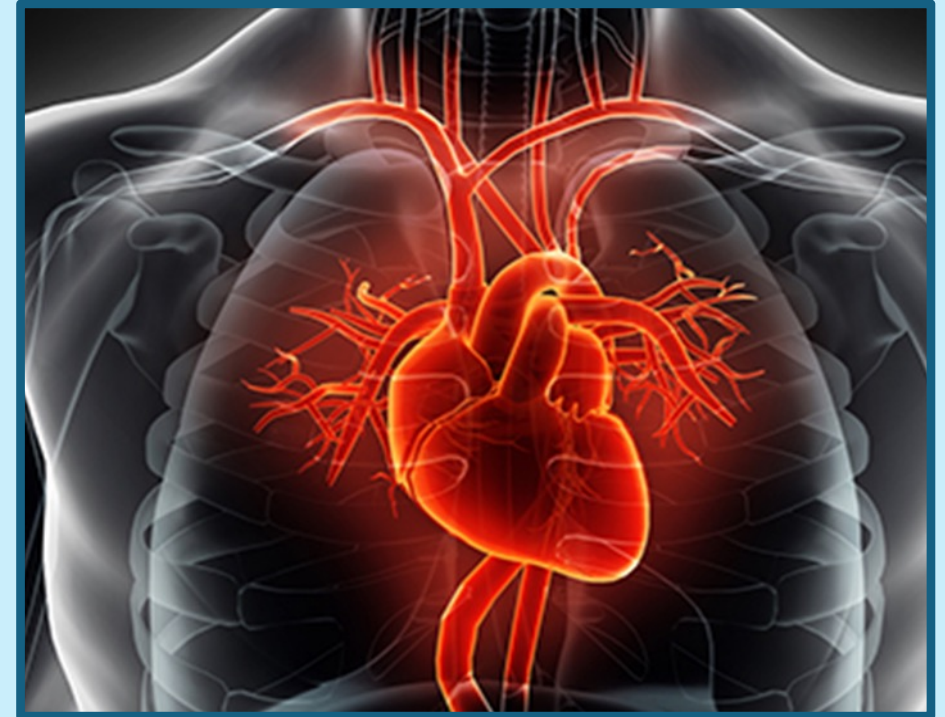


Advances in the treatment of severe heart failure

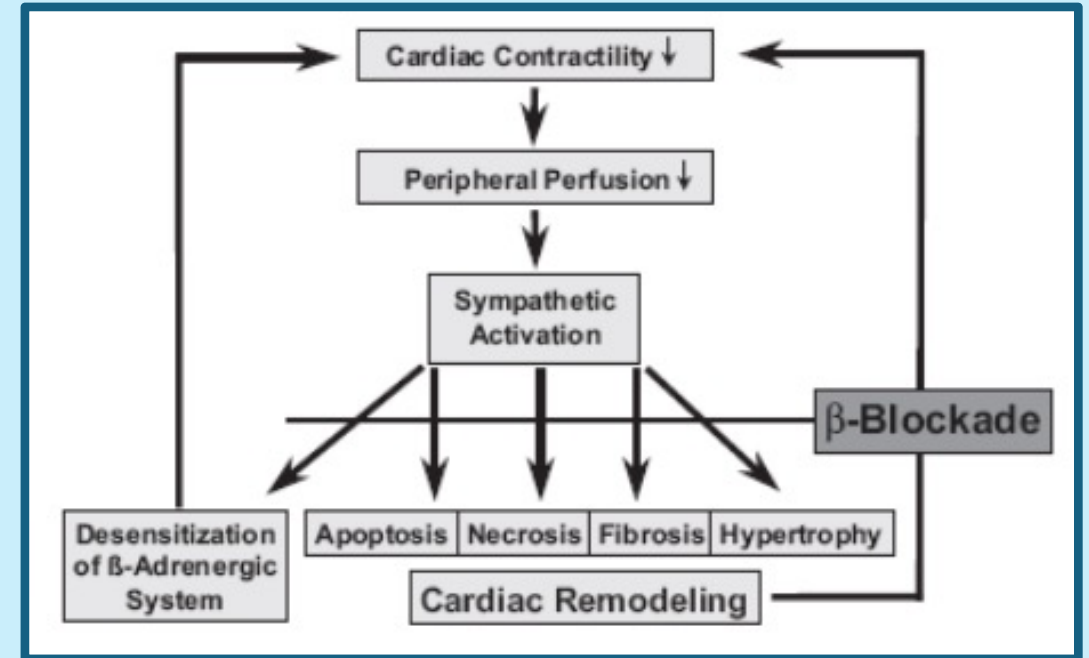
The burden of heart failure

- Greater than 6.7 million Americans are currently diagnosed with heart failure
 - The lifetime risk has now reached 1 in 4
- Mortality and morbidity is high and increasing
 - More than 425,000 deaths each year
 - Over 5 million people annually hospitalized
- Patients with heart failure suffer from a poor quality of life, with an average SF-36 score of only 33.3



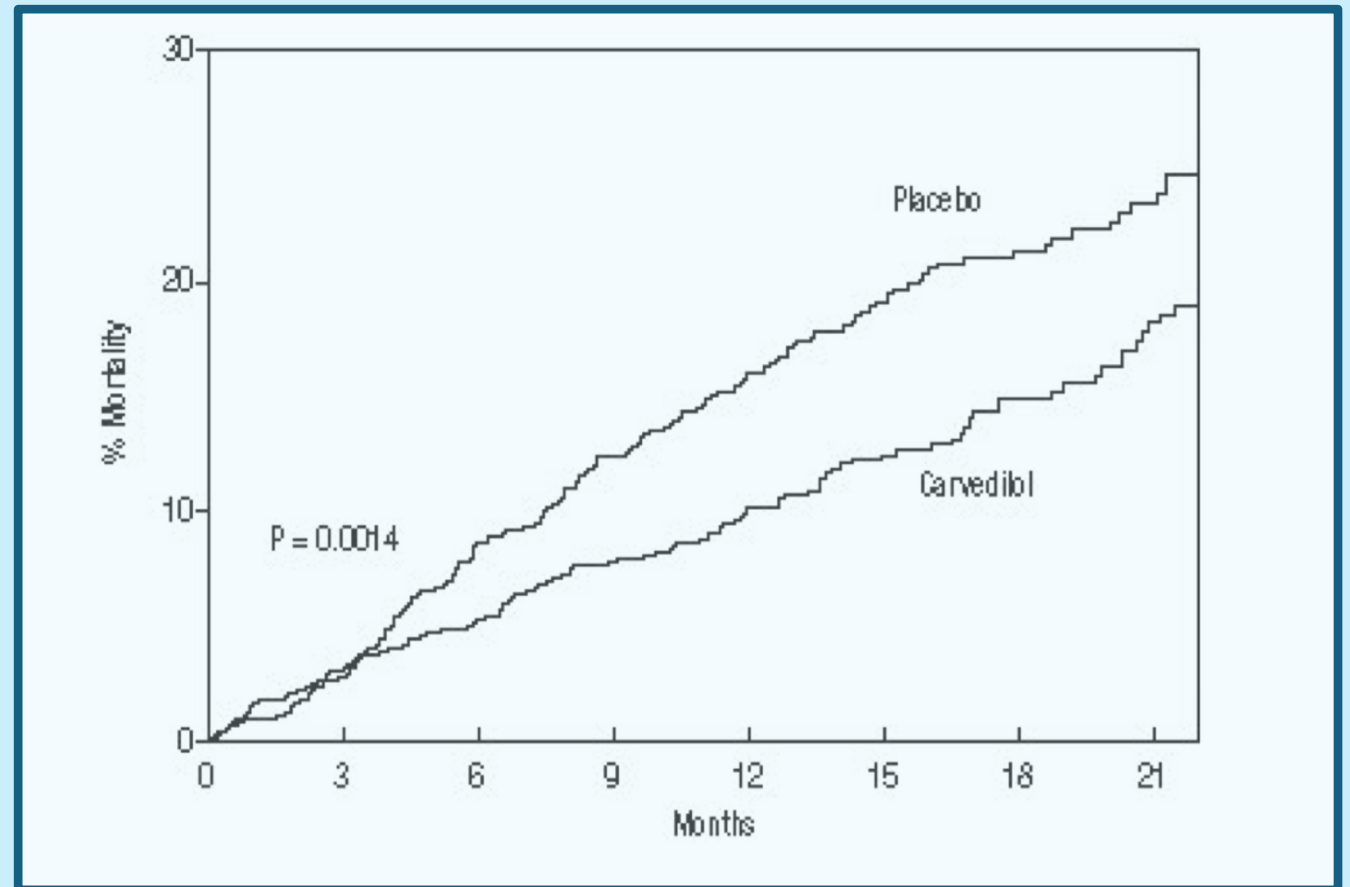
Carvedilol's unique mechanism of action

- Sympathetic activation results in cardiac myocyte injury in the failing human heart
- Beta-1, beta-2, and alpha-1 receptors are may be activated in the failing heart
- Carvedilol provides comprehensive adrenergic blockade by blocking beta-1, beta-2, and alpha-1 receptors



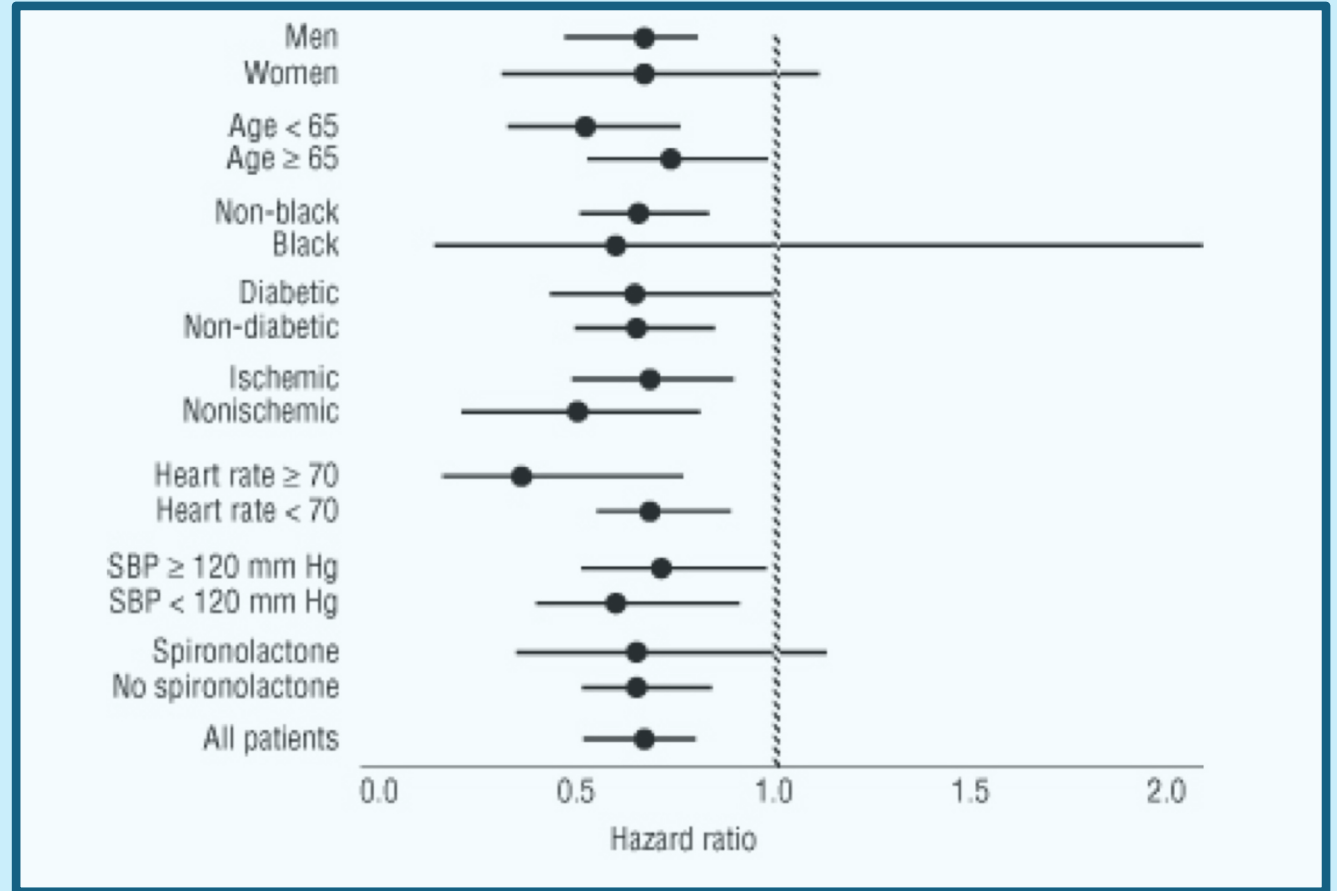
Severe heart failure: 35% reduction in mortality

- The trial was stopped early after a 35% reduction in all cause mortality
- For every 14 patients treated, 1 life was saved



Mortality reduction across subgroups

- Carvedilol had consistent effects across all subgroups examined
- Benefits were seen in both the highest and lowest risk groups



Adverse events >3% regardless of cause

- Carvedilol has been evaluated for safety in more than 4,500 subjects worldwide
- Discontinuation rates were similar between carvedilol and placebo

Body System/ Adverse Event	Mild-to-Moderate HF		Severe HF	
	COREG (n = 765)	Placebo (n = 437)	COREG (n = 1,156)	Placebo (n = 1,133)
Body as a Whole				
Asthenia	7	7	11	9
Fatigue	24	22	—	—
Digoxin level increased	5	4	2	1
Edema generalized	5	3	6	5
Edema dependent	4	2	—	—
Cardiovascular				
Bradycardia	9	1	10	3
Hypotension	9	3	14	8
Syncope	3	3	8	5
Angina pectoris	2	3	6	4
Central Nervous System				
Dizziness	32	19	24	17
Headache	8	7	5	3
Gastrointestinal				
Diarrhea	12	6	5	3
Nausea	9	5	4	3
Vomiting	6	4	1	2
Metabolic				
Hyperglycemia	12	8	5	3
Weight increase	10	7	12	11
BUN increased	6	5	—	—
NPN increased	6	5	—	—
Hypercholesterolemia	4	3	1	1
Edema peripheral	2	1	7	6

Carvedilol dosing for heart failure

- Start at 3.125 mg twice daily and increase to 6.25, 12.5, and then 25 mg twice daily over intervals of two weeks
- Maintain lower doses if higher doses are not tolerated

