

Figure 1 - Calculation of lifespan gain. The time to death can be estimated for any pair of patients, from first to die (top) to last to die (bottom). The incremental survival can be calculated as the horizontal distance between the two curves, which can be calculated until one curve stops (dotted arrow).

Trial	Year	Treatment	Inclusion Criteria			Deaths	n	Average Follow-Up (months)	Centiles Compared	Max. Placebo Lifespan (months)	Medication Usage		
			EF	NYHA	Other						ACEi/ARB	BB (%)	AA
ACE Inhibitors													
CONSENSUS		Effects of enalapril on mortality in severe congestive heart failure. Results of the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS). The CONSENSUS Trial Study Group. <i>N. Engl. J. Med.</i> 1987;316(23):1429-1435.	Enalapril	Radiological	IV	118	253	6	46.5	5.2		3	53
SOLVD		Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. The SOLVD Investigators. <i>N. Engl. J. Med.</i> 1991;325(5):293-302.	Enalapril	<35		962	2569	41	36	36.8		8	9
AIRE		Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. The Acute Infarction Ramipril Efficacy (AIRE) Study Investigators. <i>Lancet</i> 1993;342(8875):821-828.	Ramipril		MI	392	1986	15	24	18.6		22	
										Weighted mean		14	13
Beta Blockers													
Anderson <i>et al.</i>		Anderson JL, Lutz JR, Gilbert EM, <i>et al.</i> A randomized trial of low-dose beta-blockade therapy for idiopathic dilated cardiomyopathy. <i>Am. J. Cardiol.</i> 1985;55(4):471-475.	Metoprolol	<40	DCM	9	50	19	17.5	14.8			
CIBIS		A randomized trial of beta-blockade in heart failure. The Cardiac Insufficiency Bisoprolol Study (CIBIS). CIBIS Investigators and Committees. <i>Circulation</i> 1994;90(4):1765-1773.	Bisoprolol	<40	III/IV	120	641	23	28.5	32	90		0
MOCHA		Bristow MR, Gilbert EM, Abraham WT, <i>et al.</i> Carvedilol produces dose-related improvements in left ventricular function and survival in subjects with chronic heart failure. MOCHA Investigators. <i>Circulation</i> 1996;94(11):2807-2816.	Carvedilol	<35		25	345	6	7.5	4.1	94		
US Carvedilol HF Study Group		Packer M, Bristow MR, Cohn JN, <i>et al.</i> The effect of carvedilol on morbidity and mortality in patients with chronic heart failure. U.S. Carvedilol Heart Failure Study Group. <i>N. Engl. J. Med.</i> 1996;334(21):1349-1355.	Carvedilol	<35		53	1094	7	4.25	4.2	95		
Herlitz <i>et al.</i>		Herlitz J, Waagstein F, Lindqvist J, Swedberg K, Hjalmarson A. Effect of metoprolol on the prognosis for patients with suspected acute myocardial infarction and indirect signs of congestive heart failure (a subgroup analysis of the Göteborg Metoprolol Trial). <i>Am. J. Cardiol.</i> 1997;80(9B):40J-44J.	Metoprolol		MI	29	262	3	12.5	1.3			
CIBIS II		The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): a randomised trial. <i>Lancet</i> 1999;353(9146):9-13.	Bisoprolol	<35	III/IV	384	2647	16	17.5	16.2	96		
MERIT-HF		Effect of metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure (MERIT-HF). <i>Lancet</i> 1999;353(9169):2001-2007.	Metoprolol	<40	II-IV	362	3991	12	10.75	13	96		
CAPRICORN		Dargie HJ. Effect of carvedilol on outcome after myocardial infarction in patients with left-ventricular dysfunction: the CAPRICORN randomised trial. <i>Lancet</i> 2001;357(9266):1385-1390.	Carvedilol	<40	Recent MI	267	1959	16	15	15.9	98		
COPERNICUS		Packer M, Coats AJ, Fowler MB, <i>et al.</i> Effect of carvedilol on survival in severe chronic heart failure. <i>N. Engl. J. Med.</i> 2001;344(22):1651-1658.	Carvedilol	<25		320	2289	10	20.75	14.2	97		
SENIORS		Flather MD, Shibata MC, Coats AJS, <i>et al.</i> Randomized trial to determine the effect of nebivolol on mortality and cardiovascular hospital admission in elderly patients with heart failure (SENIORS). <i>Eur. Heart J.</i> 2005;26(3):215-225.	Nebivolol	<35 if no HF		361	2128	21	20	24.8	89		
										Weighted mean	95		0
Aldosterone Antagonists													
RALES		Pitt B, Zannad F, Remme WJ, <i>et al.</i> The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. <i>N. Engl. J. Med.</i> 1999;341(10):709-717.	Spironolactone	<35	III/IV	670	1663	24	39	22.9	94	10	
EPHESUS		Pitt B, Remme W, Zannad F, <i>et al.</i> Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. <i>N. Engl. J. Med.</i> 2003;348(14):1309-1321.	Eplerenone	<40	Recent MI	1032	6632	16	18.5	21.3	87	75	
EMPHASIS-HF		Zannad F, McMurray JJV, Krum H, <i>et al.</i> Eplerenone in patients with systolic heart failure and mild symptoms. <i>N. Engl. J. Med.</i> 2011;364(1):11-21.	Eplerenone	<35	II	384	2737	21	19	30	93	87	
										Weighted mean	90	65	

Table I - Studies included in this analysis.

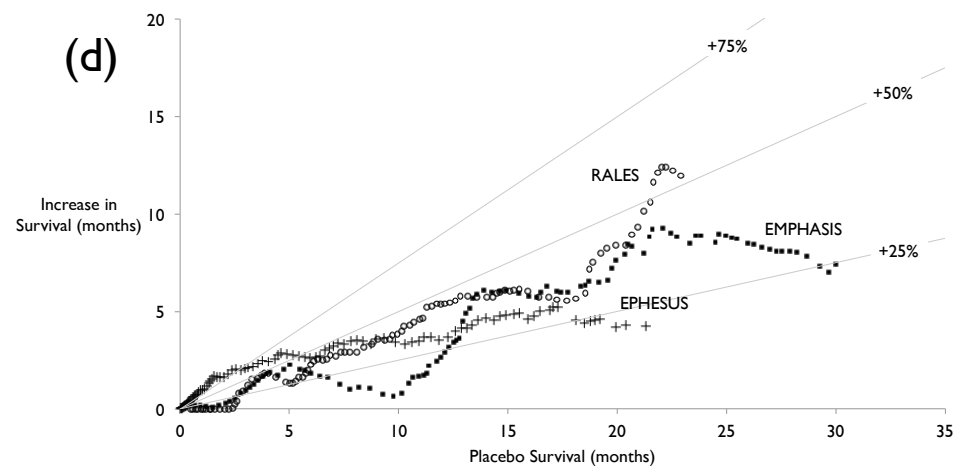
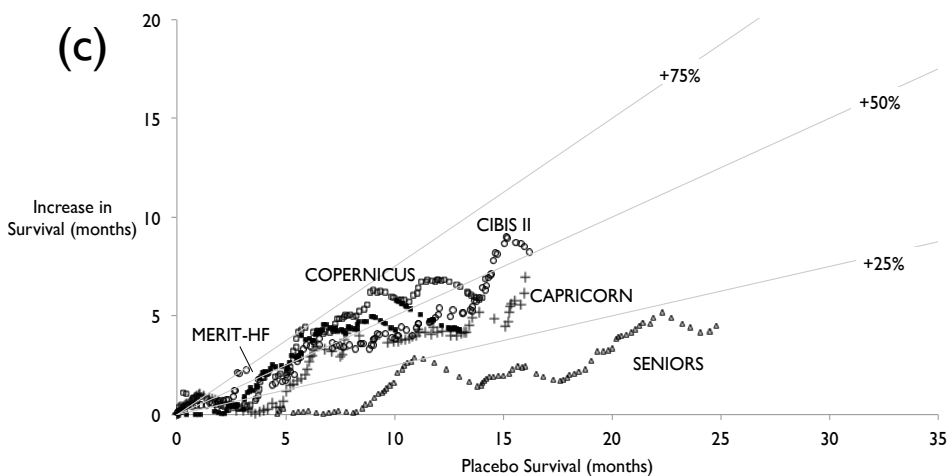
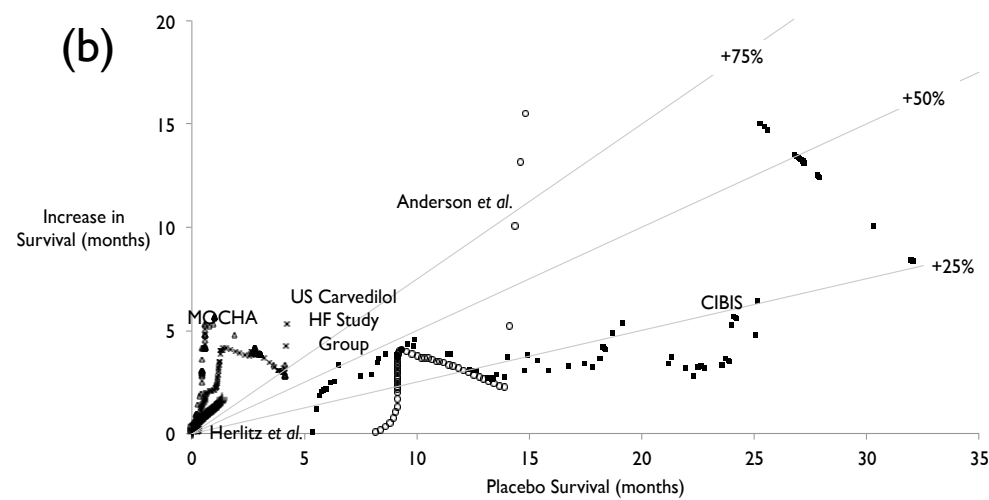
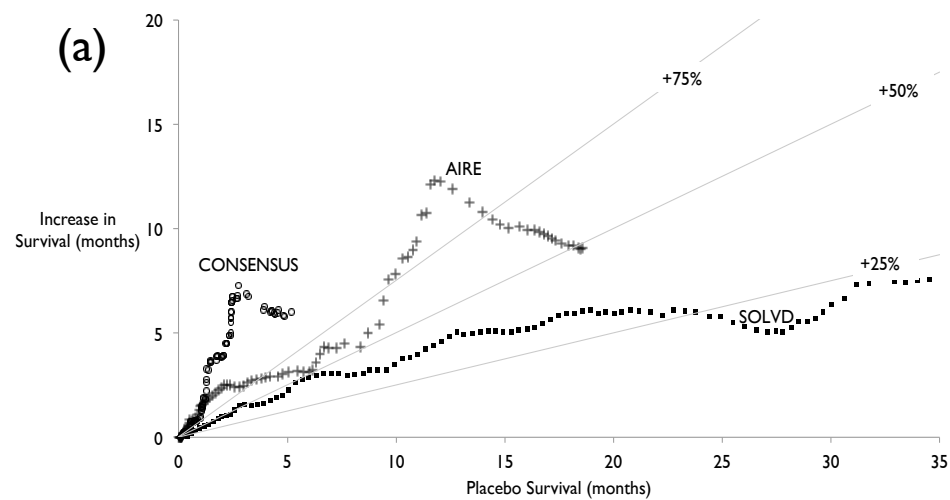


Figure 2 – Survival benefit at different durations of placebo survival. Survival benefit from (a) ACE inhibitors (b) beta-blockers – small trials (<120 deaths) (c) beta-blockers – large trials (>120 deaths) and (d) aldosterone antagonists.