

# Mind the Mortality Gap: Comparing Average and Age-Distribution Approaches to Estimating Background Survival for Health Economic Models

## Objectives

Cost-effectiveness models typically adopt a lifetime time horizon, requiring the estimation of survival beyond the follow-up observed in a clinical trial. Models often include functionality to ensure that the estimated survival of patients with the disease is less than or equal to that observed in the age- and sex-adjusted general population. The proliferation of cure models in oncology indications has made background (or 'other-cause') mortality rates an increasingly important factor when estimating the cost effectiveness of an intervention. In

cohort-based models, this is traditionally done by using the life-table hazard rates for the mean age of the study population for males and females, which are then weighted based on the distribution of patient sex within the trial. This method assumes the age of patients is normally distributed, which often means the demographic of the trial and clinical practice is not reflected. Lee *et al.* (2024) proposed an alternative method that captures the distribution of patient ages within a study when estimating the age- and sex-matched background mortality (1).

## Methods

We simulated six adult populations containing 300 patients, each consisting of a 50:50 split of males and females, but each with a different age profile, determined according to specifying different proportions within a given age band (e.g., 30 to 40 years). To simulate each population, we specified the proportion of patients in an age band, with bands running from 18–30 years old, then 10-year bands up to a maximum age of 90 years old. The simulation process then randomly assigned specific ages to the patients within each band assuming a uniform distribution within each band. The resulting distributions are presented in Figure 1.

The information required to calculate background mortality using both methods was derived from the simulated datasets. The population mean was calculated to derive background mortality using the life-table estimates based on the mean age at baseline (referred to as the

'mean approach' hereafter). The method reported by Lee *et al.* (referred to as the 'distribution approach') requires a cumulative density function for males and females. Both approaches utilized the UK LifeTables for 2022–24 published by the Office for National Statistics (ONS) (2).

The two approaches ('mean approach' and 'distribution approach') were used to estimate survival over a lifetime time horizon, defined as up to a maximum age of 100 years. The mean LYs were calculated for each method via the area-under-the-curve over the lifetime horizon, and the difference in LYs was used to compare the two approaches. Undiscounted and discounted LYs (at 3.5% per annum) were calculated. The expected lifetime survival curve using each method was also plotted to allow for visual comparison.

This study compares the background mortality estimates generated using each approach for several different populations, to understand how estimates of life years (LYs) are impacted by analysis methodology.

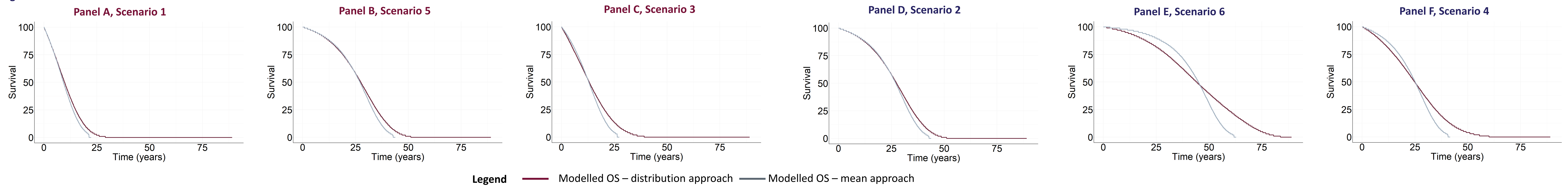
Figure 1: Population distributions

Age band (Years)	Scenario					
	1	2	3	4	5	6
18-29	0.00%	0.00%	0.00%	0.00%	0.00%	26.67%
30-39	0.00%	1.33%	0.00%	16.00%	0.00%	18.00%
40-49	0.00%	11.67%	0.00%	16.00%	0.00%	21.33%
50-59	0.00%	28.33%	50.00%	18.00%	0.00%	19.33%
60-69	0.67%	36.33%	50.00%	18.00%	22.67%	11.67%
70-79	49.33%	17.33%	0.00%	16.00%	46.00%	2.67%
80-89	49.33%	4.33%	0.00%	16.00%	28.00%	0.33%
90-99	0.67%	0.67%	0.00%	0.00%	3.33%	0.00%

## Results

Details of the estimated survival are presented in Table 1 and the modeled survival curves for each population and method is presented in Figure 2, with each panel showing a difference scenario explored.

Figure 2: Survival curves



← Smallest difference in incremental, undiscounted LYs | Largest difference in incremental, undiscounted LYs →

Table 1: Simulation results

#	Panel	Mean age (SD)	Distribution approach		Mean approach		Incremental LYs between methods	
			Undiscounted LYs	Discounted LYs	Undiscounted LYs	Discounted LYs	Undiscounted LYs	Discounted LYs
1	A	80.4 (4.2)	9.66	7.79	8.87	7.32	0.79	0.47
2	D	62.0 (9.7)	23.30	14.86	22.00	14.78	1.3	0.08
3	C	75.7 (7.8)	13.05	9.79	11.89	9.33	1.16	0.46
4	F	59.6 (16.7)	26.55	15.14	23.69	15.53	2.86	-0.39
5	B	59.6 (5.5)	24.66	15.81	23.69	15.53	0.97	0.28
6	E	42.4 (15.2)	40.78	20.48	39.43	20.94	1.35	-0.46

Undiscounted LYs were higher in all scenarios when using the distribution approach compared to the mean age. The discounted results did not follow the same consistent pattern. The results for undiscounted and discounted outcomes were consistent in scenarios where the groups were older or the spread of ages was smaller, as expected the difference in LY estimates were reduced. For the scenarios with younger populations with greater variability in age, we observed greater discounted LYs when using the mean age approach compared to the distribution approach. The difference in discounted and undiscounted results can be explored further via inspection of the plotted survival curves (Figure 2) as LYs are accrued differently over time depending on the approach. Where there is a large variability in patient ages within a population, the methods lead to substantially different overall survival

estimates over time. The distribution method leads to greater initial mortality followed by a slower mortality rate in the long-term. This is because the method is initially capturing the greater mortality rate among the patients that are older than the population mean; whereas in the mean age approach there is very little initial mortality, as the method assumes that the whole cohort starts at the mean age, which is associated with a low mortality risk. The mortality risk of the entire population then increases collectively over time, creating the steep decrease in survival.

## Conclusion

Different approaches to estimating background mortality can lead to marked variations in the modeled outcomes.

Modeling the distribution of ages within a population consistently leads to a greater initial hazard than when all patients are assumed to be the mean age of the cohort.

The results are more pronounced when the population has a lower mean age and when the variability within the demographic is greater.

The choice of methods could have implications for estimating cost effectiveness through its influence on background mortality to inform cure models or when capping overall survival in terminal cancer indications, as well as other therapeutic areas.

## References

- Lee D, Hart R, Burns D, McCarthy G. The Impact of the Approach to Accounting for Age and Sex in Economic Models on Predicted Quality-Adjusted Life-Years. *Appl Health Econ Health Policy*. 2025 Jan;23(1):131-40. Available from: <https://www.ons.gov.uk/peoplepopulationandcommunity/birthdeathsandmarriages/lifeexpectancies/bulletins/nationallifetablesunitedkingdom/2022to2024>. Accessed on: April 2026.
- Office for National Statistics (ONS). National life tables – life expectancy in the UK: 2022 to 2024. 2025. Available from: <https://www.ons.gov.uk/peoplepopulationandcommunity/birthdeathsandmarriages/lifeexpectancies/bulletins/nationallifetablesunitedkingdom/2022to2024>. Accessed on: April 2026.

## Abbreviations

- LY – Life year
- ONS – Office for National Statistics
- SD – Standard deviation