

Supplementary Online Content

Gaziano TA, Fonarow GC, Claggett B, et al. Cost-effectiveness analysis of sacubitril/valsartan vs enalapril in US patients with heart failure and reduced ejection fraction. *JAMA Cardiol*. doi: 10.1001/jamacardio.2016.1747

eAppendix. Utility for the Cost Effectiveness Model

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Utility for the Cost Effectiveness Model

Utility for the cost-effectiveness model was based on EQ5D data from the PARADIGM-HF trial which was collected at baseline and then at 4,8,12,24 and 36 months after the baseline responses. In the EQ-5D, a score of 1 represents perfect health whereas a score of 0 represents death. The EQ-5D index requires responses to all five domains to be estimable; in the event of a missing response, the EQ-5D index will be assumed missing. Unless otherwise specified, missing data was assumed missing at random. In general, loss to follow-up was very low (20 patients out of 8,442 patients randomized) and the quantity of missing data was low. Subjects in countries for which translations of the EQ-5D questionnaire were not available did not complete the EQ-5D questionnaire, but this mechanism was considered missing at random and was not anticipated to lead to bias in the sacubitril/valsartan treatment effect size on EQ-5D. Below is a table with the availability of EQ-5D data throughout the trial.

Data availability on EQ-5D

Time point	Enalapril			LCZ696			p-value
	N	n	m	N	n	m	
At baseline	4,212	4,145	1.6%	4,187	4,126	1.5%	0.6269
4 months	4,125	3,898	5.5%	4,112	3,910	4.9%	0.2281
8 months	4,036	3,731	7.6%	4,041	3,775	6.6%	0.0858
12 months	3,913	3,570	8.8%	3,919	3,630	7.4%	0.0229
24 months	2,809	2,497	11.1%	2,886	2,586	10.4%	0.3871
36 months	1,384	1,209	12.6%	1,362	1,219	10.5%	0.0797

N: Number of individuals still in the study

n: Number of individuals with data on EQ-5D

m: Percentage of individuals who remain in the study and have missing data on EQ-5D

p-value: based on a test of proportions investigating whether the extent of missing data on EQ-5D differs between Enalapril and LCZ696

In order to determine the extent to which EQ-5D changes over time, a mixed-effects model was developed which considered the role of sacubitril/valsartan and other effects on EQ-5D over time. The final model used calculated utility as a function of treatment status baseline EQ-5D, hospitalization within the previous 30 days, baseline age, and time from start of trial. Coefficients are listed in the table below. Monthly utilities were then calculated and discounted at 3%.

	Coefficient	SE	z	P > z	95% LCI	95% UCI
Sacubitril/Valsartan	0.0084	0.0024	3.5300	0.0000	0.0037	0.0131
Baseline EQ-5D	0.5697	0.0078	73.2200	0.0000	0.5544	0.5849
Hospitalized within previous 30 days	-0.0771	0.0041	-18.9300	0.0000	-0.0851	-0.0691
Baseline age	-0.0011	0.0001	-10.1100	0.0000	-0.0013	-0.0009
Time (years)	-0.0057	0.0007	-8.7400	0.0000	-0.0070	-0.0044
Constant	0.8991	0.0070	128.0900	0.0000	0.8854	0.9129