case for **PFS**



Utility adjustment

- **TTD-based:** The utility values for the **general population** of different age and gender[6] were **applied multiplicatively** into the model.
- **Age-based:** The coefficient of TTD[4] related to utility was utilized to calculate the **disutility associated with different TTD periods** during the model cycles and **adjust progression-based utilities accordingly**.

Time to death	Coefficients	Adjusted PFS utility	Adjusted PP utility
0-3 months	-0.144	0.593	0.521
3-6 months	-0.180	0.557	0.485
6-12 months	-0.099	0.638	0.566
12-18 months	-0.213	0.524	0.452
18-24 months	-0.095	0.642	0.570
24-36 months	-0.104	0.633	0.561
36-48 months	-0.033	0.704	0.632
48-60 months	-0.100	0.637	0.565
> 60 months	-	0.737	0.665

RESULTS

TTD-based adjustment delays the QoL decline when the survival time is extended

- Total **QALYs of DBd** with TTD-based adjustment were **higher** than QALYs with age-based adjustment, while the QALYs of **Bd were lower**.

		Age adjusted		TTD adjusted	
		DBd	**Bd**	**DBd**	**Bd**
Discounted QALY	QALY gain	5.233	2.110	5.260	1.888
	Incremental QALY		-3.123		-3.372
Discounted cost	Total cost	£319,557	£73,816	£319,557	£73,816
	Incremental cost		-£245,741		-£245,741
ICER	**Per QALY**		**£78,687**		**£72,884**

In all scenarios, incremental QALYs were higher with TTD adjustments, leading to lower ICERs.

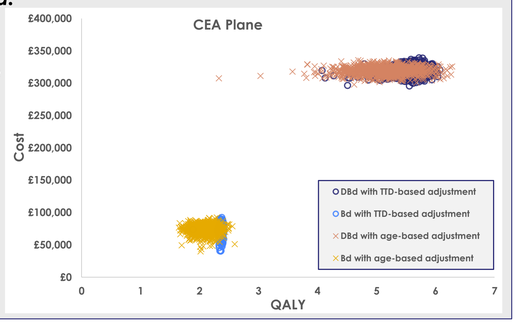
- When using the optimistic lognormal distribution to extrapolate DBd OS, the difference of incremental QALYs between adjustment approaches was 27.7% larger than the base case.
- The pessimistic Gompertz function reduced incremental QALYs between approaches.

Scenarios	Age-based adjustment		TTD-based adjustment	
	Incremental QALYs	ICER (£/QALY)	Incremental QALYs	ICER (£/QALY)
Base case	-3.123	78,687	-3.372	72,884
time horizon - 15 years	-2.438	98,773	-2.639	91,252
Age - 85 years	-0.702	337,714	-0.884	268,039
Age - 40 years	-3.26	75,410	-3.438	71,496
PFS for Bd - Loglogistic	-3.121	78,523	-3.369	72,751
OS for Bd - Loglogistic	-2.64	92,374	-2.848	85,422
OS for DBd - Exponential	-2.854	85,766	-3.099	78,757
OS for DBd - Lognormal	-3.369	73,214	-3.687	66,725
OS for DBd - Weibull	-2.584	94,326	-2.782	87,370
OS for DBd - Gompertz	-2.283	106,270	-2.441	99,141

Legend: Small difference — Large difference (between approaches)

Probabilistic analysis highlighted:

- The probabilistic cost-effectiveness plane was more convergent when TTD was chosen to adjust utility.
- It suggested that the uncertainty of model with TTD-based adjustment was less than model with age-based adjustment.



LIMITATIONS & CONCLUSIONS

Limitations

- The sample size of Versteegh et al. (2022) was small which might lead to a large uncertainty of the coefficients.
- More scenario analysis including different clinical efficacy, indications, and other factors may impact on utility, are needed to improve the generalisability.

Conclusions

In a RRMM **case study with a large survival difference** between comparators,

- **TTD-based** health state utility **adjustments increased incremental QALYs** compared to age-based adjustments.
- **The difference in incremental QALYs between approaches diminishes as survival benefit diminishes.**

REFERENCES

Disclosures

Wen Su and Max Clayson are employees of Amaris Consulting, no professional fees or funding were received for this study.