

**Single Technology Appraisal – Bevacizumab in combination with oxaliplatin and either 5FU or capecitabine for the treatment of metastatic colorectal cancer**

**PART 4 – RESPONSE TO NON-PRIORITY ERG CLARIFICATION QUESTIONS**

The table below summarises the most relevant ICERs from each of the additional analysis performed. The analyses below take into account the modifications suggested by the ERG to the original submission.

B-XELOX and XELOX represent the regimens on the efficiency frontier of the cost effectiveness plane, B-FOLFOX-6 vs FOLFOX-6 are of relevance for patients unsuitable for capecitabine and the comparison of B-XELOX vs FOLFOX-6 is of relevance as this shows the cost effectiveness of replacing the most used regimen in England and Wales with the most cost-effective of the bevacizumab regimens examined in this analysis.

As discussed previously in parts 1-3 of our response we consider that the analysis using all 6 arms of the 966 study offers the most plausible estimate of the ICER.

**Summary of scenario analysis**

Analysis	COMPARATOR		
	Intervention	XELOX	FOLFOX-6
Chemo+Bev vs Chemo+-Placebo (all 6 arms)	B-XELOX	84,553	50,338
	B-FOLFOX-6	126,826	92,634
Chemo+Bev vs Chemo+-Placebo (all 6 arms) including Bev wastage	B-XELOX	90,945	56,738
	B-FOLFOX-6	132,621	98,436
Chemo+Bev vs Chemo+-Placebo (all 6 arms) including Oxaliplatin wastage	B-XELOX	86,637	49,710
	B-FOLFOX-6	132,260	95,357
Chemo+Bev vs Chemo+Placebo (2*2) excluding prior adjuvant patients	B-XELOX	92,698	47,754
	B-FOLFOX-6	141,752	96,687
XELOX+Bev vs XELOX+Placebo (2*2) FOLFOX+Bev vs FOLFOX+Placebo (2*2)	B-XELOX	90,779	71,923
	B-FOLFOX-6	170,531	240,324
Chemo+Bev vs Chemo+Placebo (2*2)	B-XELOX	129,911	63,702
	B-FOLFOX-6	200,770	134,309

**Scenario 1: all 6 arms of NO16966, XELOX and FOLFOX arms pooled**

	B-FOLFOX-4	B-FOLFOX-6	B-XELOX	XELOX	FOLFOX-6	FOLFOX-4	FOLFIRI mdg	FOLFIRI dg
<b>ICER (£)</b>								
<b>B-XELOX intervention</b>	N/A	N/A	N/A	<b>84,553</b>	50,338	32,193	46,780	31,263
<b>B-FOLFOX-6 intervention</b>	N/A	N/A	N/A	126,826	<b>92,634</b>	74,386	77,654	62,125
<b>B-FOLFOX-4 intervention</b>	N/A	N/A	N/A	148,345	114,057	<b>96,018</b>	93,385	77,856

**Results of PSA**

	B-XELOX vs XELOX			B-FOLFOX-6 vs FOLFOX-6		
			<b>ICER</b>			<b>ICER</b>
<b>Mean</b>			84,212			91,915
<b>95% percentiles</b>			(61,368, 147,392)			(65,675, 163,577)

**Scenario 2: all 6 arms of NO16966, XELOX and FOLFOX arms pooled including bevacizumab wastage**

	B-FOLFOX-4	B-FOLFOX-6	B-XELOX	XELOX	FOLFOX-6	FOLFOX-4	FOLFIRI mdg	FOLFIRI dg
<b>ICER (£)</b>								
<b>B-XELOX intervention</b>	N/A	N/A	N/A	<b>90,945</b>	56,738	38,593	51,454	35,937
<b>B-FOLFOX-6 intervention</b>	N/A	N/A	N/A	132,621	<b>98,436</b>	80,182	81,890	66,361
<b>B-FOLFOX-4 intervention</b>	N/A	N/A	N/A	154,139	119,853	<b>101,820</b>	97,621	82,092

**Results of PSA**

	B-XELOX vs XELOX			B-FOLFOX-6 vs FOLFOX-6		
			ICER			ICER
<b>Mean</b>			91,198			98,488
<b>95% percentiles</b>			(67,740, 152,900)			(71,338, 163,458)

**Scenario 3: all 6 arms of NO16966, XELOX and FOLFOX arms pooled including oxaliplatin wastage**

	B-FOLFOX-4	B-FOLFOX-6	B-XELOX	XELOX	FOLFOX-6	FOLFOX-4	FOLFIRI mdg	FOLFIRI dg
<b>ICER (£)</b>								
<b>B-XELOX intervention</b>	N/A	N/A	N/A	<b>86,637</b>	49,710	36,697	51,873	36,356
<b>B-FOLFOX-6 intervention</b>	N/A	N/A	N/A	132,260	<b>95,357</b>	82,240	85,198	69,669
<b>B-FOLFOX-4 intervention</b>	N/A	N/A	N/A	147,290	110,286	<b>97,382</b>	96,186	80,656

**Results of PSA**

	B-XELOX vs XELOX			B-FOLFOX-6 vs FOLFOX-6		
			<b>ICER</b>			<b>ICER</b>
<b>Mean</b>			86,083			94,355
<b>95% percentiles</b>			(62,820, 149,013)			(67,704, 163,867)

**Scenario 4: Analysis using the 2x2 part of N16966, XELOX and FOLFOX arms pooled excluding prior adjuvant patients**

	B-FOLFOX-4	B-FOLFOX-6	B-XELOX	XELOX	FOLFOX-6	FOLFOX-4	FOLFIRI mdg	FOLFIRI dg
<b>ICER (£)</b>								
<b>B-XELOX intervention</b>	N/A	N/A	N/A	<b>92,698</b>	47,754	24,886	46,958	28,127
<b>B-FOLFOX-6 intervention</b>	N/A	N/A	N/A	141,752	<b>96,687</b>	73,695	82,091	63,243
<b>B-FOLFOX-4 intervention</b>	N/A	N/A	N/A	166,701	121,448	<b>98,706</b>	99,981	81,133

**Results of PSA**

	B-XELOX vs XELOX		B-FOLFOX-6 vs FOLFOX-6	
		ICER		ICER
<b>Mean</b>		92,356		96,342
<b>95% percentiles</b>		(60,814, 229,158)		(59,793, 246,416)

**Scenario 5: Analysis using 2x2 part of NO16966, XELOX and FOLFOX arms un-pooled**

	B-FOLFOX-4	B-FOLFOX-6	B-XELOX	XELOX	FOLFOX-6	FOLFOX-4	FOLFIRI mdg	FOLFIRI dg
<b>ICER (£)</b>								
<b>B-XELOX intervention</b>	N/A	N/A	N/A	<b>90,779</b>	71,923	30,009	61,068	33,046
<b>B-FOLFOX-6 intervention</b>	N/A	N/A	N/A	170,531	<b>240,324</b>	175,245	138,484	103,078
<b>B-FOLFOX-4 intervention</b>	N/A	N/A	N/A	200,702	307,976	<b>242,897</b>	170,733	135,327

**Results of PSA**

	B-XELOX vs XELOX			B-FOLFOX-6 vs FOLFOX-6		
			<b>ICER</b>			<b>ICER</b>
<b>Mean</b>			90,187			241,000
<b>95% percentiles</b>			(45,858, 423,809)			(-2,346,787, 2,113,555)

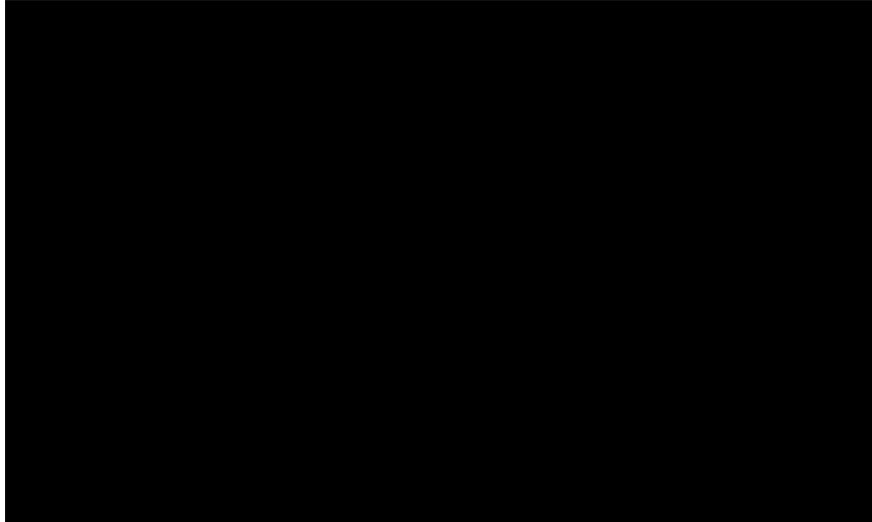
**Scenario 6: Analysis using 2x2 part of NO16966, XELOX and FOLFOX arms pooled**

	B-FOLFOX-4	B-FOLFOX-6	B-XELOX	XELOX	FOLFOX-6	FOLFOX-4	FOLFIRI mdg	FOLFIRI dg
<b>ICER (£)</b>								
<b>B-XELOX intervention</b>	N/A	N/A	N/A	<b>129,911</b>	63,702	29,996	56,559	32,282
<b>B-FOLFOX-6 intervention</b>	N/A	N/A	N/A	200,770	<b>134,309</b>	100,541	100,981	76,677
<b>B-FOLFOX-4 intervention</b>	N/A	N/A	N/A	236,843	170,315	<b>136,547</b>	123,638	99,334

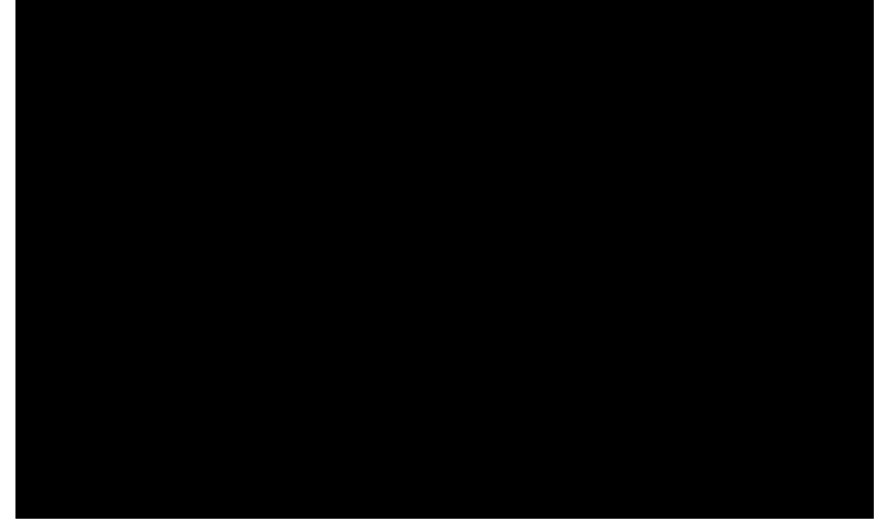
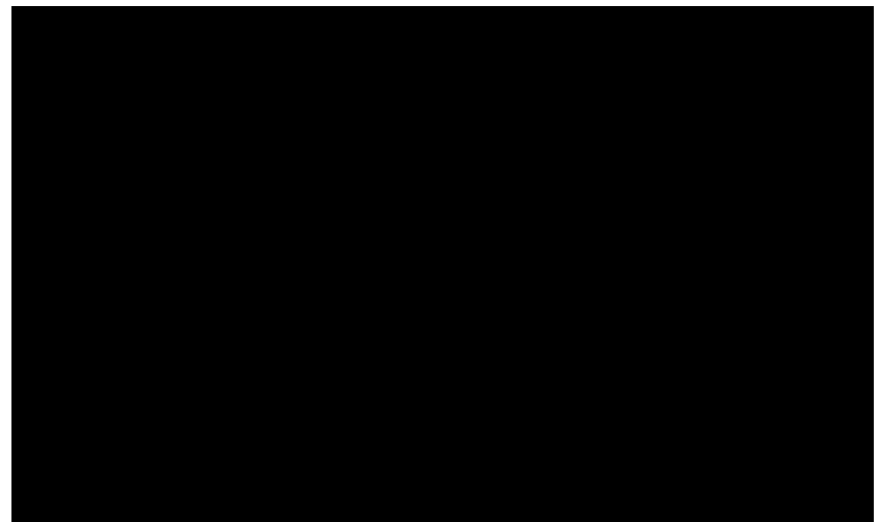
**Results of PSA**

	B-XELOX vs XELOX			B-FOLFOX-6 vs FOLFOX-6		
			ICER			ICER
<b>Mean</b>			130,281			133,921
<b>95% percentiles</b>			(-231,910, 713,057)			(63,416, 764,148)

**Scenario 1 B-XELOX vs XELOX above B-FOLFOX-6 vs FOLFOX-6 below**

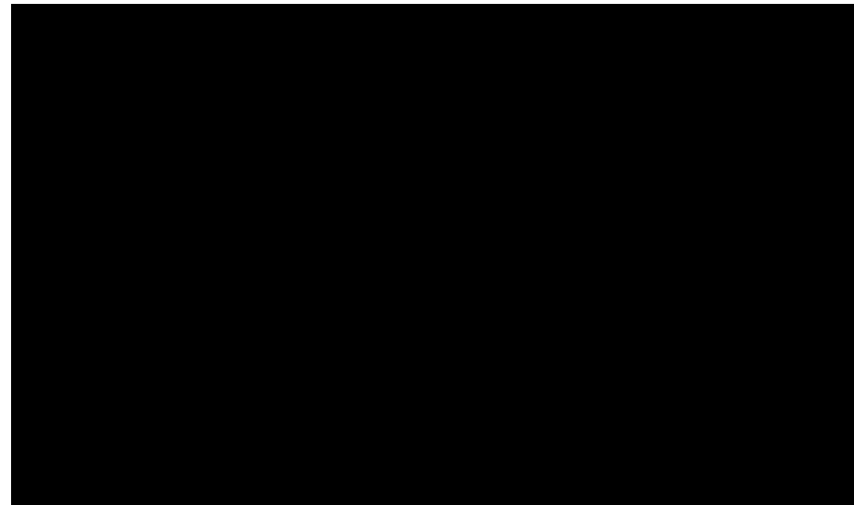
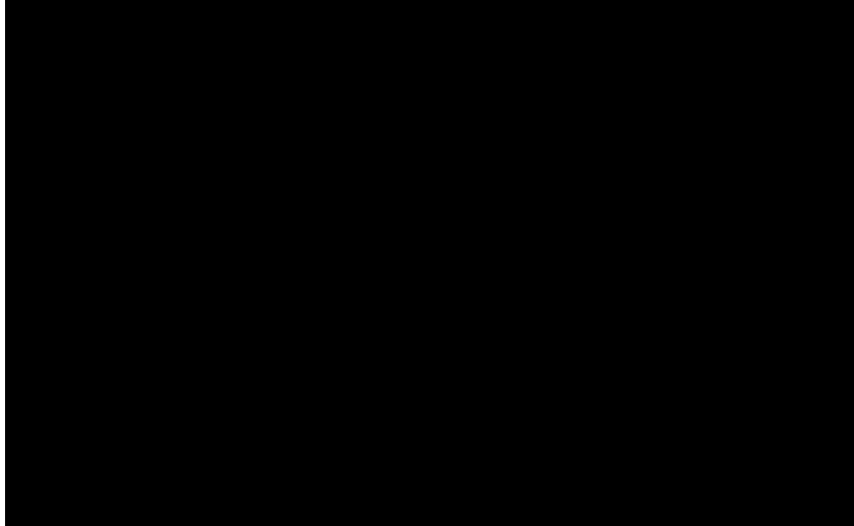


**Scenario 2 B-XELOX vs XELOX above B-FOLFOX-6 vs FOLFOX-6 below**

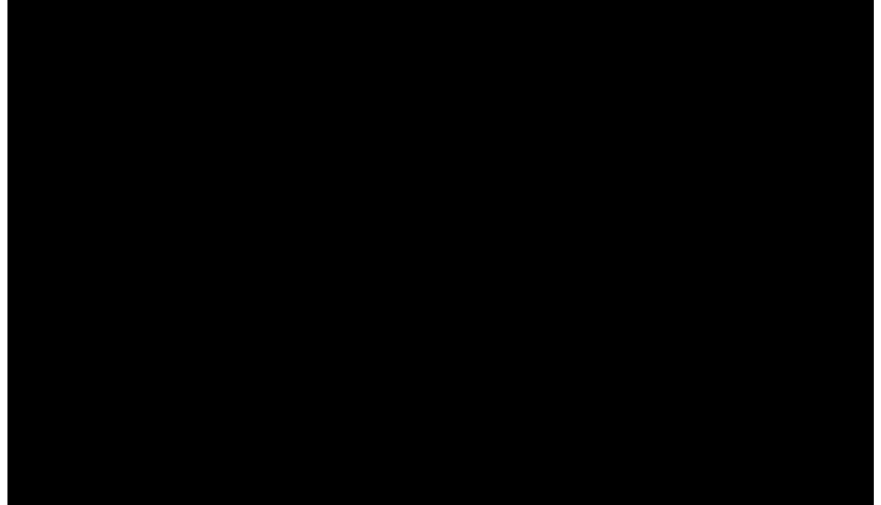




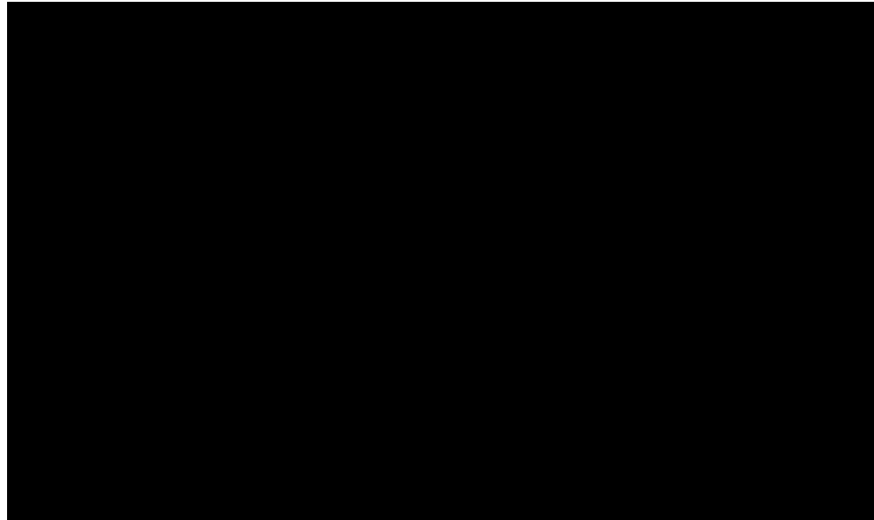
**Scenario 3 B-XELOX vs XELOX above B-FOLFOX-6 vs FOLFOX-6 below**



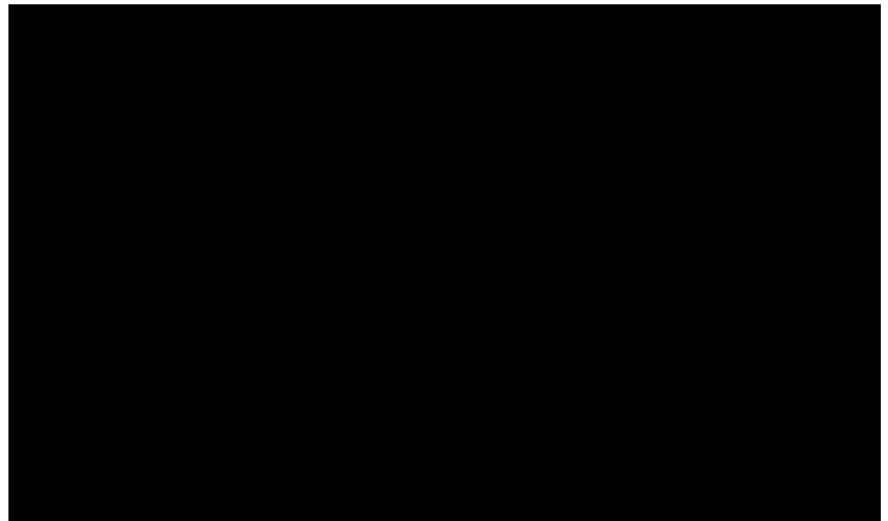
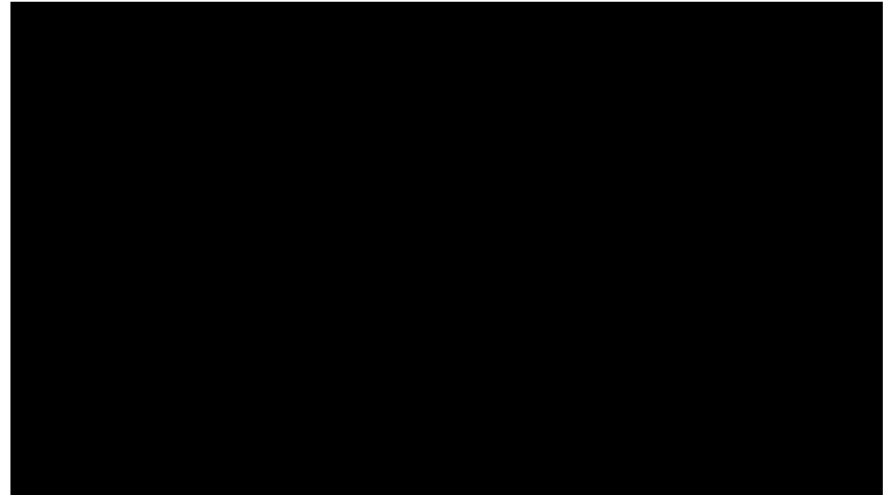
**Scenario 4 B-XELOX vs XELOX above B-FOLFOX-6 vs FOLFOX-6 below**



**Scenario 4 B-XELOX vs XELOX above B-FOLFOX-6 vs FOLFOX-6 below**



**Scenario 5 B-XELOX vs XELOX above B-FOLFOX-6 vs FOLFOX-6 below**



**Scenario 6 B-XELOX vs XELOX above B-FOLFOX-6 vs FOLFOX-6 below**

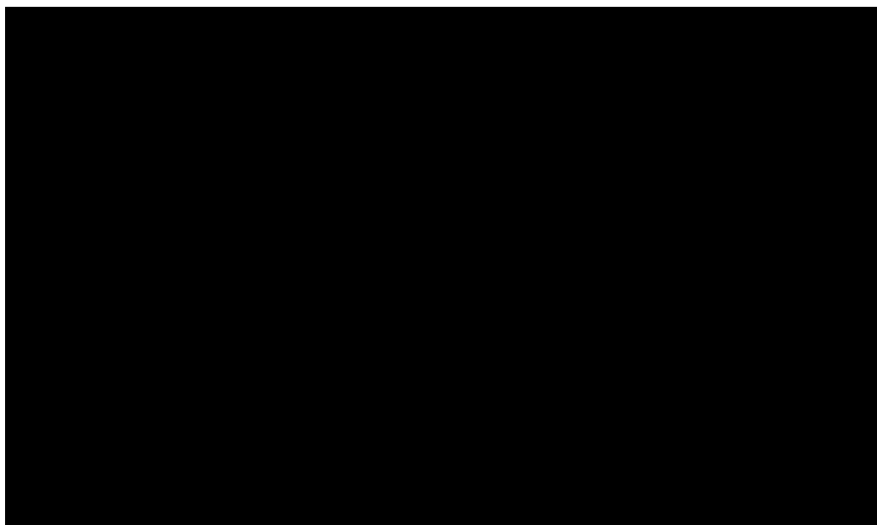
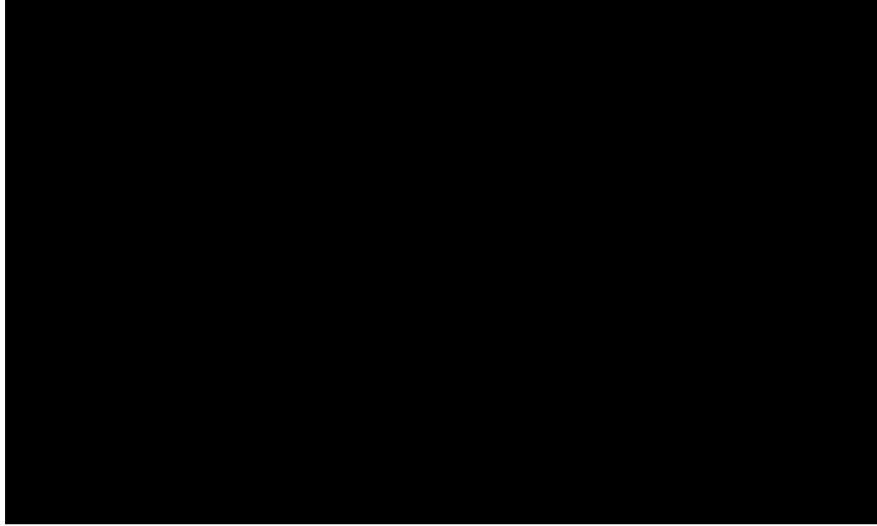


Figure 1: S1 CEAC

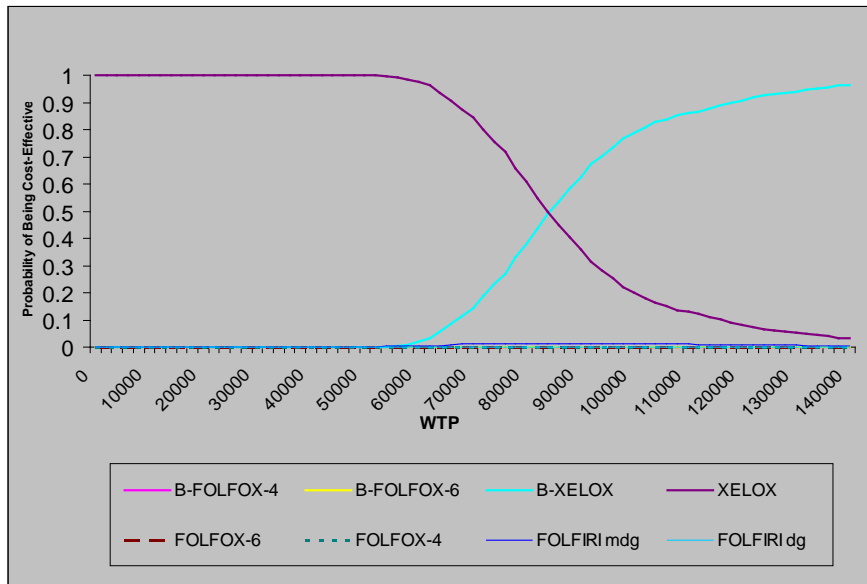
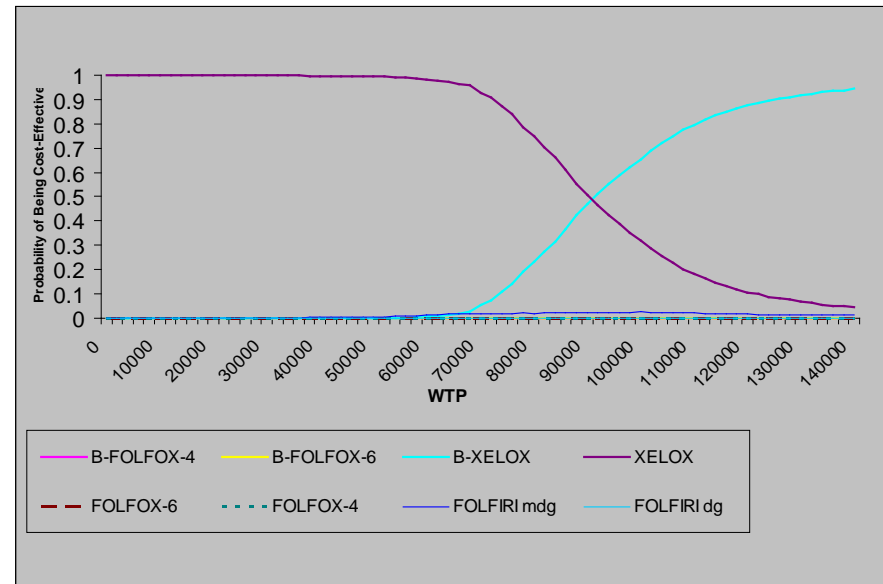
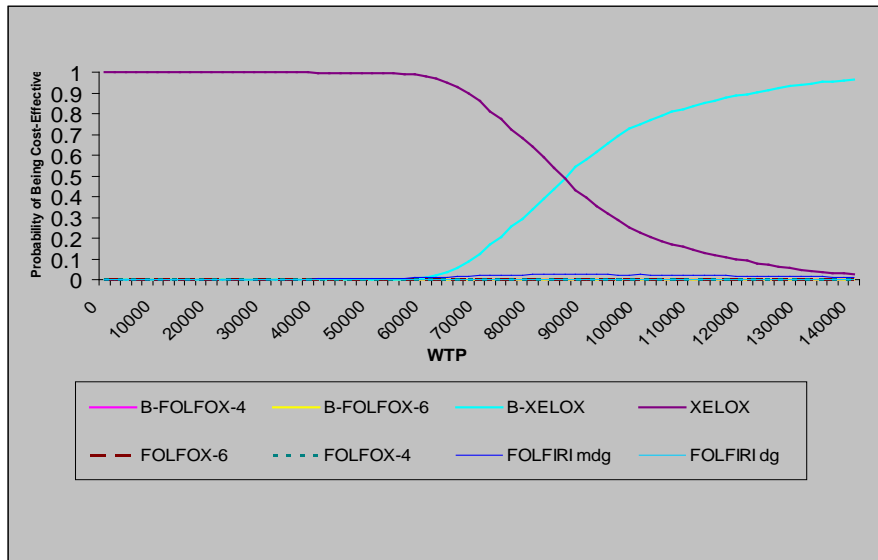


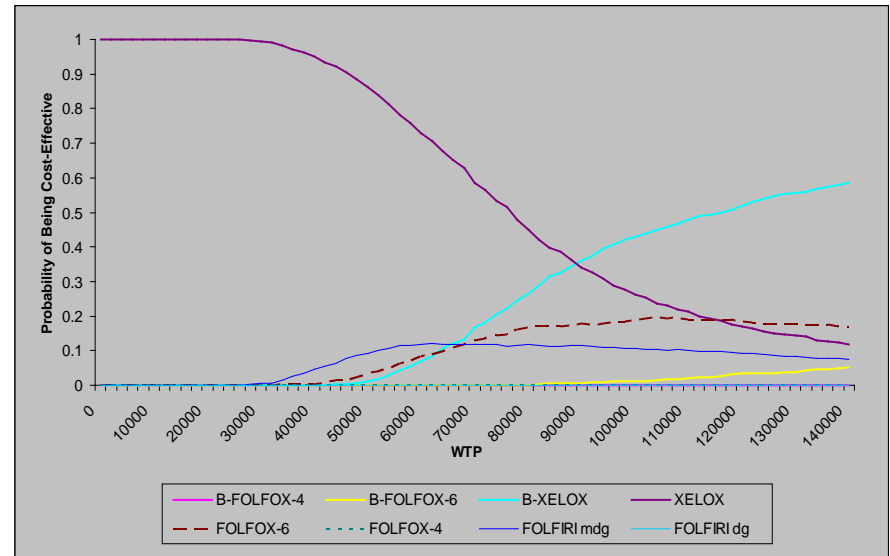
Figure 2: S2 (CEAC)



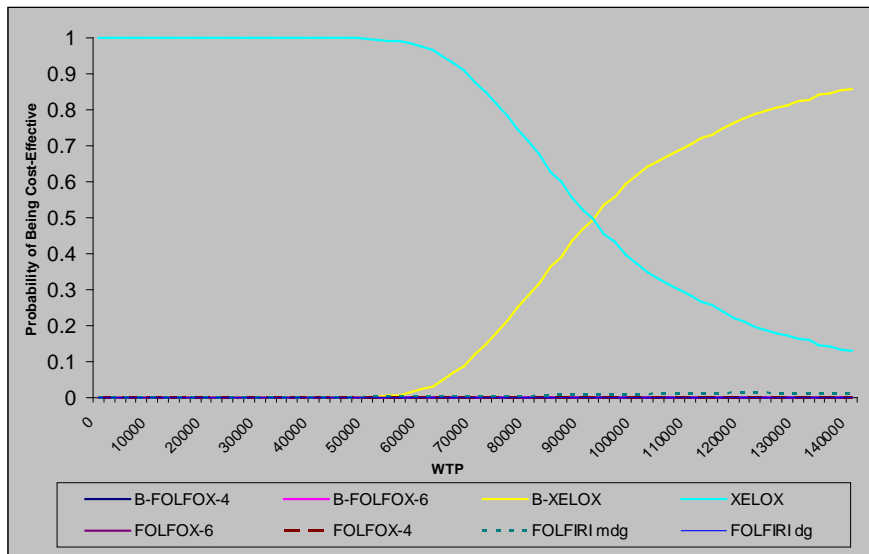
### Scenario 3 CEAC



### Scenario 5 CEAC



### Scenario 4 CEAC



### Scenario 6 CEAC

