

Long-Term Clinical Outcomes in People with Heart Failure with Preserved Ejection Fraction (HFpEF) or Heart Failure with Mid-Range Ejection Fraction (HFmrEF) Treated with Standard of Care (SoC)

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Background

- Heart failure (HF) is a highly prevalent, chronic, and progressive condition affecting approximately 64 million people worldwide and 6 million people in the United States (US)^{1,2}
- HFpEF/HFmrEF constitutes approximately half of all HF³
 - In this study, HFpEF/HFmrEF includes all HF with LVEF ≥40%
- Three large phase 3 trials have been conducted in contemporary HFpEF/HFmrEF populations since 2019:
 - PARAGON-HF⁴
 - EMPEROR-Preserved⁵
 - DELIVER⁶

Objective

- We sought to model the clinical outcomes in a cohort of patients with symptomatic (New York Heart Association [NYHA] class II-IV) HFpEF/HFmrEF treated with SoC over a lifetime horizon.

Methods

- A three-state Markov model (Figure 1) with 1-month cycle length was developed based on enrolled populations for PARAGON-HF, EMPEROR-Preserved, and DELIVER studies⁴⁻⁶
 - Weighted mean age 72 years, 53.6% male
- SoC was defined as the baseline distribution of selected cardiovascular medications reported at baseline in clinical trials
 - In addition, 20% of patients assumed to be treated with sodium-glucose cotransporter-2 (SGLT2) inhibitor
- Event rates derived from recent HFpEF/HFmrEF trials as a weighted average of comparator arm and SGLT2 inhibitor arm outcomes (Table 1)
- Background mortality was based on US life tables⁷
- All outcomes discounted at 3% per year with half-cycle corrections

Figure 1. Model Structure

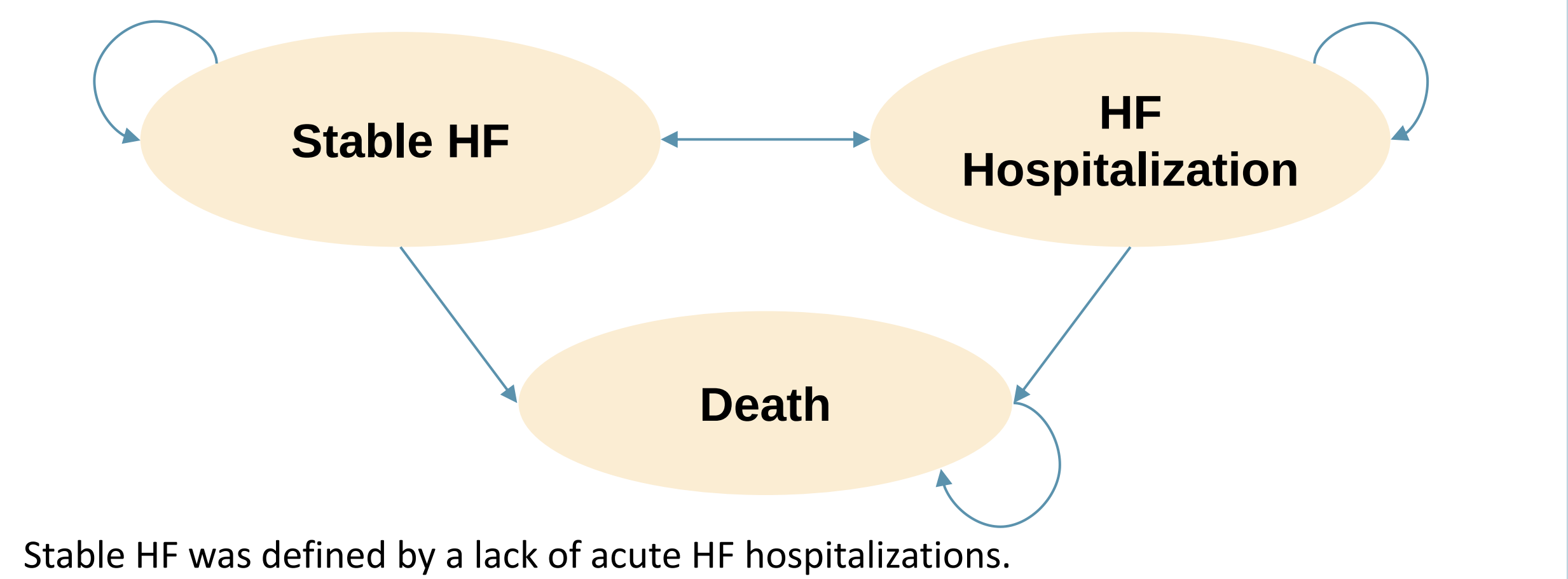


Table 1. Model Inputs

Parameter	Value	Source
Event Probabilities, per month		
HF Hospitalization, from stable HF	0.57%	PARAGON-HF, EMPEROR-Preserved, DELIVER ⁴⁻⁶
Hyperkalemia	0.21%	
Composite renal endpoint	0.13%	
Cardiovascular death	0.28%	
All-cause death	0.52%	
Rehospitalization for HF	6.8%	Peters et al 2022 ⁸
Hyperkalemia Management		
Managed outpatient	41%	EMPEROR-Preserved and PARAGON-HF ^{4,5}
Managed inpatient	59%	
Composite renal endpoint events*		
Sustained eGFR decline, outpatient	23%	EMPEROR-Preserved and PARAGON-HF ^{4,5}
Sustained eGFR decline, inpatient	32%	
Kidney failure	45%	PARAGON-HF ⁴
Mortality Risk		
HF hospitalization (vs stable HF)	9.39	Carson et al 2015 ⁹
Composite renal endpoint	2.24	Löfman et al 2019 ¹⁰

*Sustained eGFR decline ≥40% from baseline over at least 30 days or kidney failure

Results

- Cumulative results over a lifetime and 10-year horizon are shown in Table 2
- From age 72, the average life expectancy in the modeled cohort is an additional 9.0 (undiscounted) or 7.5 (discounted) years
- Results of one-way sensitivity analysis indicate that estimated life expectancy was most sensitive to rates of non-cardiovascular and cardiovascular death, followed by mortality risk associated with HF hospitalization (Figure 3)

Table 2. Model Results

Outcome	Time Horizon	
	Lifetime	10 years
Cumulative HF hospitalizations per person	0.68	0.52
≥1 HF hospitalization, %	43%	37%
Cardiovascular death, %	34%	26%
Hyperkalemia events per person	0.26	0.20
Composite renal endpoint events per person	2.15	0.12

Figure 2A. HF Hospitalizations Over a Lifetime Horizon in Modeled Cohort

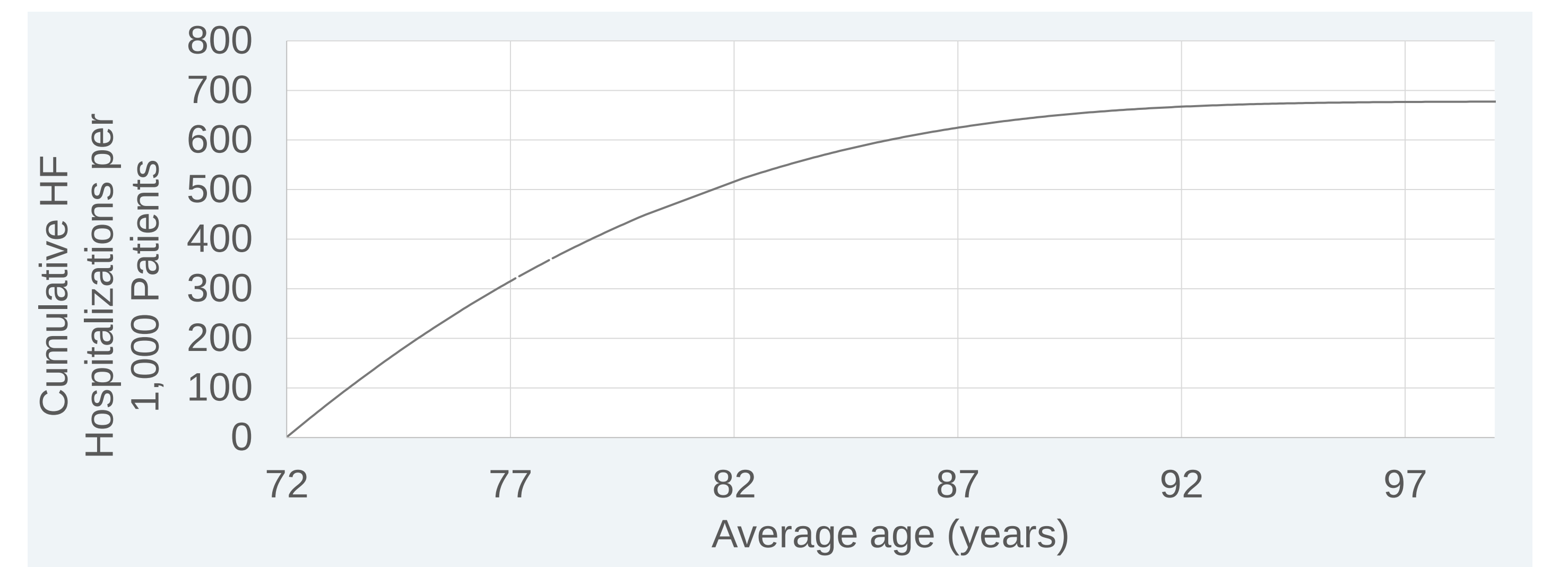


Figure 2B. Cardiovascular Deaths Over a Lifetime Horizon in Modeled Cohort

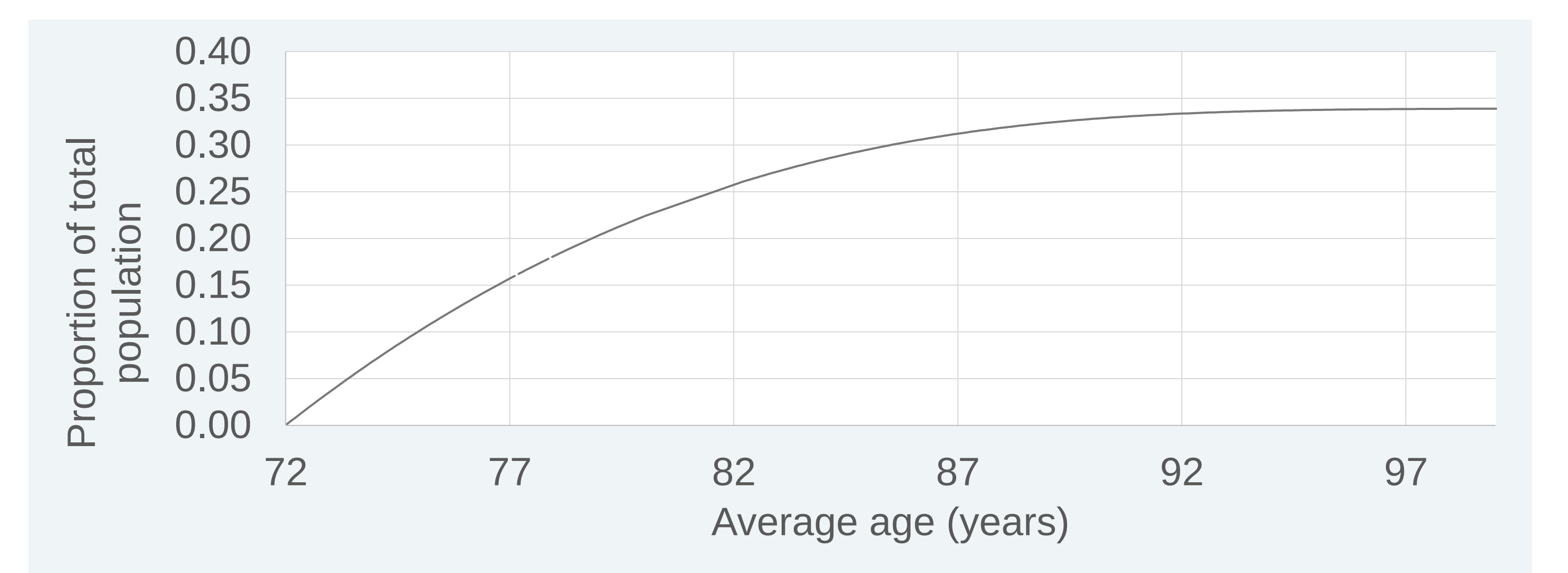
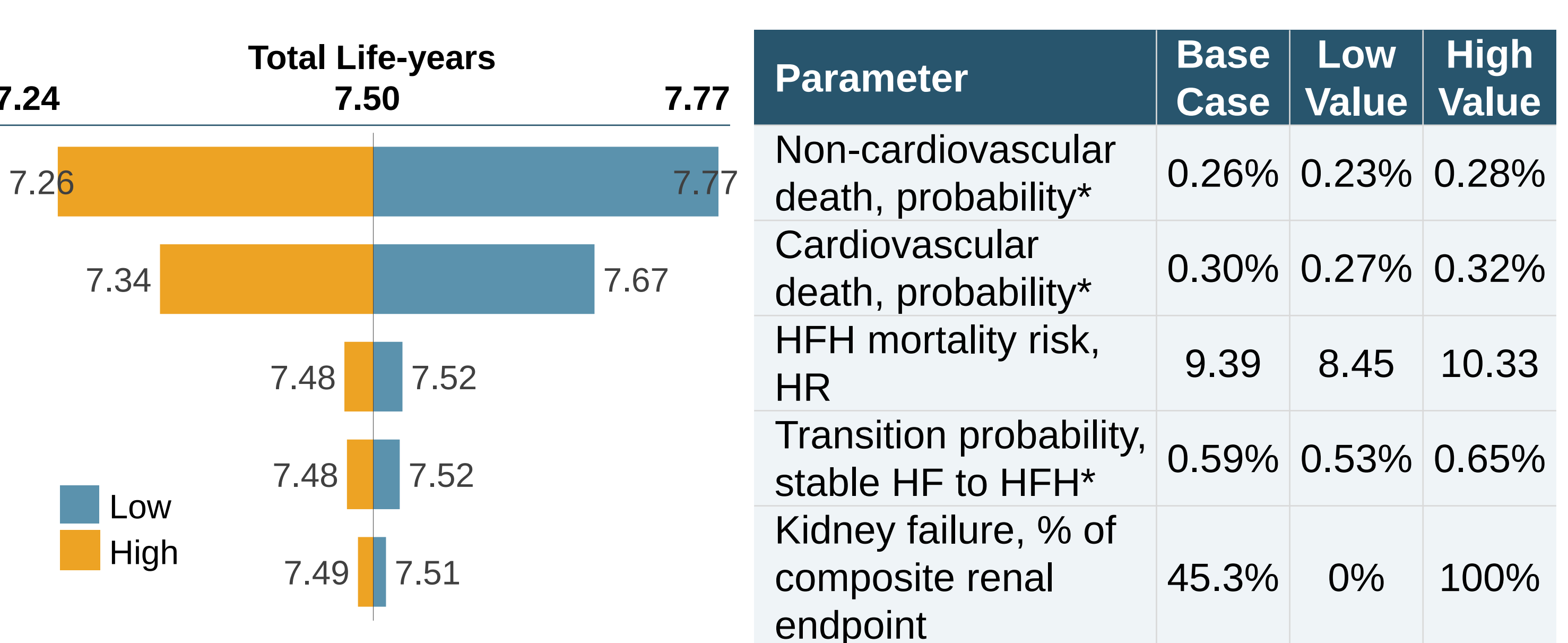


Figure 3. Tornado Diagram and One-Way Sensitivity Analysis Results



*All probabilities are per cycle (monthly)
HFH – heart failure hospitalization; HR – hazard ratio.

Conclusions

- Symptomatic HF with LVEF ≥40% is associated with high rates of HF hospitalization and risk of cardiovascular death
- Even with newer treatments in HFpEF/HFmrEF, there is still significant unmet clinical need
- Optimizing care and treatment may contribute to greater life expectancy and fewer adverse outcomes for patients with HFpEF/HFmrEF

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