

Decomposing Overall Mortality Into Latent Disease-Specific Health States Mortality to Inform Cost-Effectiveness Modelling

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INTRODUCTION

- A Markov Model assessed the cost-effectiveness of BGF 320/18/9.6 µg versus FF/UMEC/VI100/62.5/25 µg¹
- Health states were defined based on FEV1 severity (moderate, severe, and very severe)
- Mortality data for FF/UMEC/VI was only available at the aggregate level from a MAIC and required decomposition into mortality associated with FEV1 health states²
- MAIC adjusted KM curves from ETHOS and IMPACT are presented in the supplement
- Aim:** To estimate standardized mortality estimates per latent FEV1 health state adjusting for general population mortality from aggregated mortality data to run a Markov model for 5-year time horizon evaluation

METHODS



All-cause mortality was obtained from UK life tables³



The cumulative mortality curves from MAIC were digitized to extract the cumulative probability of death over-time at 1-month intervals as per model cycle length



A hazard ratio was calibrated using the baseline distribution in different FEV1 states (i.e., 29%, 61%, and 10%) and excess relative risk of dying (i.e., 1.4, 2.6, and 2.6) for FF/UMEC/VI by minimizing the MSE (Table 1)

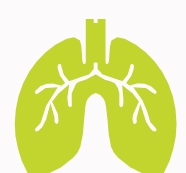


Table 2 depicts the cut-off criteria for mild, moderate, severe and very severe FEV1

Table 1: Mortality relative risks derived from the published literature

| FEV1 health state-related mortality | Relative risk |
|---|---------------|
| Moderate FEV1 no exacerbation-related mortality* | 1.40 |
| Severe FEV1 no exacerbation-related mortality* | 2.60 |
| Very severe FEV1 no exacerbation-related mortality* | 2.60 |

Source: Shavelle et al. 2009⁴
*Relative risk versus annual general population mortality

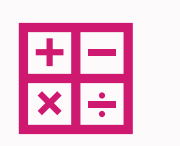
Table 2: Spirometric cut points for airflow obstruction in COPD

| Severity | FEV1 (% predicted) |
|-------------|----------------------------|
| Mild | FEV1 ≥ 80% predicted |
| Moderate | 50% ≤ FEV1 < 80% predicted |
| Severe | 30% ≤ FEV1 < 50% predicted |
| Very Severe | FEV1 < 30% predicted |

Source: GOLD 2024⁵



For mortality beyond one year, the 12-month relative hazard was assumed to remain constant or increase linearly to match the FF/UMEC/VI hazard at 5 years



In the model the calculation of mortality was performed using various steps as depicted in Figure 1

RESULTS

- At one year, the decomposed mortality by moderate, severe, very severe health states for BGF (0.86%, 1.59%, and 1.59%, respectively) was lower compared to FF/UMEC/VI (1.41%, 2.61%, and 2.61%, respectively) (Figure 2)
- BGF was found to increase the life-years by 7.5% over 5 years when assuming a constant rate and by 5.1% when assuming a linear decrease in treatment effect from 1 to 5 years compared to FF/UMEC/VI

Figure 2: Decomposed mortality rates at one-year associated with FEV1 health states

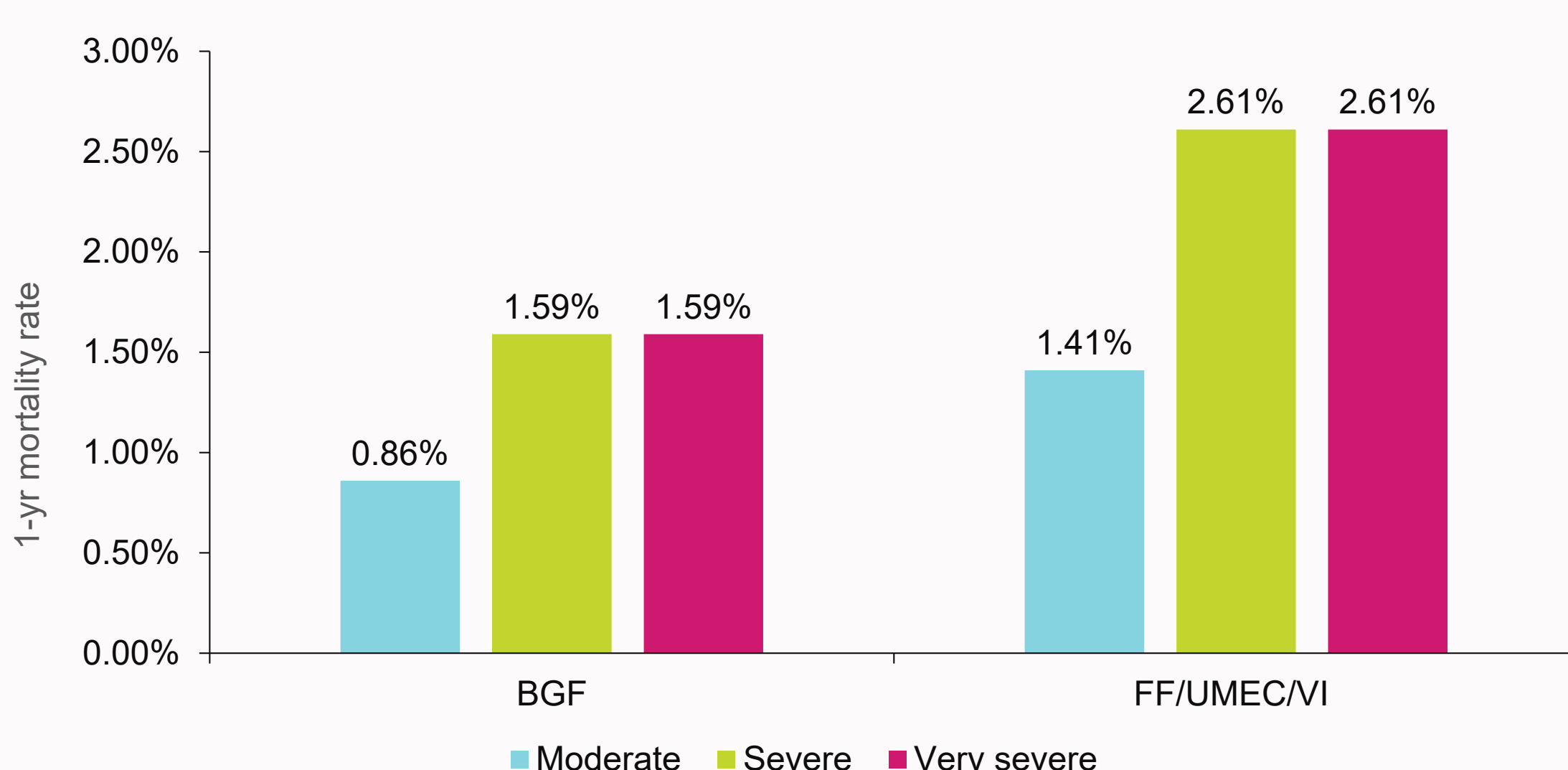


Figure 1: Detailed description on Mortality calculations

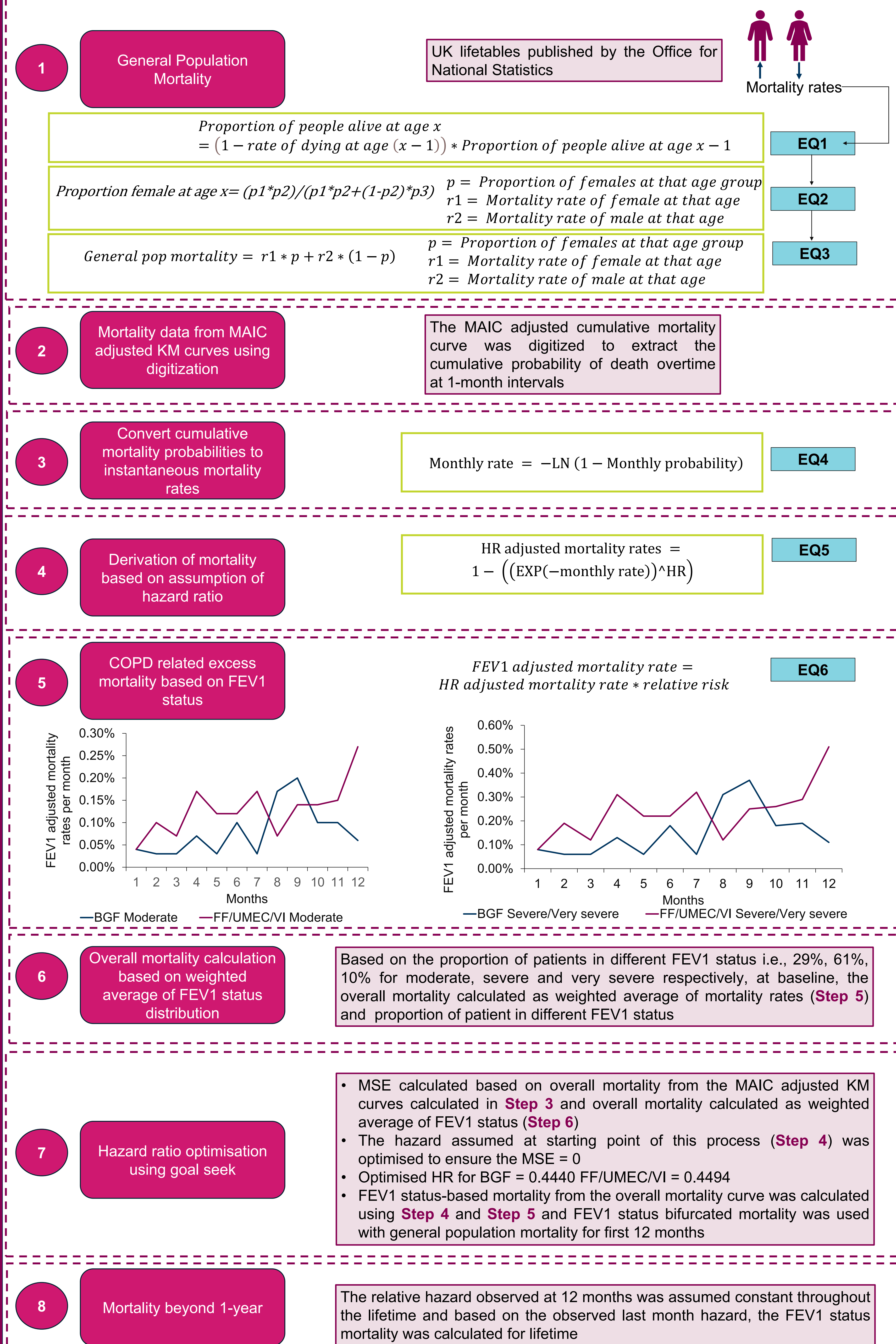
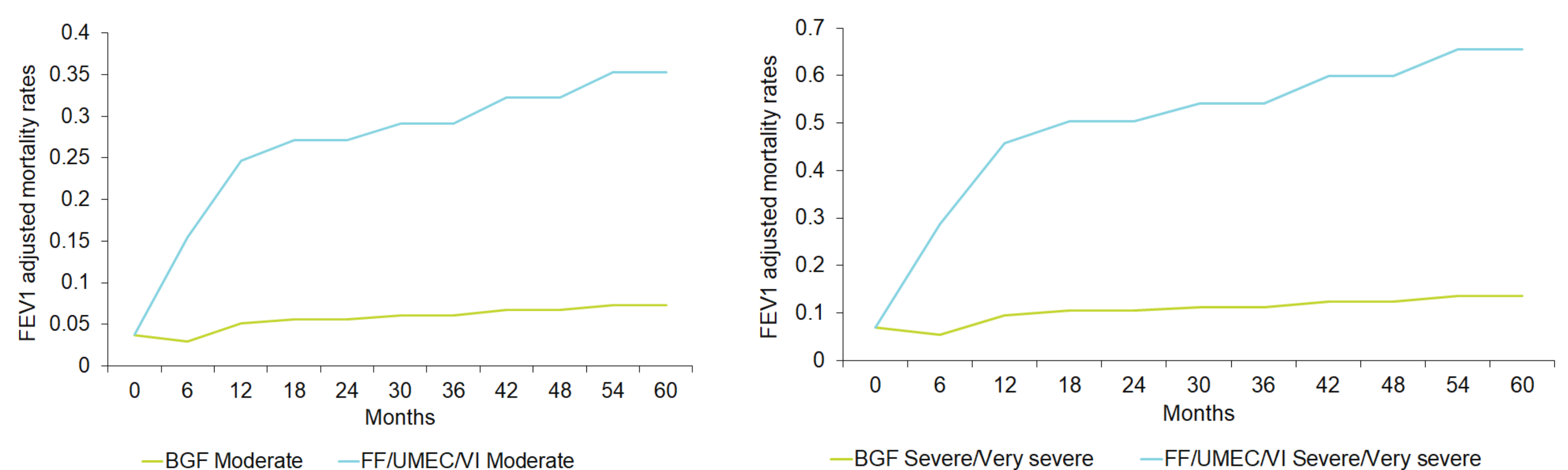


Figure 3: Graphical representation of FEV1 health state mortality rate up to 5 years



CONCLUSION

- The methodology to decompose overall mortality into health state-specific mortality, accounting for general population mortality, was successfully implemented. This approach can be applied in health economic models to predict health state specific mortality from overall mortality accounting for general population mortality

Abbreviations

ACM, all-cause mortality; BGF, budesonide/glycopyrronium/formoterol fumarate; CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in one second; FF/UMEC/VI, fluticasone furoate/umeclidinium/vilanterol; GOLD, Global Initiative for Chronic Obstructive Lung Disease; HR, hazard ratio; ITT, intent-to-treat; MAIC, matching-adjusted indirect comparison; KM, Kaplan-Meier; MSE, mean square error; SLR, systematic literature review; UK, United Kingdom

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Disclosures

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