

Cost effectiveness of Optimal Medical Therapy in Heart Failure with Reduced Ejection Fraction

APPENDIX II: supplementary results

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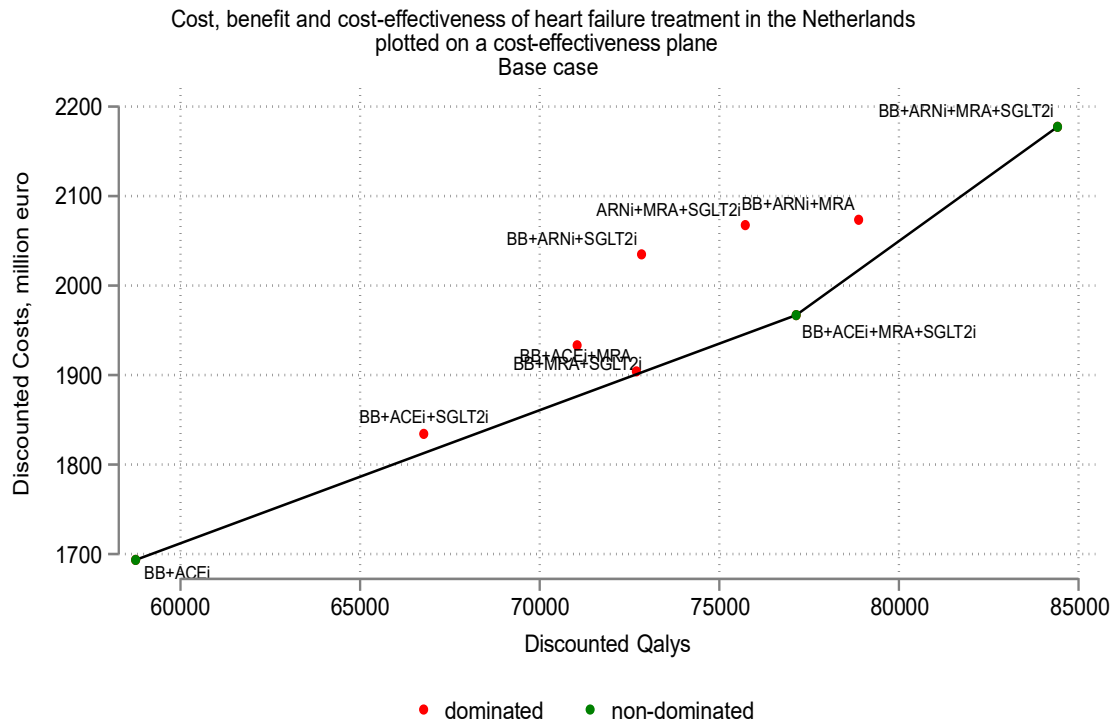
1. Introduction

This appendix contains supplementary results. Section 2 compares extrapolation methodologies for (the effect of) transition probabilities (see Appendix I for the methodology underlying these results). Section 3 presents subgroup analyses, while section 4 presents details for the sensitivity analyses, some of which are summarized in the main report in the form of tornado diagrams. The general conclusion across all supplemental results is that quadruple therapy with an ARNi remains costs effective at a threshold value of €50.000 (and in most cases also at a threshold value of €30.000).

2. Comparison of different extrapolation methodologies

Base case

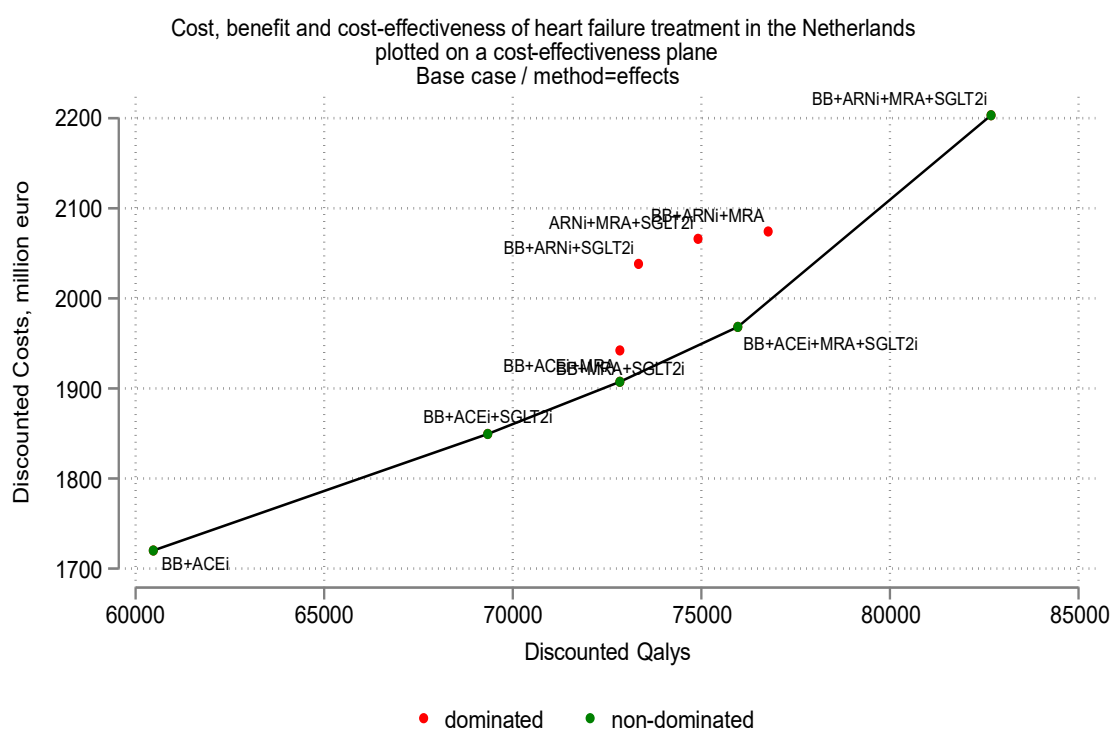
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 € / QALY gained)	ICER(1000 € / QALY gained)
BB+ARNi+MRA+SGLT2i	2177	84.4	18.8	28.9
BB+ARNi+MRA	2074	78.9	61.3	.
BB+ACEi+MRA+SGLT2i	1967	77.1	-71.0	14.9
ARNi+MRA+SGLT2i	2068	75.7	11.3	.
BB+ARNi+SGLT2i	2035	72.8	907.6	.
BB+ACEi+MRA	1904	72.7	-17.7	.
BB+MRA+SGLT2i	1933	71.0	23.2	.
BB+ACEi+SGLT2i	1834	66.8	17.6	.
BB+ACEi	1693	58.8	.	.



A cohort of 10,000 Dutch heart failure patients were simulated lifelong.
ACEi: ACE-inhibitor; ARB: angiotensin-II-receptor antagonist BB: betablocker;
MRA: mineralocorticoid receptor antagonist ARNi: angiotensin receptor-neprilysin inhibitor

Base case / method=effects

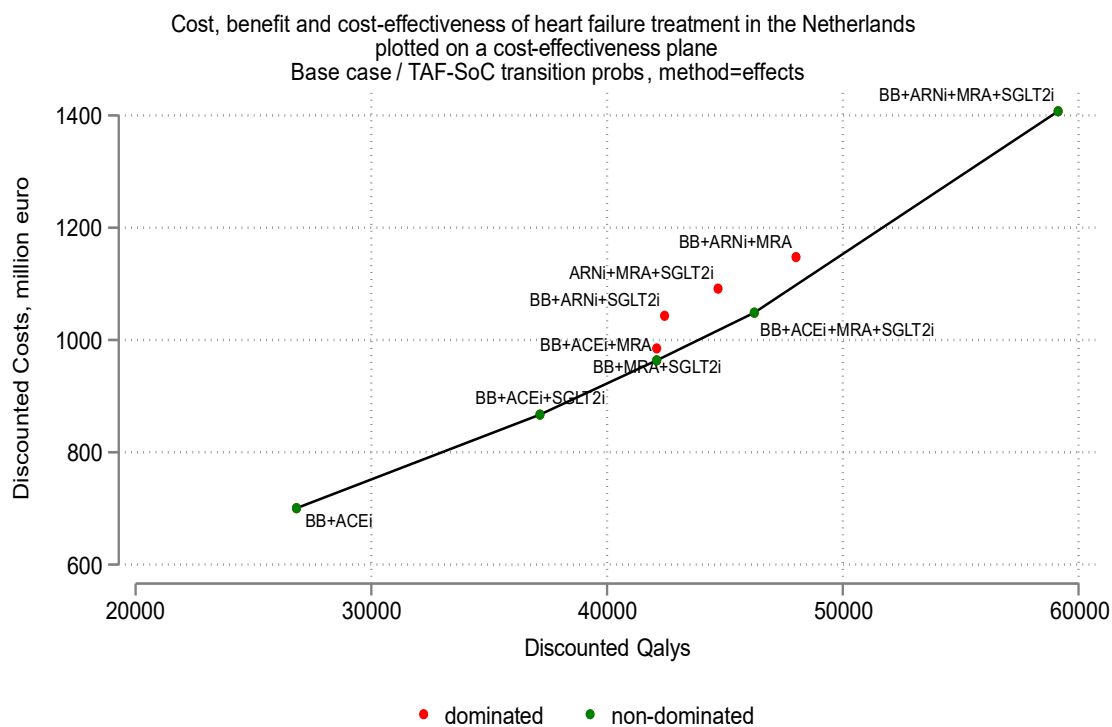
Costs, Qalys, CERs and ICERs				
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	2203	82.7	21.8	35.0
BB+ARNi+MRA	2074	76.8	131.5	.
BB+ACEi+MRA+SGLT2i	1968	76.0	-92.7	19.5
ARNi+MRA+SGLT2i	2066	74.9	17.7	.
BB+ARNi+SGLT2i	2038	73.3	194.0	.
BB+ACEi+MRA	1907	72.8	16.5	16.5
BB+MRA+SGLT2i	1942	72.8	.	.
BB+ACEi+SGLT2i	1849	69.3	14.6	14.6
BB+ACEi	1720	60.5	.	.



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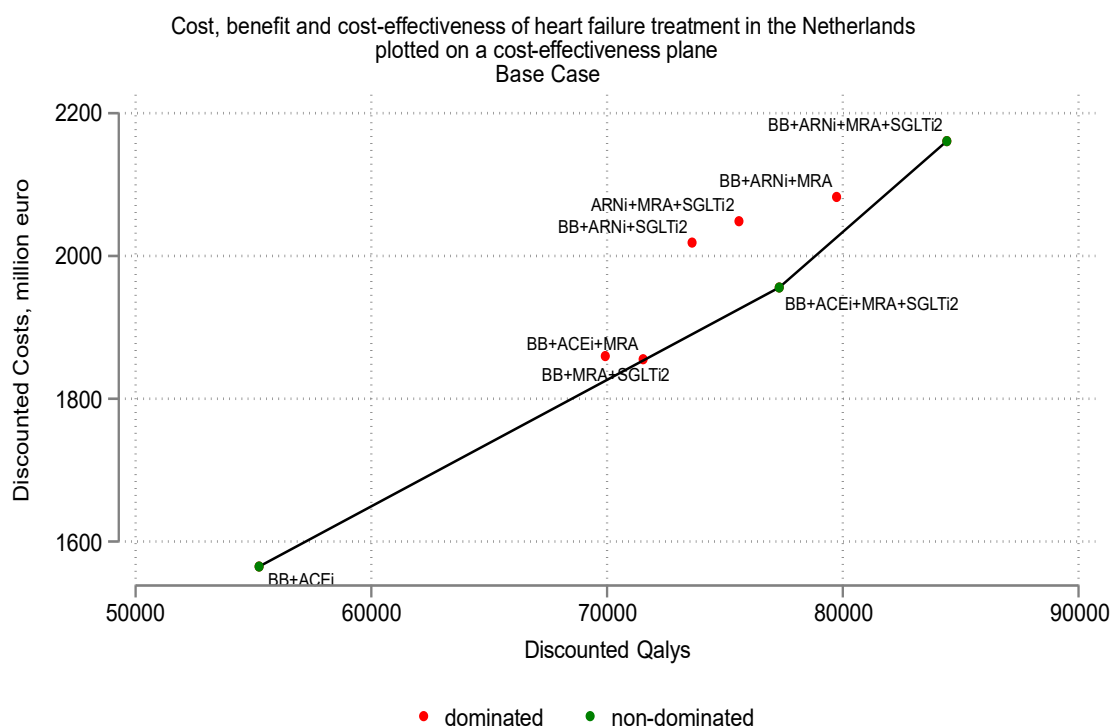
Base case / TAF-SoC transition probs, method=effects

Costs, Qalys, CERs and ICERs				
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	1407	59.1	23.4	27.8
BB+ARNi+MRA	1148	48.0	56.1	.
BB+ACEi+MRA+SGLT2i	1049	46.2	-27.8	20.5
ARNi+MRA+SGLT2i	1091	44.7	21.3	.
BB+ARNi+SGLT2i	1043	42.4	173.2	.
BB+MRA+SGLT2i	985	42.1	.	.
BB+ACEi+MRA	964	42.1	19.5	19.5
BB+ACEi+SGLT2i	867	37.2	16.1	16.1
BB+ACEi	700	26.8	.	.



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Costs, Qalys, CERs and ICERs				
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2	2161	84.4	16.7	28.8
BB+ARNi+MRA	2083	79.7	52.1	.
BB+ACEi+MRA+SGLT2	1956	77.3	-54.3	17.7
ARNi+MRA+SGLT2	2049	75.6	15.1	.
BB+ARNi+SGLT2	2019	73.6	78.7	.
BB+ACEi+MRA	1855	71.5	-2.8	.
BB+MRA+SGLT2	1860	69.9	20.1	.
BB+ACEi	1565	55.2	.	.

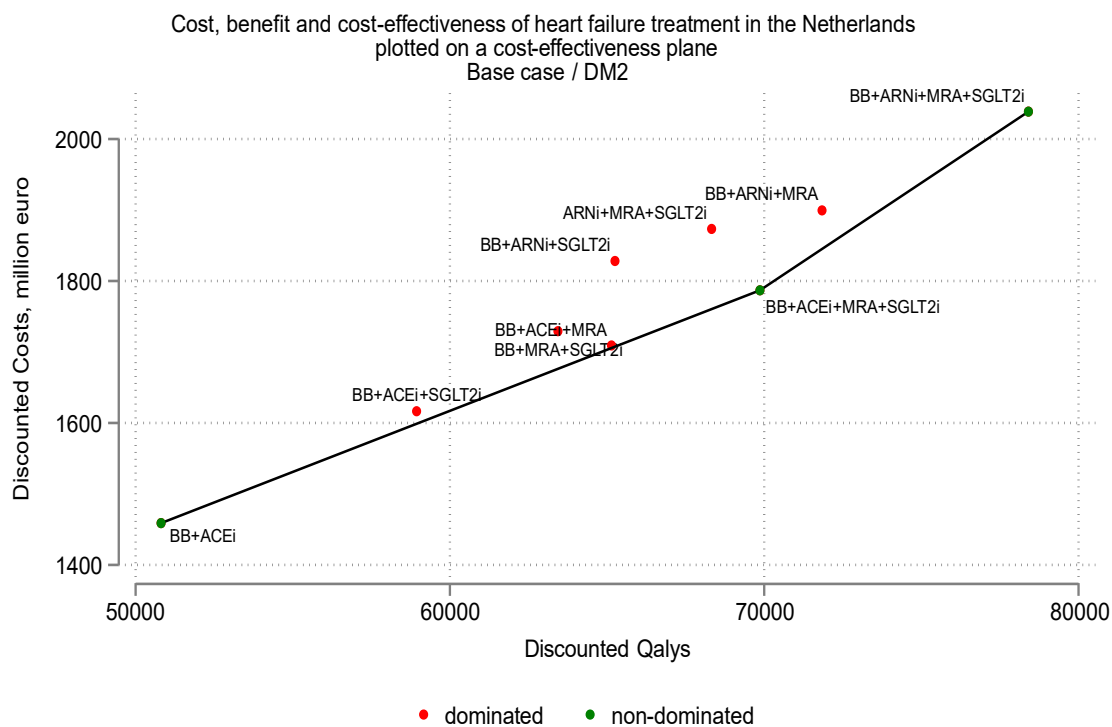


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Subgroup analyses

Base case / DM2

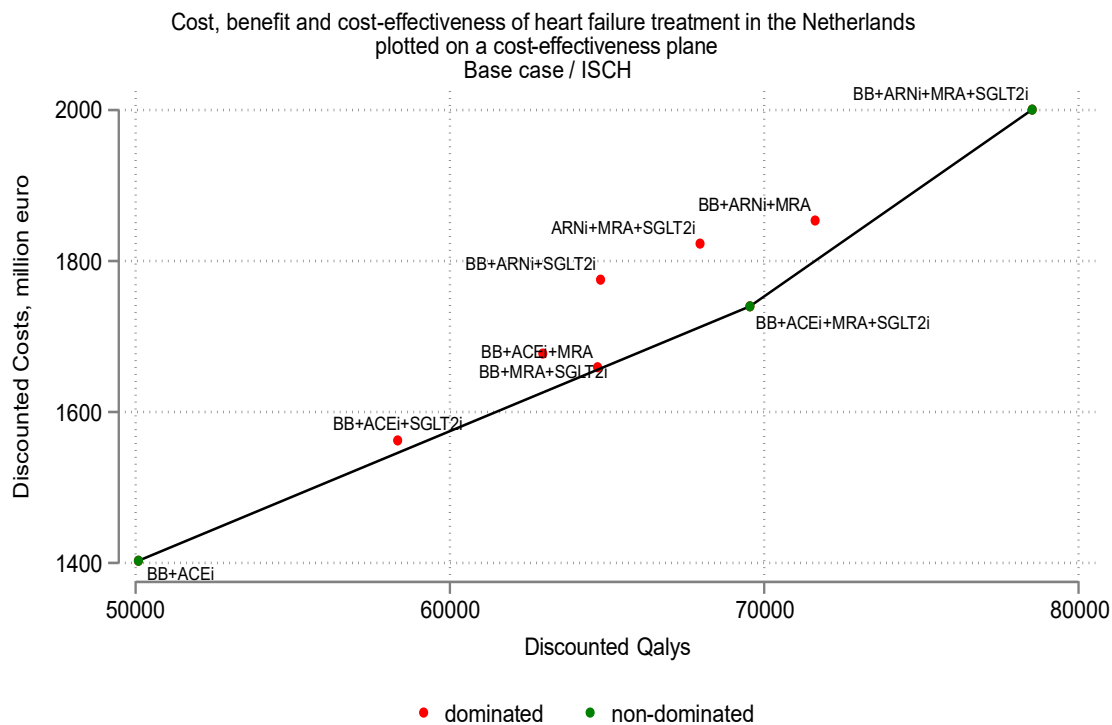
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	2039	78.4	21.2	29.5
BB+ARNi+MRA	1899	71.8	57.0	.
BB+ACEi+MRA+SGLT2i	1787	69.9	-56.3	17.2
ARNi+MRA+SGLT2i	1873	68.3	14.7	.
BB+ARNi+SGLT2i	1828	65.3	1062.4	.
BB+ACEi+MRA	1709	65.1	-11.8	.
BB+MRA+SGLT2i	1729	63.4	25.1	.
BB+ACEi+SGLT2i	1617	58.9	19.4	.
BB+ACEi	1459	50.8	.	.



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Base case / ISCH

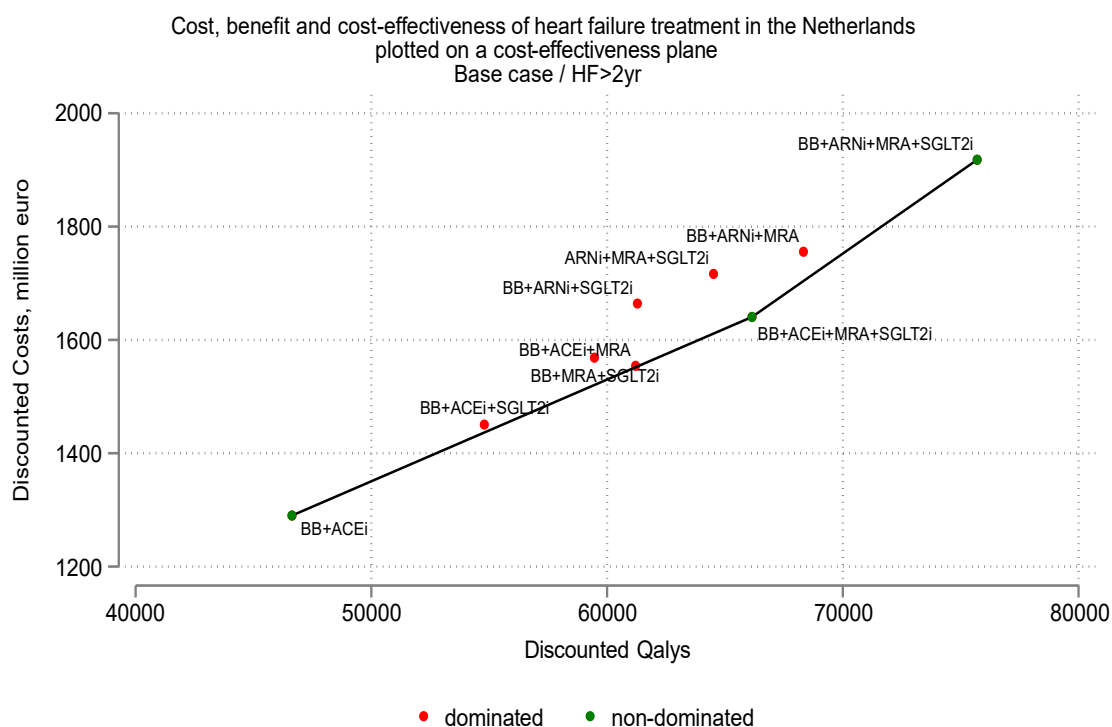
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	2001	78.5	21.3	29.0
BB+ARNi+MRA	1854	71.6	54.8	.
BB+ACEi+MRA+SGLT2i	1740	69.5	-52.3	17.3
ARNi+MRA+SGLT2i	1823	68.0	15.1	.
BB+ARNi+SGLT2i	1775	64.8	1216.2	.
BB+ACEi+MRA	1659	64.7	-10.4	.
BB+MRA+SGLT2i	1677	63.0	24.9	.
BB+ACEi+SGLT2i	1562	58.3	19.3	.
BB+ACEi	1403	50.1	.	.



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Base case / HF>2yr

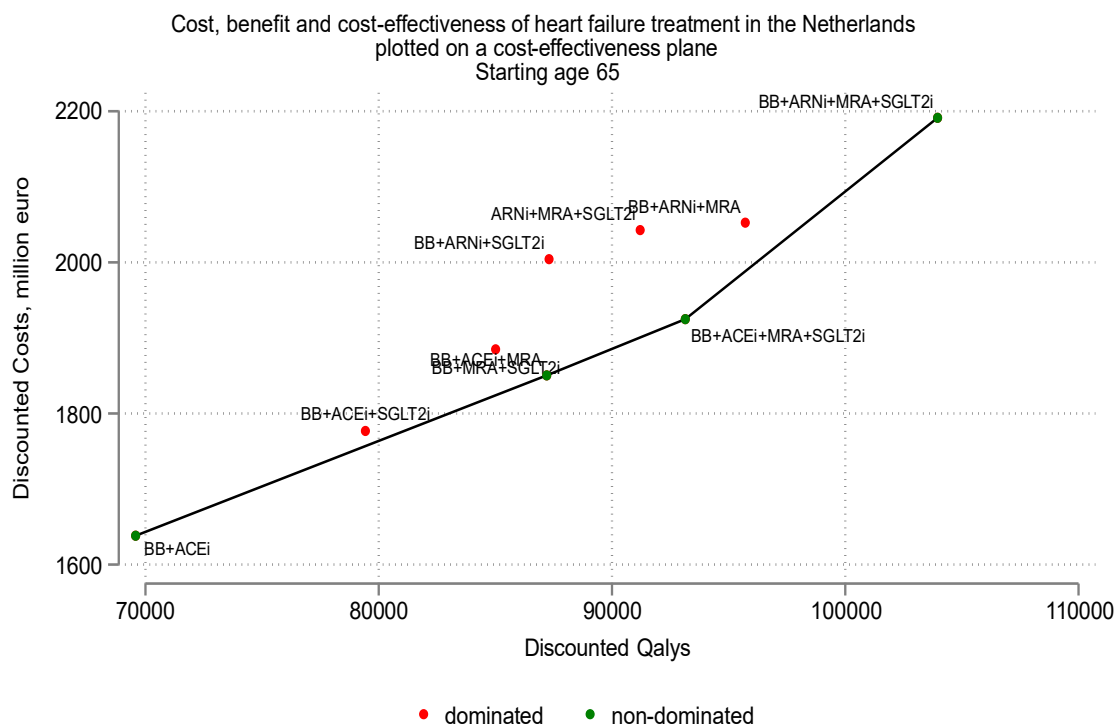
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 € /QALY gained)	ICER(1000 € /QALY gained)
BB+ARNi+MRA+SGLT2i	1918	75.7	22.0	29.0
BB+ARNi+MRA	1756	68.3	52.8	.
BB+ACEi+MRA+SGLT2i	1640	66.1	-46.5	18.0
ARNi+MRA+SGLT2i	1716	64.5	16.2	.
BB+ARNi+SGLT2i	1664	61.3	1464.2	.
BB+ACEi+MRA	1554	61.2	-8.2	.
BB+MRA+SGLT2i	1569	59.5	25.3	.
BB+ACEi+SGLT2i	1451	54.8	19.7	.
BB+ACEi	1290	46.6	.	.



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Starting age 65

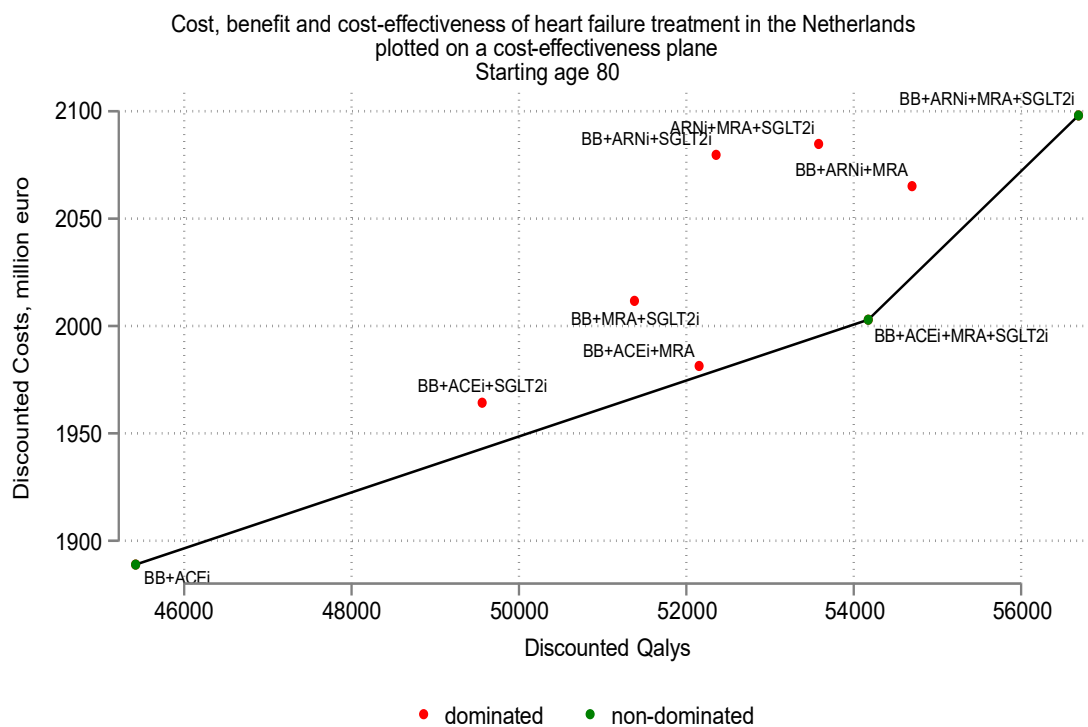
Treatment Combination	Discounted costs, €mIn	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	2191	104.0	16.8	24.6
BB+ARNi+MRA	2053	95.7	49.7	.
BB+ACEi+MRA+SGLT2i	1925	93.1	-60.9	12.5
ARNi+MRA+SGLT2i	2043	91.2	9.9	.
BB+ARNi+SGLT2i	2004	87.3	1537.3	.
BB+ACEi+MRA	1850	87.2	-15.7	12.0
BB+MRA+SGLT2i	1885	85.0	19.4	.
BB+ACEi+SGLT2i	1777	79.4	14.1	.
BB+ACEi	1638	69.6	.	.



A cohort of 10,000 Dutch heart failure patients were simulated lifelong.
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Starting age 80

Costs, Qalys, CERs and ICERs				
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	2098	56.7	16.6	37.9
BB+ARNi+MRA	2065	54.7	118.9	.
BB+ACEi+MRA+SGLT2i	2003	54.2	-138.0	13.0
ARNi+MRA+SGLT2i	2085	53.6	4.2	.
BB+ARNi+SGLT2i	2080	52.4	484.0	.
BB+ACEi+MRA	1981	52.2	-39.2	.
BB+MRA+SGLT2i	2012	51.4	26.1	.
BB+ACEi+SGLT2i	1964	49.6	18.2	.
BB+ACEi	1889	45.4	.	.

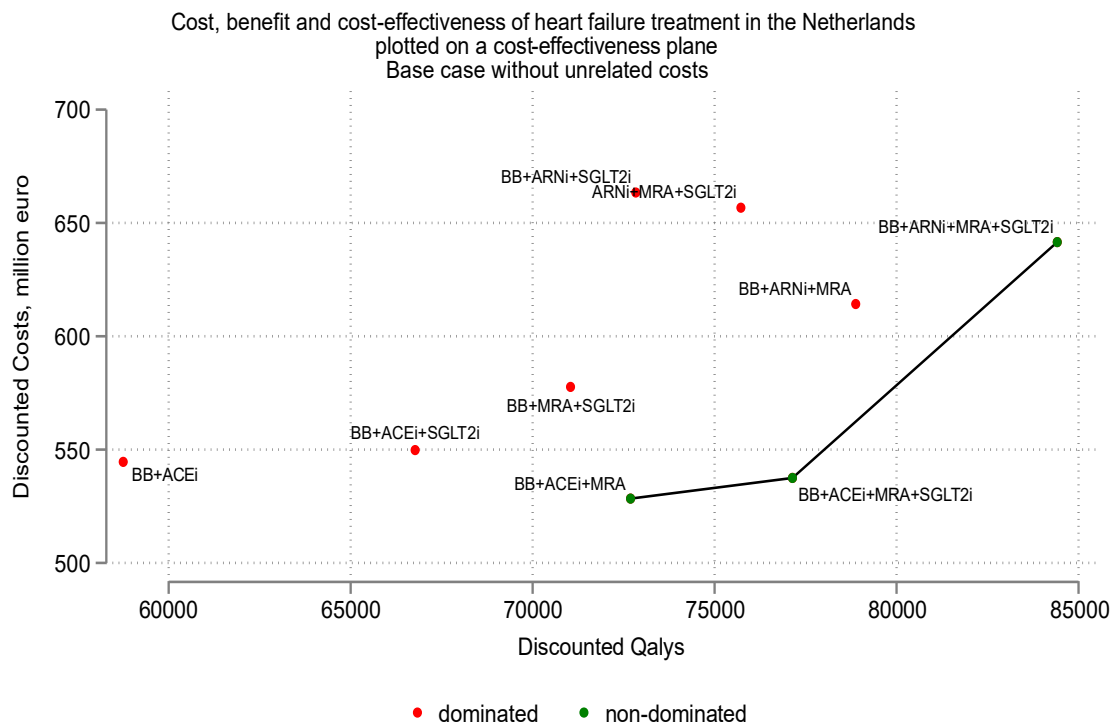


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Sensitivity analyses

Base case without unrelated costs

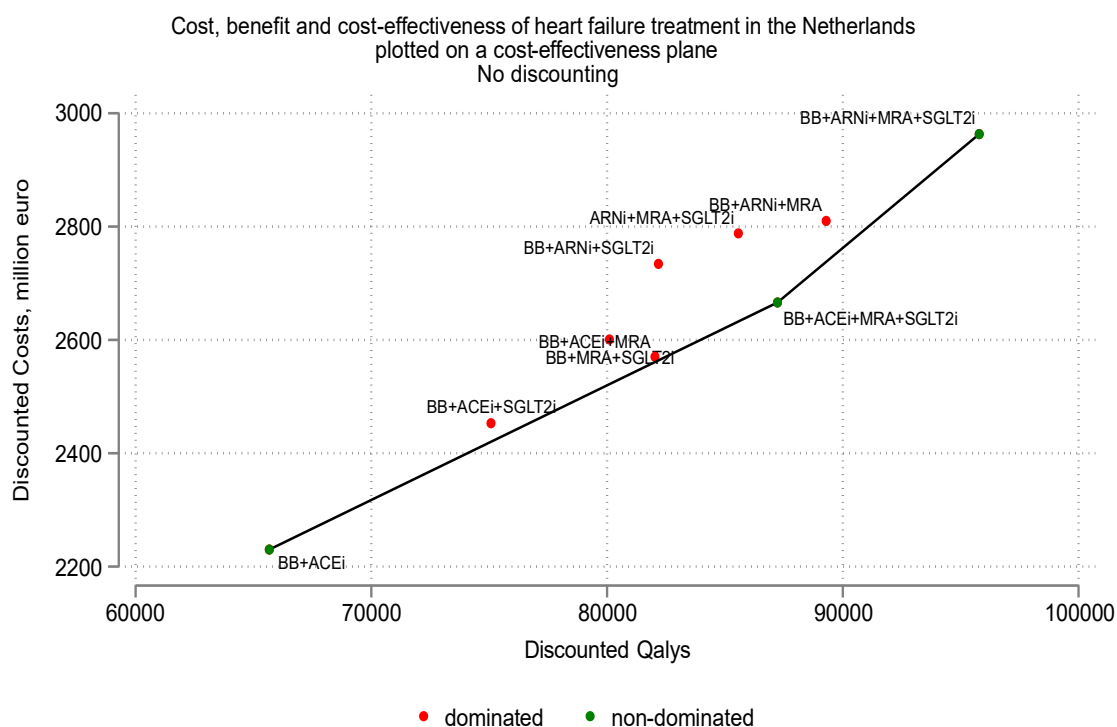
Costs, Qalys, CERs and ICERs				
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	642	84.4	4.9	14.3
BB+ARNi+MRA	614	78.9	44.1	.
BB+ACEi+MRA+SGLT2i	538	77.1	-84.1	2.1
ARNi+MRA+SGLT2i	657	75.7	-2.3	.
BB+ARNi+SGLT2i	663	72.8	937.0	.
BB+ACEi+MRA	528	72.7	-29.9	-1.2
BB+MRA+SGLT2i	578	71.0	6.5	.
BB+ACEi+SGLT2i	550	66.8	0.6	.
BB+ACEi	545	58.8	.	.



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No discounting

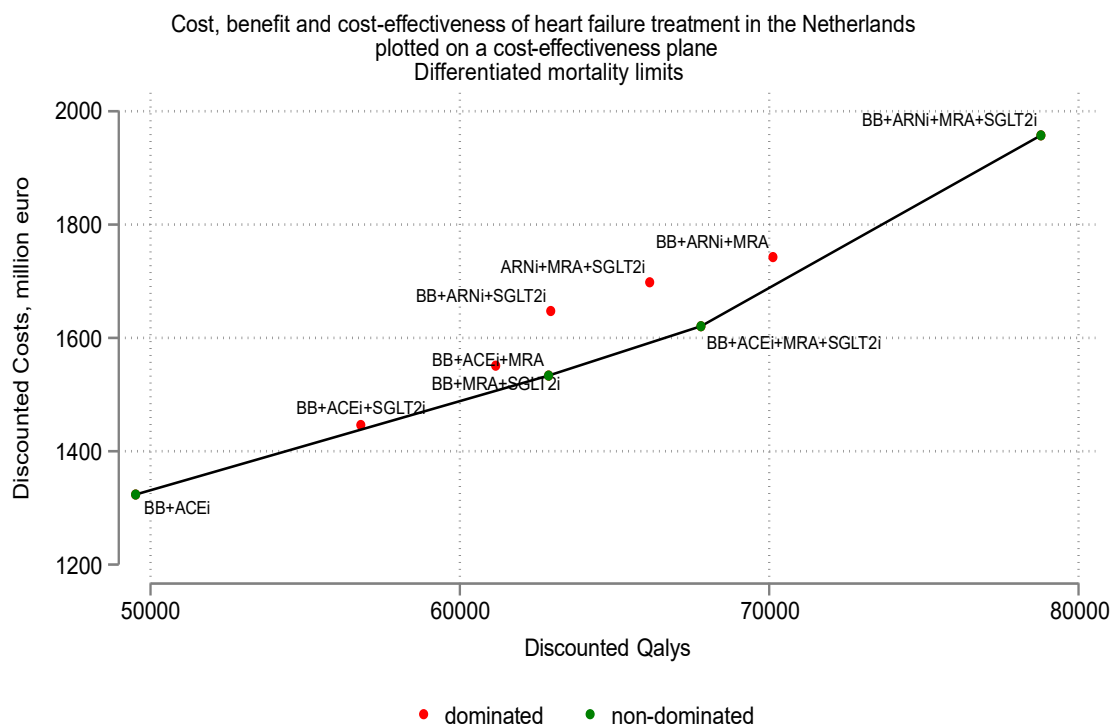
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	2963	95.8	23.6	34.7
BB+ARNi+MRA	2810	89.3	69.7	.
BB+ACEi+MRA+SGLT2i	2666	87.2	-73.4	20.2
ARNi+MRA+SGLT2i	2788	85.6	15.9	.
BB+ARNi+SGLT2i	2734	82.2	1111.2	.
BB+ACEi+MRA	2570	82.0	-15.8	.
BB+MRA+SGLT2i	2601	80.1	29.4	.
BB+ACEi+SGLT2i	2453	75.1	23.7	.
BB+ACEi	2230	65.7	.	.



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Differentiated mortality limits

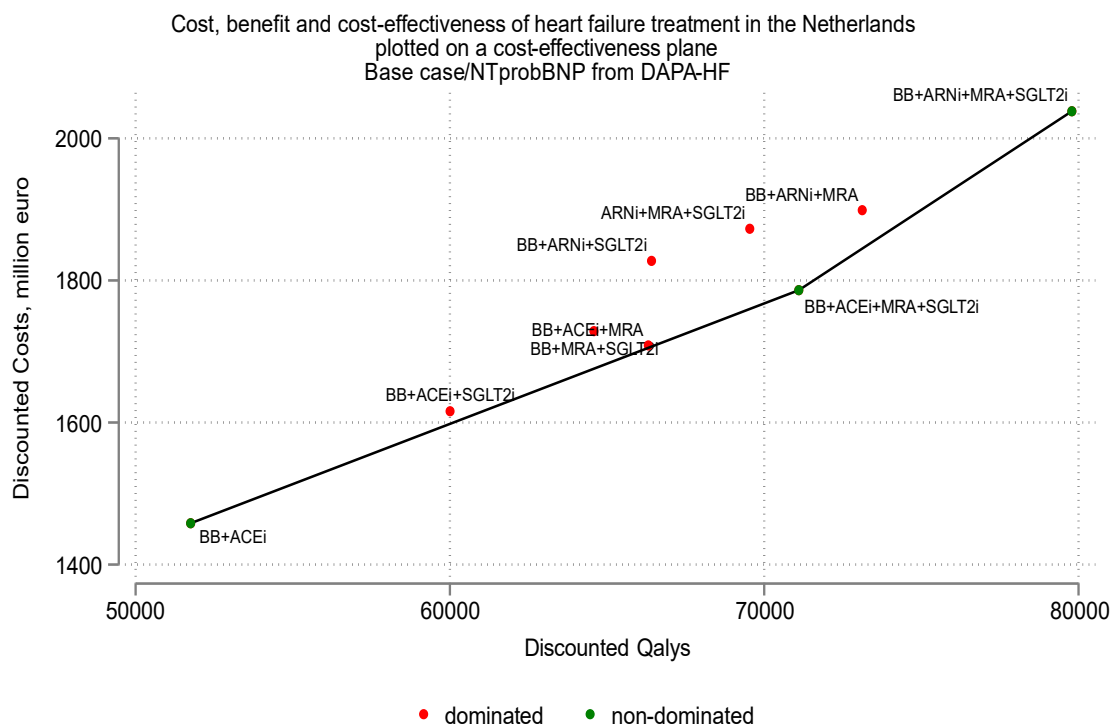
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	1957	78.8	24.8	30.7
BB+ARNi+MRA	1743	70.1	52.5	.
BB+ACEi+MRA+SGLT2i	1621	67.8	-46.8	17.7
ARNi+MRA+SGLT2i	1698	66.1	15.8	.
BB+ARNi+SGLT2i	1647	62.9	1653.0	.
BB+ACEi+MRA	1534	62.9	-10.2	15.7
BB+MRA+SGLT2i	1551	61.2	24.0	.
BB+ACEi+SGLT2i	1446	56.8	16.8	.
BB+ACEi	1324	49.5	.	.



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Base case/NTprobBNP from DAPA-HF

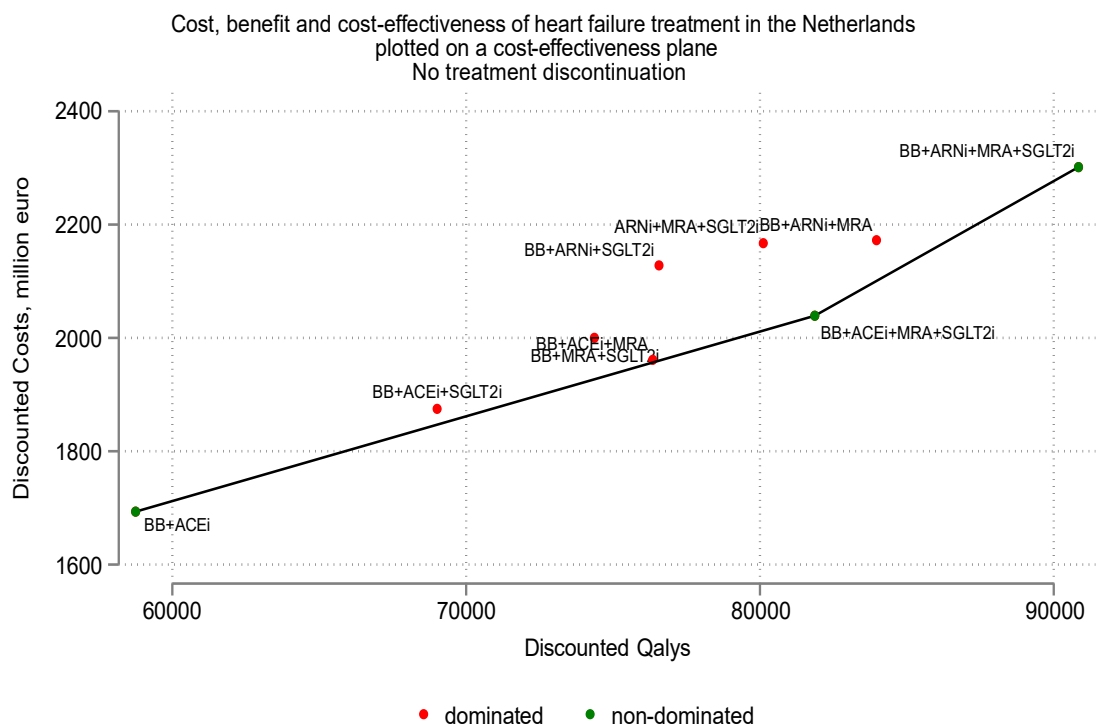
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	2038	79.8	20.9	29.0
BB+ARNi+MRA	1899	73.1	55.8	.
BB+ACEi+MRA+SGLT2i	1786	71.1	-55.4	17.0
ARNi+MRA+SGLT2i	1873	69.5	14.5	.
BB+ARNi+SGLT2i	1828	66.4	1155.0	.
BB+ACEi+MRA	1709	66.3	-11.6	.
BB+MRA+SGLT2i	1729	64.6	24.6	.
BB+ACEi+SGLT2i	1616	60.0	19.1	.
BB+ACEi	1458	51.8	.	.



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No treatment discontinuation

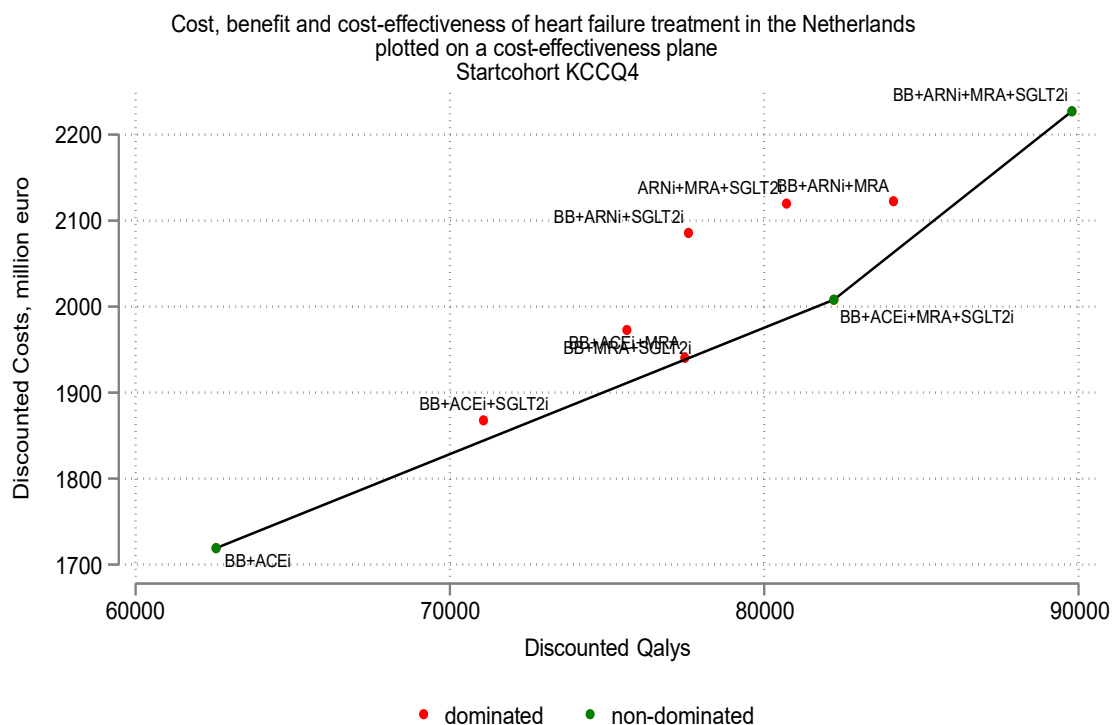
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	2301	90.8	18.8	29.2
BB+ARNi+MRA	2172	84.0	63.5	.
BB+ACEi+MRA+SGLT2i	2039	81.9	-73.1	15.0
ARNi+MRA+SGLT2i	2167	80.1	11.0	.
BB+ARNi+SGLT2i	2128	76.6	777.2	.
BB+ACEi+MRA	1961	76.4	-19.5	.
BB+MRA+SGLT2i	2000	74.4	23.4	.
BB+ACEi+SGLT2i	1875	69.0	17.7	.
BB+ACEi	1693	58.8	.	.



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Startcohort KCCQ4

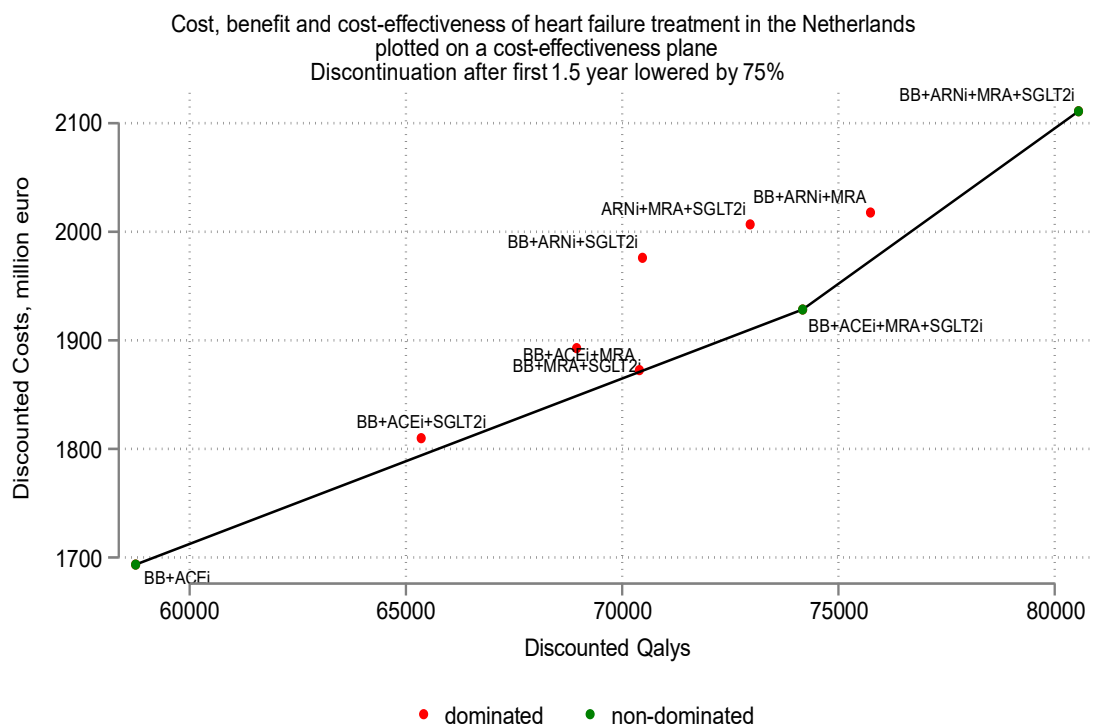
Costs, Qalys, CERs and ICERs				
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	2227	89.8	18.4	28.9
BB+ARNi+MRA	2123	84.1	60.4	.
BB+ACEi+MRA+SGLT2i	2008	82.2	-74.1	14.7
ARNi+MRA+SGLT2i	2120	80.7	10.9	.
BB+ARNi+SGLT2i	2086	77.6	1226.3	.
BB+ACEi+MRA	1940	77.5	-17.5	.
BB+MRA+SGLT2i	1973	75.6	23.0	.
BB+ACEi+SGLT2i	1868	71.1	17.5	.
BB+ACEi	1719	62.6	.	.



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Discontinuation after first 1.5 year lowered by 75%

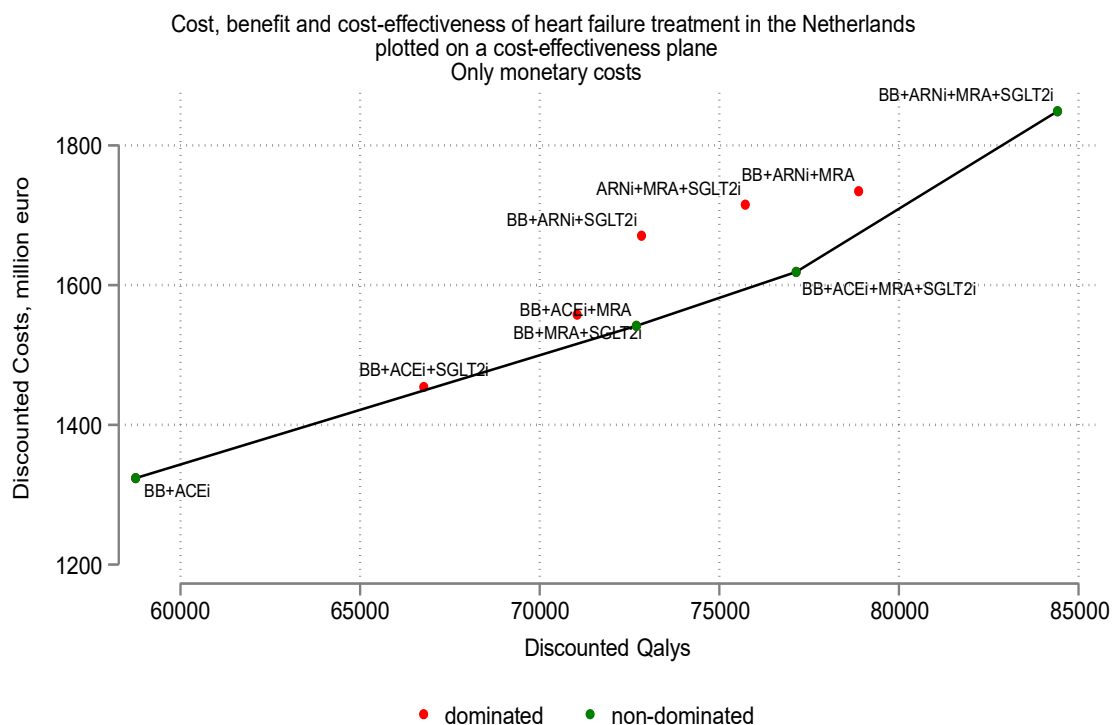
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	2111	80.6	19.4	28.6
BB+ARNi+MRA	2018	75.7	56.9	.
BB+ACEi+MRA+SGLT2i	1928	74.2	-64.6	15.2
ARNi+MRA+SGLT2i	2007	73.0	12.4	.
BB+ARNi+SGLT2i	1976	70.5	1449.2	.
BB+ACEi+MRA	1873	70.4	-13.9	.
BB+MRA+SGLT2i	1893	68.9	23.1	.
BB+ACEi+SGLT2i	1810	65.4	17.6	.
BB+ACEi	1693	58.8	.	.



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Only monetary costs

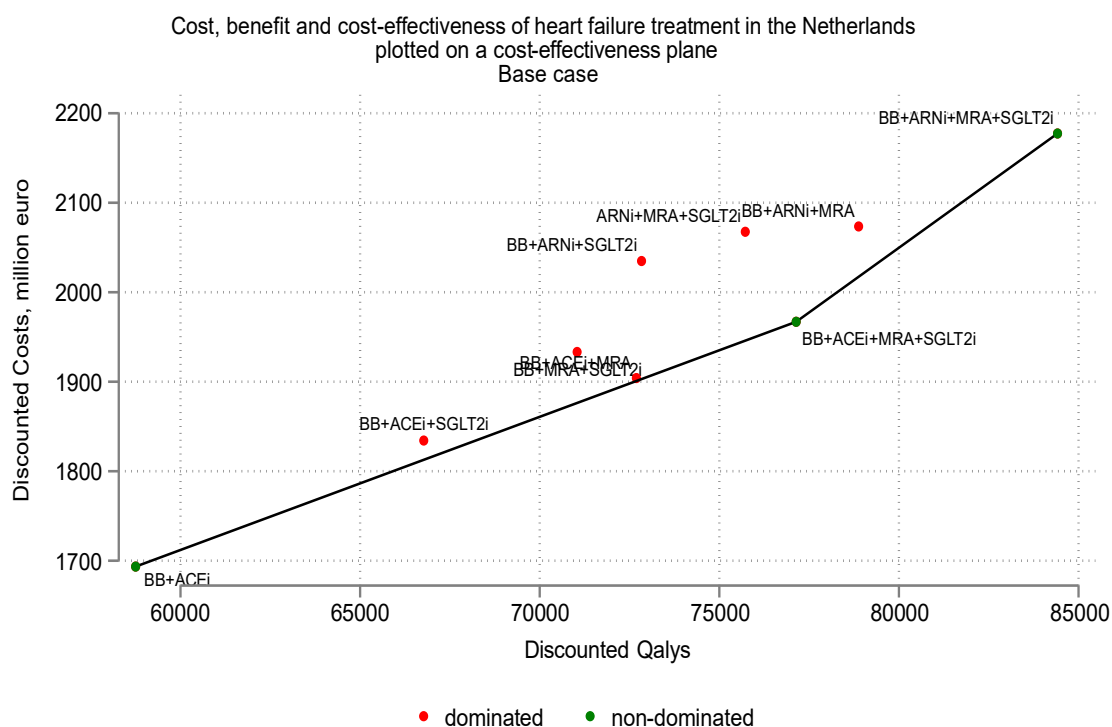
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BB+ARNi+MRA+SGLT2i	1849	84.4	20.7	31.6
BB+ARNi+MRA	1734	78.9	66.4	.
BB+ACEi+MRA+SGLT2i	1619	77.1	-67.9	17.4
ARNi+MRA+SGLT2i	1715	75.7	15.4	.
BB+ARNi+SGLT2i	1671	72.8	895.0	.
BB+ACEi+MRA	1542	72.7	-9.7	15.6
BB+MRA+SGLT2i	1558	71.0	24.2	.
BB+ACEi+SGLT2i	1454	66.8	16.3	.
BB+ACEi	1324	58.8	.	.



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Base case

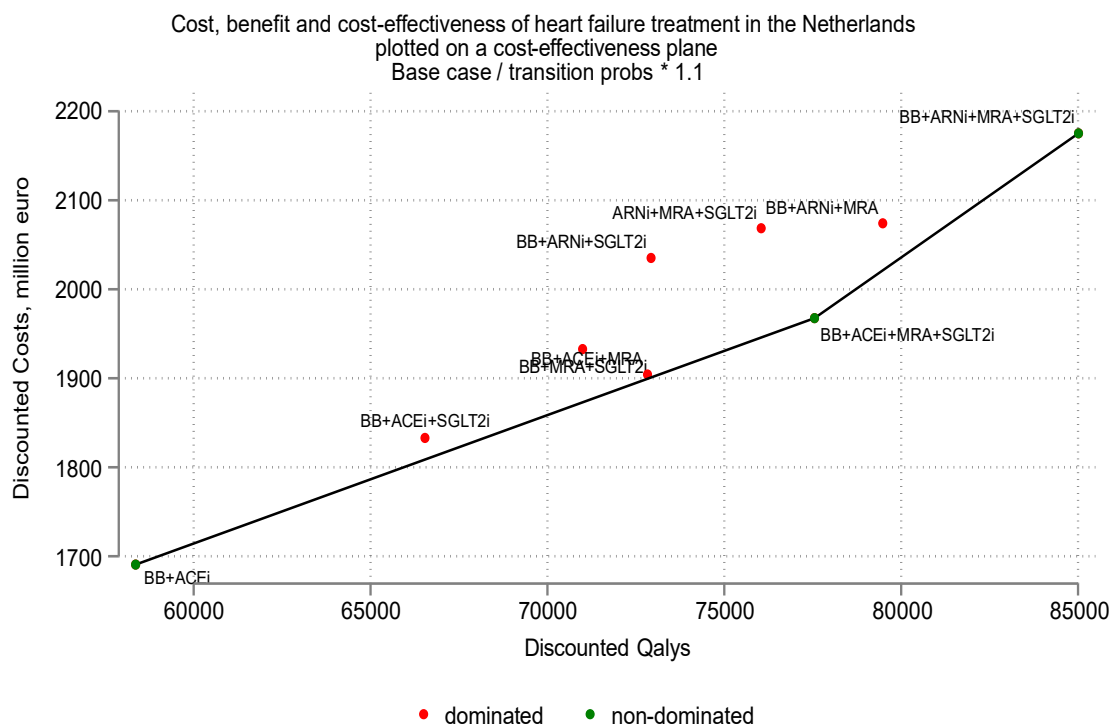
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BB+ARNi+MRA	2074	78.9	61.3	.
BB+ACEi+MRA+SGLT2i	1967	77.1	-71.0	14.9
ARNi+MRA+SGLT2i	2068	75.7	11.3	.
BB+ARNi+SGLT2i	2035	72.8	907.6	.
BB+ACEi+MRA	1904	72.7	-17.7	.
BB+MRA+SGLT2i	1933	71.0	23.2	.
BB+ACEi+SGLT2i	1834	66.8	17.6	.
BB+ACEi	1693	58.8	.	.



A cohort of 10,000 Dutch heart failure patients were simulated lifelong.
ACEi: ACE-inhibitor; ARB: angiotensin-II-receptor antagonist BB: betablocker;
MRA: mineralocorticoid receptor antagonist ARNi: angiotensin receptor-neprilysin inhibitor

Base case / transition probs * 1.1

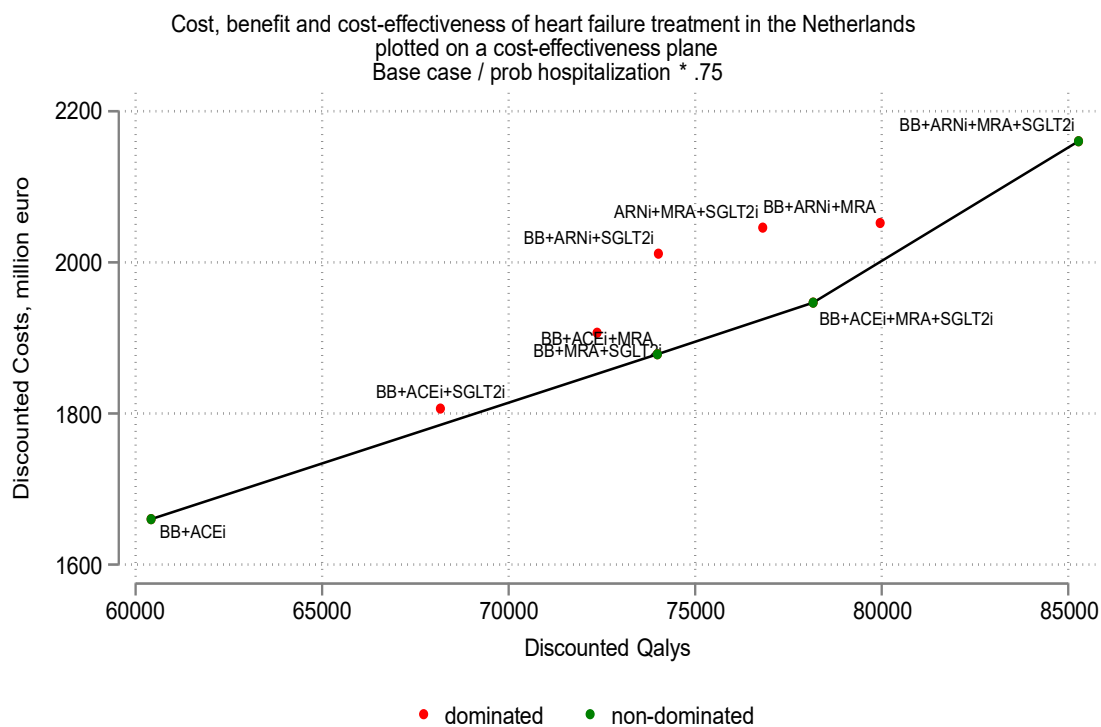
Costs, Qalys, CERs and ICERs				
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	2175	85.0	18.3	27.8
BB+ARNi+MRA	2074	79.5	55.2	.
BB+ACEi+MRA+SGLT2i	1968	77.6	-67.0	14.4
ARNi+MRA+SGLT2i	2069	76.0	10.7	.
BB+ARNi+SGLT2i	2035	72.9	1292.5	.
BB+ACEi+MRA	1904	72.8	-15.6	.
BB+MRA+SGLT2i	1933	71.0	22.4	.
BB+ACEi+SGLT2i	1833	66.5	17.4	.
BB+ACEi	1691	58.4	.	.



A cohort of 10,000 Dutch heart failure patients were simulated lifelong.
ACEi: ACE-inhibitor; ARB: angiotensin-II-receptor antagonist BB: betablocker;
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Base case / prob hospitalization * .75

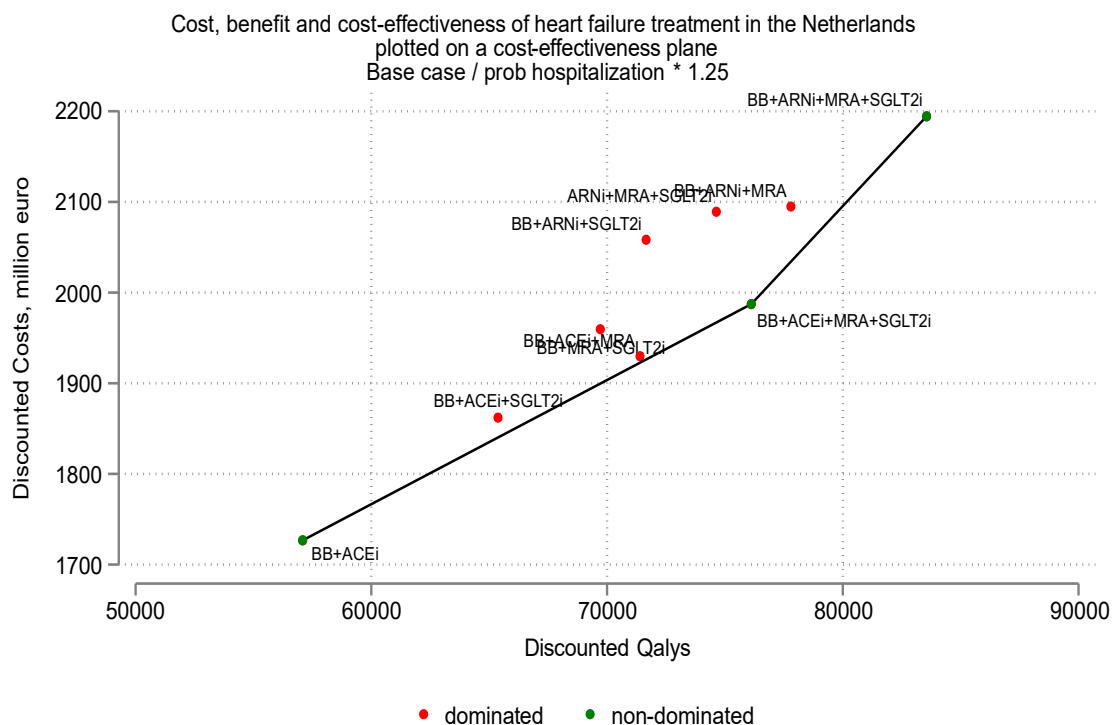
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	2160	85.3	20.4	30.0
BB+ARNi+MRA	2052	80.0	58.7	.
BB+ACEi+MRA+SGLT2i	1947	78.2	-73.4	16.4
ARNi+MRA+SGLT2i	2046	76.8	12.3	.
BB+ARNi+SGLT2i	2011	74.0	4737.3	.
BB+ACEi+MRA	1878	74.0	-17.6	16.1
BB+MRA+SGLT2i	1907	72.4	23.9	.
BB+ACEi+SGLT2i	1806	68.2	18.9	.
BB+ACEi	1660	60.4	.	.



A cohort of 10,000 Dutch heart failure patients were simulated lifelong.
ACEi: ACE-inhibitor; ARB: angiotensin-II-receptor antagonist BB: betablocker;
MRA: mineralocorticoid receptor antagonist ARNi: angiotensin receptor-neprilysin inhibitor

Base case / prob hospitalization * 1.25

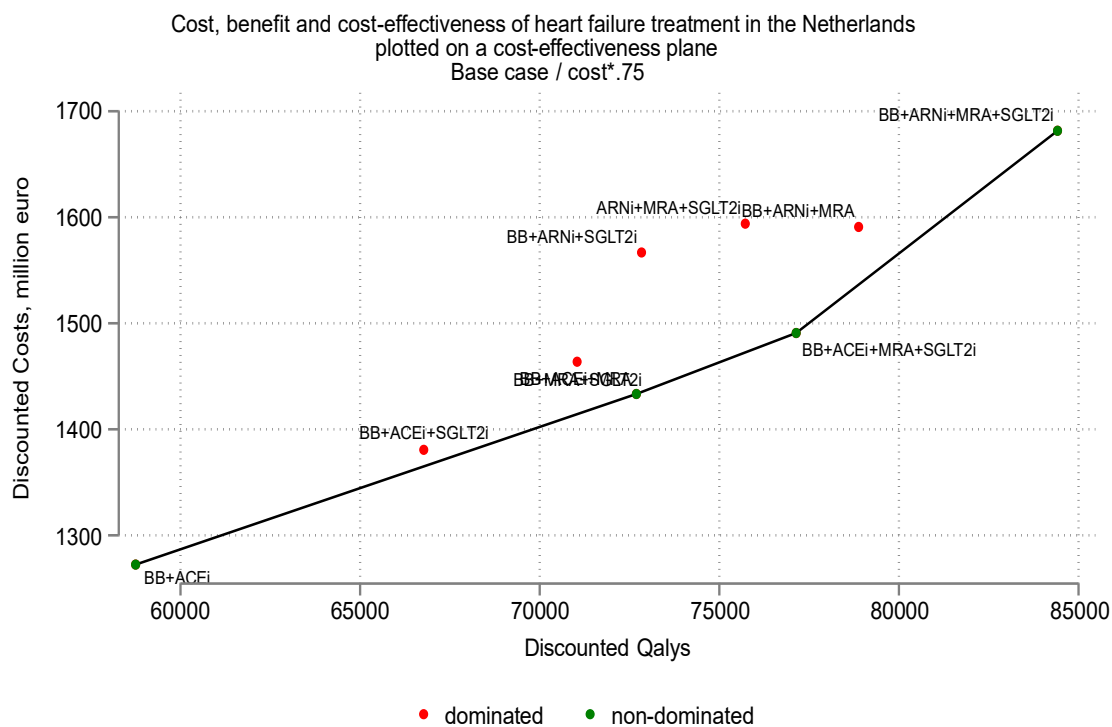
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	2194	83.6	17.3	27.9
BB+ARNi+MRA	2095	77.8	64.1	.
BB+ACEi+MRA+SGLT2i	1987	76.1	-68.7	13.7
ARNi+MRA+SGLT2i	2089	74.6	10.4	.
BB+ARNi+SGLT2i	2058	71.7	494.0	.
BB+ACEi+MRA	1930	71.4	-17.7	.
BB+MRA+SGLT2i	1960	69.7	22.5	.
BB+ACEi+SGLT2i	1862	65.4	16.3	.
BB+ACEi	1727	57.1	.	.



A cohort of 10,000 Dutch heart failure patients were simulated lifelong.
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Base case / cost*.75

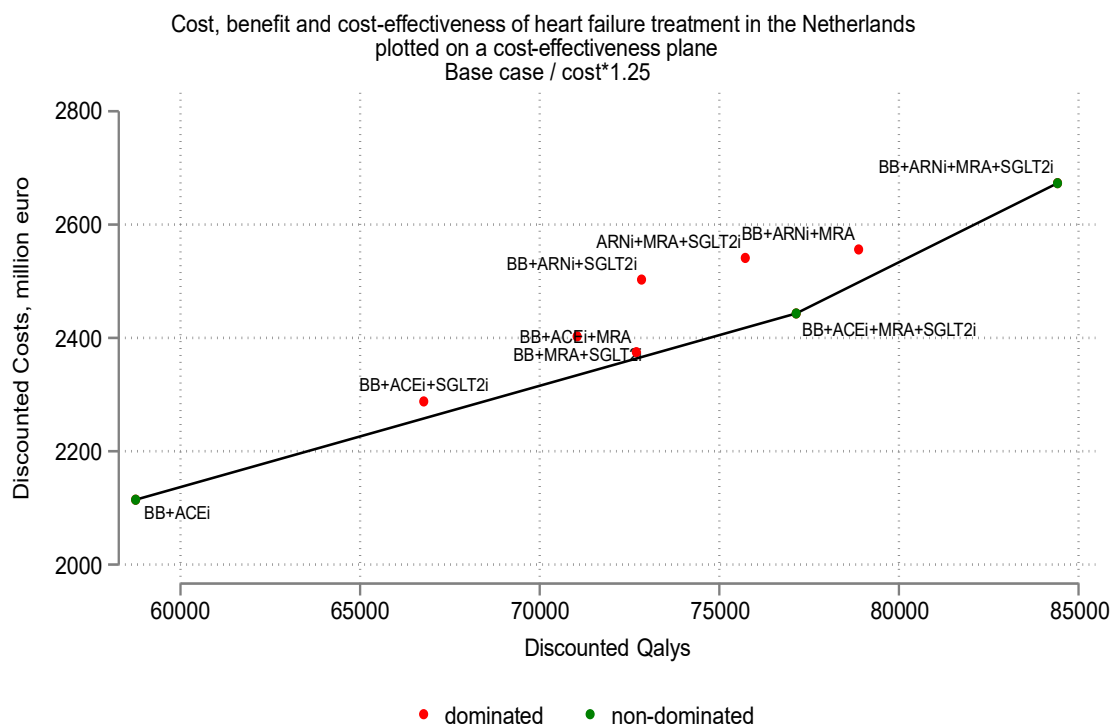
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 € /QALY gained)	ICER(1000 € /QALY gained)
BB+ARNi+MRA+SGLT2i	1682	84.4	16.4	26.2
BB+ARNi+MRA	1591	78.9	57.6	.
BB+ACEi+MRA+SGLT2i	1491	77.1	-72.8	12.9
ARNi+MRA+SGLT2i	1594	75.7	9.4	.
BB+ARNi+SGLT2i	1567	72.8	926.4	.
BB+ACEi+MRA	1433	72.7	-18.4	11.5
BB+MRA+SGLT2i	1464	71.0	19.5	.
BB+ACEi+SGLT2i	1381	66.8	13.5	.
BB+ACEi	1272	58.8	.	.



A cohort of 10,000 Dutch heart failure patients were simulated lifelong.
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MRA: mineralocorticoid receptor antagonist ARNi: angiotensin receptor-neprilysin inhibitor

Base case / cost*1.25

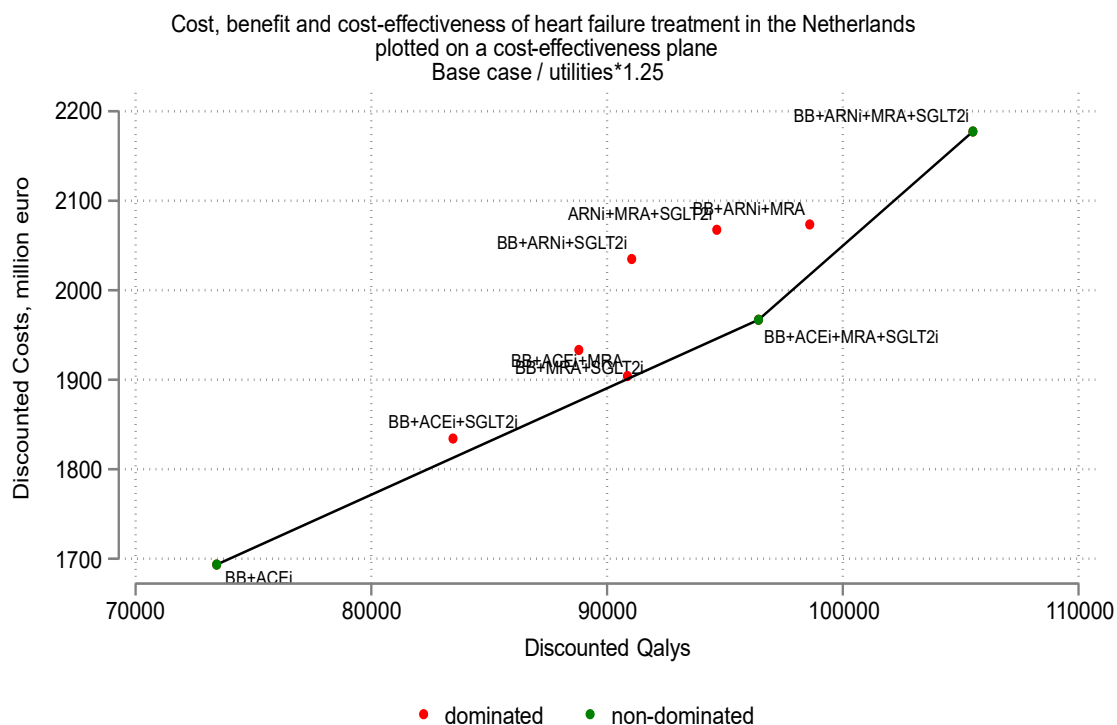
Costs, Qalys, CERs and ICERs				
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	2673	84.4	21.1	31.6
BB+ARNi+MRA	2556	78.9	65.0	.
BB+ACEi+MRA+SGLT2i	2443	77.1	-69.2	17.9
ARNi+MRA+SGLT2i	2541	75.7	13.2	.
BB+ARNi+SGLT2i	2503	72.8	888.9	.
BB+ACEi+MRA	2375	72.7	-16.9	.
BB+MRA+SGLT2i	2403	71.0	26.9	.
BB+ACEi+SGLT2i	2288	66.8	21.6	.
BB+ACEi	2114	58.8	.	.



A cohort of 10,000 Dutch heart failure patients were simulated lifelong.
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MRA: mineralocorticoid receptor antagonist ARNi: angiotensin receptor-neprilysin inhibitor

Base case / utilities*1.25

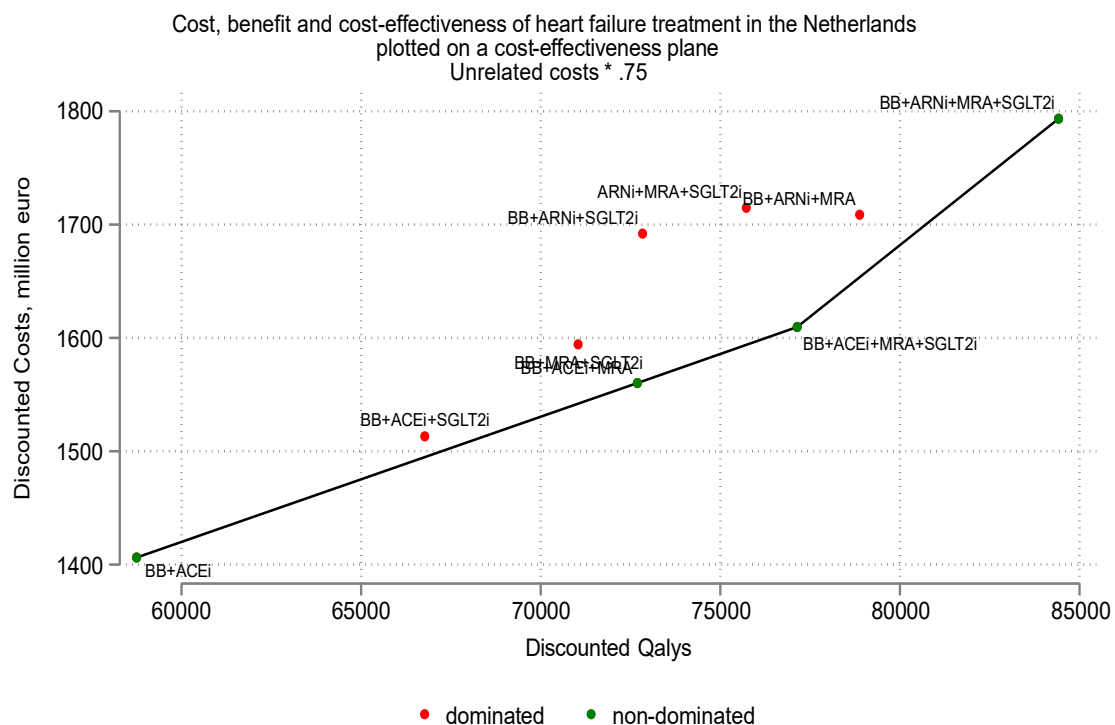
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	2177	105.5	15.0	23.1
BB+ARNi+MRA	2074	98.6	49.0	.
BB+ACEi+MRA+SGLT2i	1967	96.4	-56.8	11.9
ARNi+MRA+SGLT2i	2068	94.7	9.0	.
BB+ARNi+SGLT2i	2035	91.0	726.1	.
BB+ACEi+MRA	1904	90.9	-14.1	.
BB+MRA+SGLT2i	1933	88.8	18.5	.
BB+ACEi+SGLT2i	1834	83.5	14.0	.
BB+ACEi	1693	73.4	.	.



A cohort of 10,000 Dutch heart failure patients were simulated lifelong.
ACEi: ACE-inhibitor; ARB: angiotensin-II-receptor antagonist BB: betablocker;
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Unrelated costs * .75

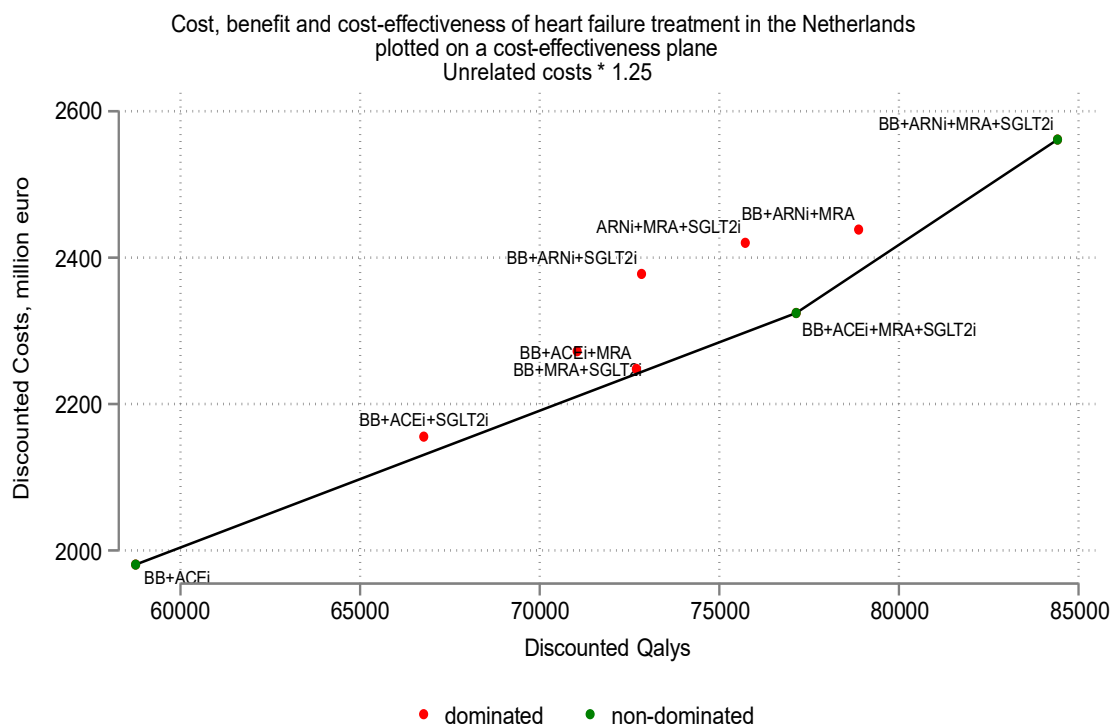
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 € /QALY gained)	ICER(1000 € /QALY gained)
BB+ARNi+MRA+SGLT2i	1793	84.4	15.3	25.3
BB+ARNi+MRA	1709	78.9	57.0	.
BB+ACEi+MRA+SGLT2i	1610	77.1	-74.2	11.1
ARNi+MRA+SGLT2i	1715	75.7	7.9	.
BB+ARNi+SGLT2i	1692	72.8	915.0	.
BB+ACEi+MRA	1560	72.7	-20.7	11.0
BB+MRA+SGLT2i	1594	71.0	19.0	.
BB+ACEi+SGLT2i	1513	66.8	13.3	.
BB+ACEi	1406	58.8	.	.



A cohort of 10,000 Dutch heart failure patients were simulated lifelong.
ACEi: ACE-inhibitor; ARB: angiotensin-II-receptor antagonist BB: betablocker;
MRA: mineralocorticoid receptor antagonist ARNi: angiotensin receptor-neprilysin inhibitor

Unrelated costs * 1.25

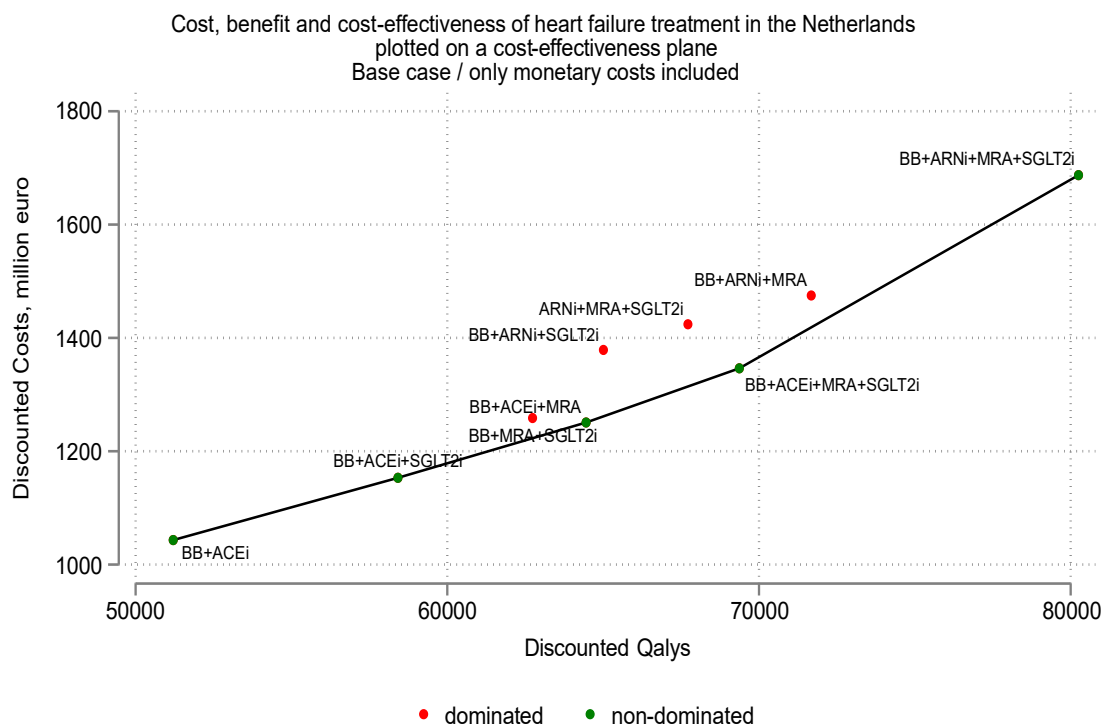
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 € /QALY gained)	ICER(1000 € /QALY gained)
BB+ARNi+MRA+SGLT2i	2561	84.4	22.2	32.6
BB+ARNi+MRA	2438	78.9	65.6	.
BB+ACEi+MRA+SGLT2i	2324	77.1	-67.7	18.7
ARNi+MRA+SGLT2i	2420	75.7	14.7	.
BB+ARNi+SGLT2i	2378	72.8	900.3	.
BB+ACEi+MRA	2248	72.7	-14.6	.
BB+MRA+SGLT2i	2272	71.0	27.3	.
BB+ACEi+SGLT2i	2155	66.8	21.8	.
BB+ACEi	1981	58.8	.	.



A cohort of 10,000 Dutch heart failure patients were simulated lifelong.
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MRA: mineralocorticoid receptor antagonist ARNi: angiotensin receptor-neprilysin inhibitor

Base case / only monetary costs included

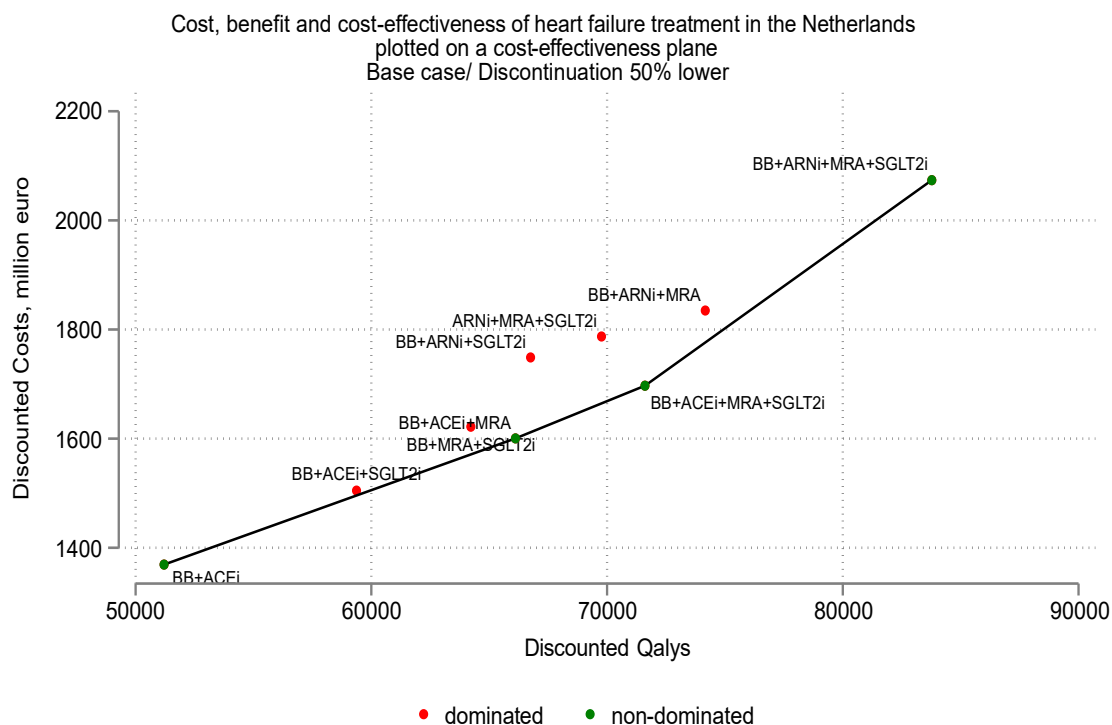
Costs, Qalys, CERs and ICERs				
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	1687	80.3	24.8	31.3
BB+ARNi+MRA	1475	71.7	55.7	.
BB+ACEi+MRA+SGLT2i	1346	69.4	-47.0	19.4
ARNi+MRA+SGLT2i	1424	67.7	16.7	.
BB+ARNi+SGLT2i	1379	65.0	230.3	.
BB+ACEi+MRA	1251	64.5	-4.6	16.2
BB+MRA+SGLT2i	1259	62.7	24.4	.
BB+ACEi+SGLT2i	1153	58.4	15.2	15.2
BB+ACEi	1043	51.2	.	.



A cohort of 10,000 Dutch heart failure patients were simulated lifelong.
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MRA: mineralocorticoid receptor antagonist ARNi: angiotensin receptor-neprilysin inhibitor

Base case/ Discontinuation 50% lower

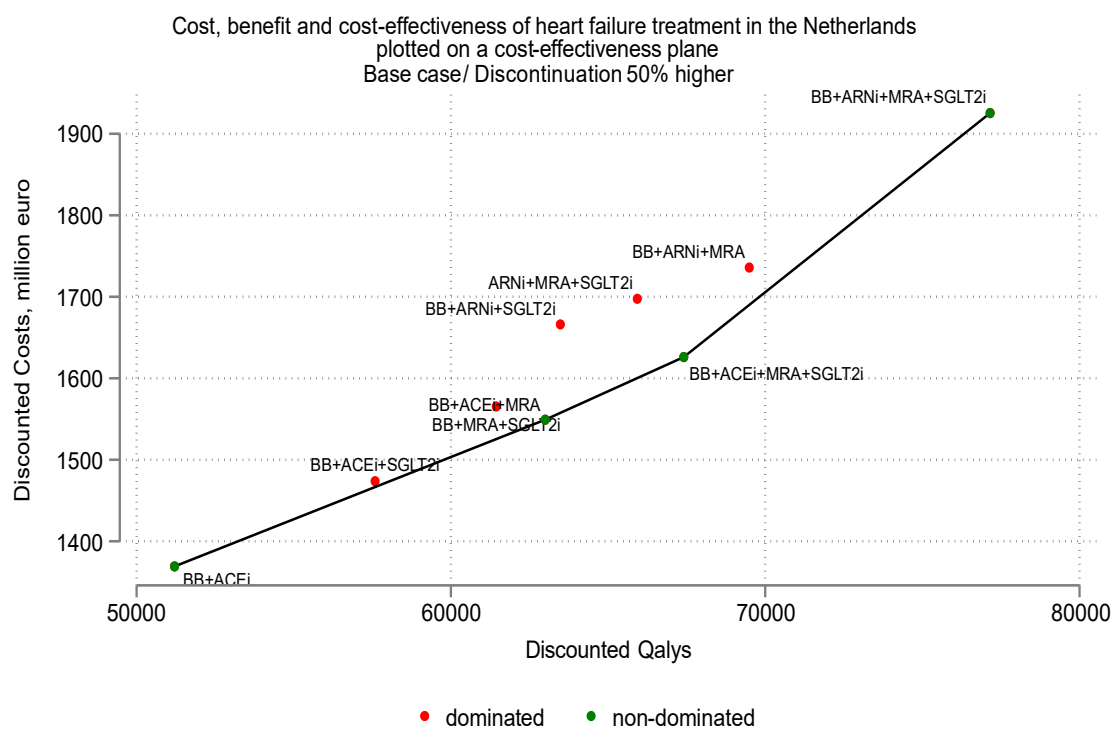
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	2074	83.8	24.9	31.0
BB+ARNi+MRA	1835	74.2	53.8	.
BB+ACEi+MRA+SGLT2i	1697	71.6	-48.9	17.6
ARNi+MRA+SGLT2i	1787	69.8	12.8	.
BB+ARNi+SGLT2i	1749	66.8	231.0	.
BB+ACEi+MRA	1600	66.1	-11.3	15.5
BB+MRA+SGLT2i	1622	64.2	24.1	.
BB+ACEi+SGLT2i	1505	59.4	16.6	.
BB+ACEi	1369	51.2	.	.



A cohort of 10,000 Dutch heart failure patients were simulated lifelong.
ACEi: ACE-inhibitor; ARB: angiotensin-II-receptor antagonist BB: betablocker;
MRA: mineralocorticoid receptor antagonist ARNi: angiotensin receptor-neprilysin inhibitor

Base case/ Discontinuation 50% higher

Costs, Qalys, CERs and ICERs				
Treatment Combination	Discounted costs, €mln	Discounted QALYs, 1000	CER(1000 €/QALY gained)	ICER(1000 €/QALY gained)
BB+ARNi+MRA+SGLT2i	1925	77.2	24.7	30.7
BB+ARNi+MRA	1736	69.5	52.7	.
BB+ACEi+MRA+SGLT2i	1626	67.4	-48.3	17.4
ARNi+MRA+SGLT2i	1698	65.9	12.8	.
BB+ARNi+SGLT2i	1666	63.5	242.7	.
BB+ACEi+MRA	1549	63.0	-10.4	15.3
BB+MRA+SGLT2i	1565	61.4	23.8	.
BB+ACEi+SGLT2i	1474	57.6	16.4	.
BB+ACEi	1369	51.2	.	.



A cohort of 10,000 Dutch heart failure patients were simulated lifelong.
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