Saltelli PSA

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PSA

This report documents the results of using Saltelli's method of probability sensitivity analysis on the IGNITE model.

The method chosen uses a low discrepency sequence sample of the defined space and explores permuatations of the samples in a methodical manner in such a way to maximize information returned about the probability sensitivity of the model. For this analysis we chose an N=100 values in that the primary sample is 100 points from a Halton sequence that draws 2 uncorrelated positions as defined by the parameter space. In this instance the parameter space has 48 variables. Thus for each of the 100 draws it draws from a 96 dimensional space. The secondary 48 is shuffled to destroy any residual correlation from the Halton draw. Then each parameter is permuted across these pairs in the space. This results in 9800 defined models runs.

For each run, we evaluate 3 scenarios for cost and quality. These are the 0, 2, and 3 scenarios of the ignite project.

Scenarios

- Scenario 0. (Reference) Single drug start on Clopidogrel no testing.
- Scenario 1. Single drug start on Tricagrelor no testing.
- Scenario 2. Start on Tricagrelor, switch all to Clopidogrel at 30 days.
- Scenario 3. Genotype and switch based on test.

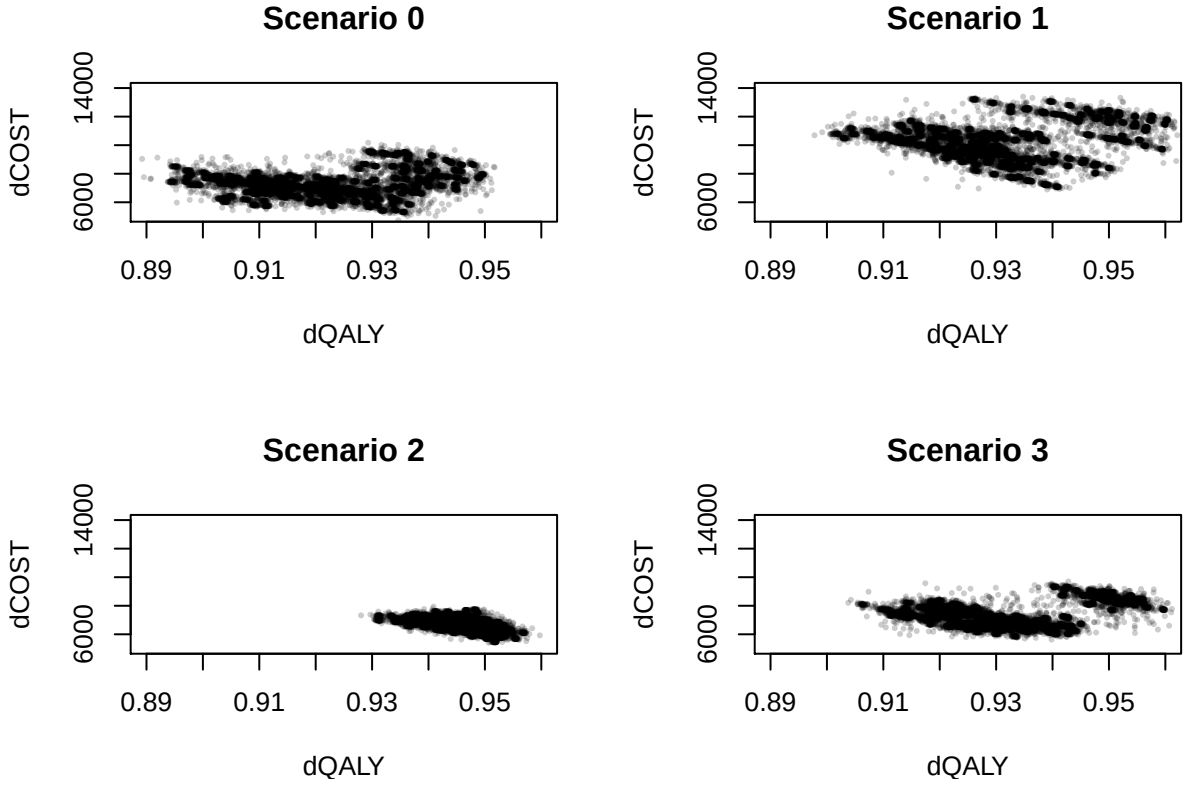
Ranges

Table 1: Parameter Ranges for PSA

Variable	Value	Low	High
vRiskST30.Non	0.0074	0.0024	0.0173
vRiskST365.Non	0.0135	0.0037	0.0347
vRiskST30.Alt.Non	0.0067	0.0002	0.0371
vRiskST365.Alt.Non	0	0.0000	0.0049
vRiskST30.LOF	0.021	0.0043	0.0615
vRiskST365.LOF	0	0.0000	0.0074
vRiskST30.Alt.LOF	0	0.0000	0.0156
vRiskST365.Alt.LOF	0.0224	0.0050	0.0712
vSt.Case.Fatality.Non	0.15	0.0010	0.3000
vSt.Case.Fatality.Alt.Non	0	0.0000	0.3000
vSt.Case.Fatality.LOF	0.18	0.0010	0.3600
vSt.Case.Fatality.Alt.LOF	0	0.0000	0.3000
vPrCABG.ST	0.08	0.0400	0.1200
vRiskMI30.Non	0.0225	0.0126	0.0371
vRiskMI365.Non	0.0379	0.0189	0.0679
vRiskMI30.Alt.Non	0.0133	0.0016	0.0481
vRiskMI365.Alt.Non	0.0484	0.0100	0.1416
vRiskMI30.LOF	0.0427	0.0157	0.0929
vRiskMI365.LOF	0.1262	0.0410	0.2945
vRiskMI30.Alt.LOF	0.0085	0.0010	0.0307
vRiskMI365.Alt.LOF	0.0327	0.0089	0.0838
vPrCABG.MI	0.08	0.0400	0.1200
vPrPCI.MI	0.55	0.4500	0.6500
vRiskStroke30.Non	0.009	0.0033	0.0196
vRiskStroke365.Non	0.0068	0.0008	0.0245
vRiskStroke30.Alt.Non	0	0.0000	0.0240
vRiskStroke365.Alt.Non	0	0.0000	0.0047
vRiskStroke30.LOF	0.0067	0.0002	0.0374
vRiskStroke365.LOF	0	0.0000	0.0075
vRiskStroke30.Alt.LOF	0	0.0000	0.0158
vRiskStroke365.Alt.LOF	0	0.0000	0.0025
vRiskDeath	0.0175	0.0000	0.1000
vRiskRV365	0.1	0.0500	0.1500
vPrCABG.RV	0.25	0.1500	0.3500
vRiskExtBleed	0.023	0.0150	0.0700
vRiskIntBleed	0.0015	0.0010	0.0020
vRiskTIMIMinor	0.02	0.0100	0.0600
vRiskFatalBleed	0.0015	0.0010	0.0030
vRR.ExtBleed.Ticagrelor	1.3	1.0500	1.6100
vRR.IntBleed.Ticagrelor	1.15	0.5500	2.4100
vRR.TIMIMinor.Ticagrelor	1.07	0.9100	1.2600
vRR.FatalBleed.Ticagrelor	0.87	0.4800	1.5900
vRiskCABGTIMImajor	0.022	0.0130	0.0310
vRR.RiskCABGTIMImajor.Ticagrelor	1.08	0.8500	1.3600
vRR.Bleed.LOF	0.84	0.7500	1.0000
costs.test	100	50.0000	250.0000
costs.clopidogrel	10	9.0000	70.0000
costs.ticagrelor	400	300.0000	425.0000

Raw Results

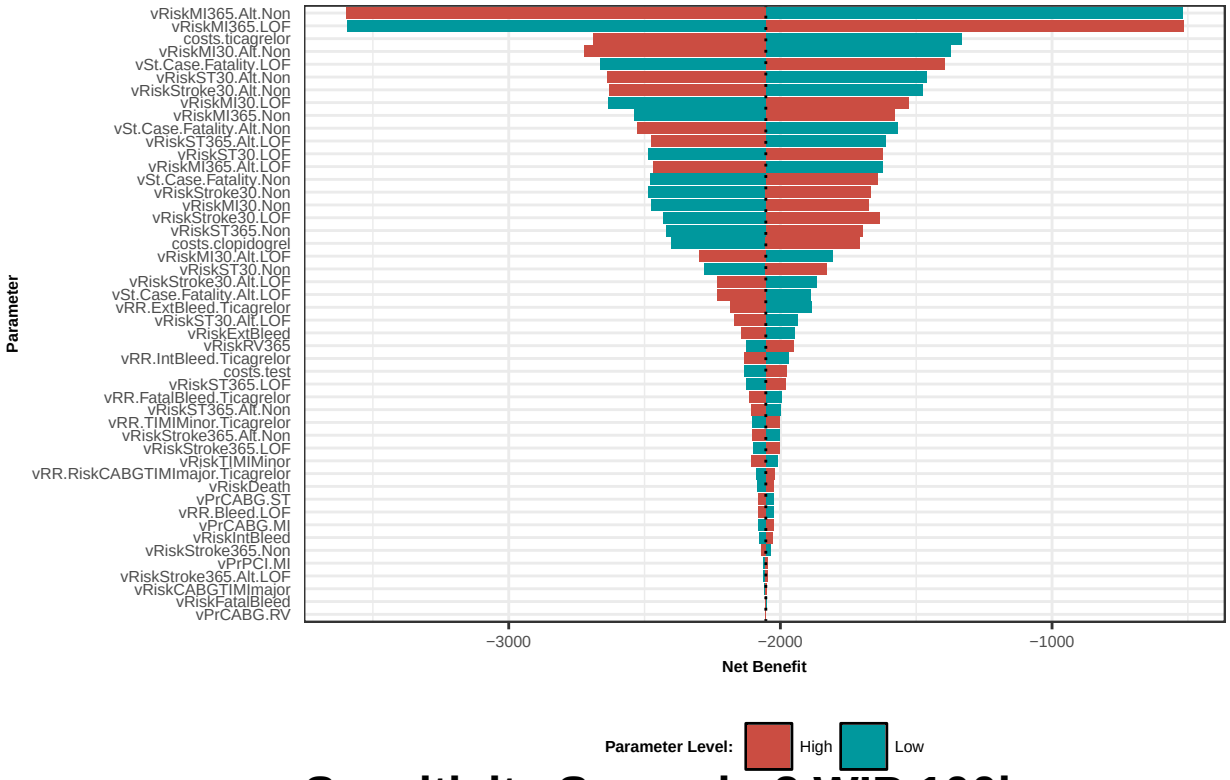
Given that the sample space is carefully designed and has a very specific structure to maximize information returned to the PSA, the raw data is not particularly useful. It's included here as an exploratory measure to show that runs did have variance and show how their structures varied.



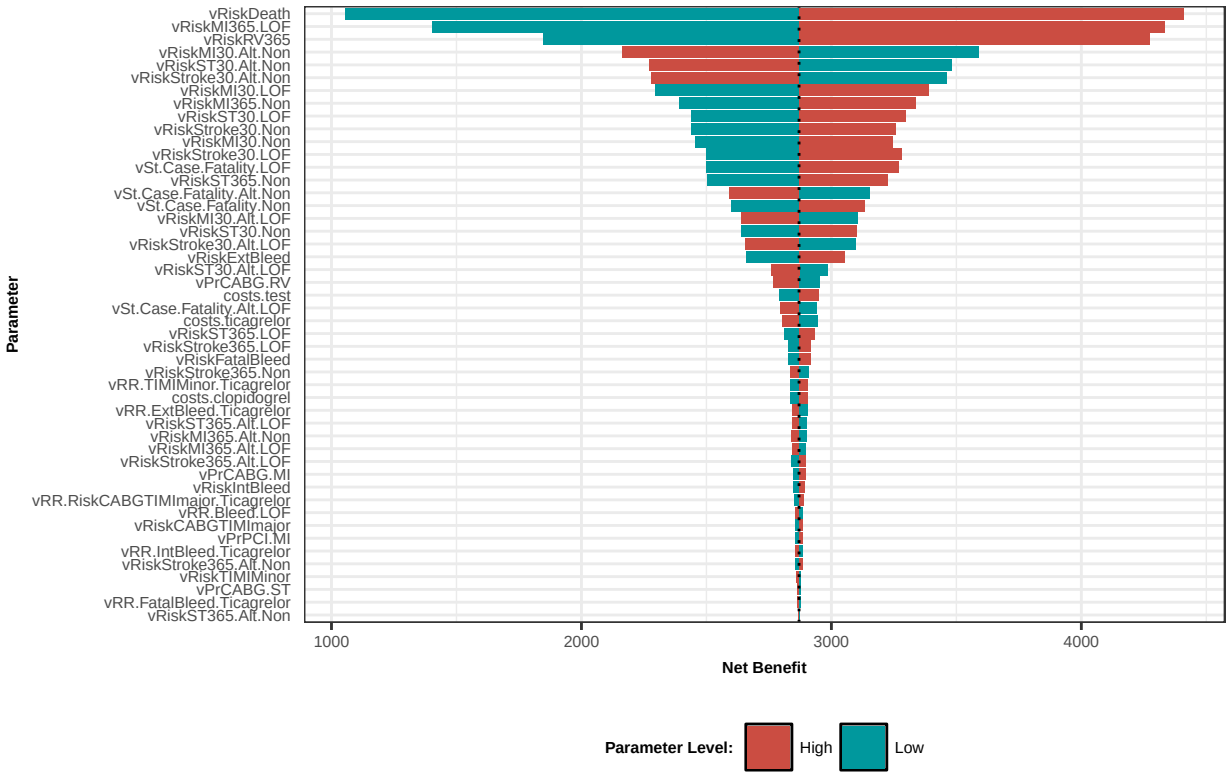
Tornado Plots

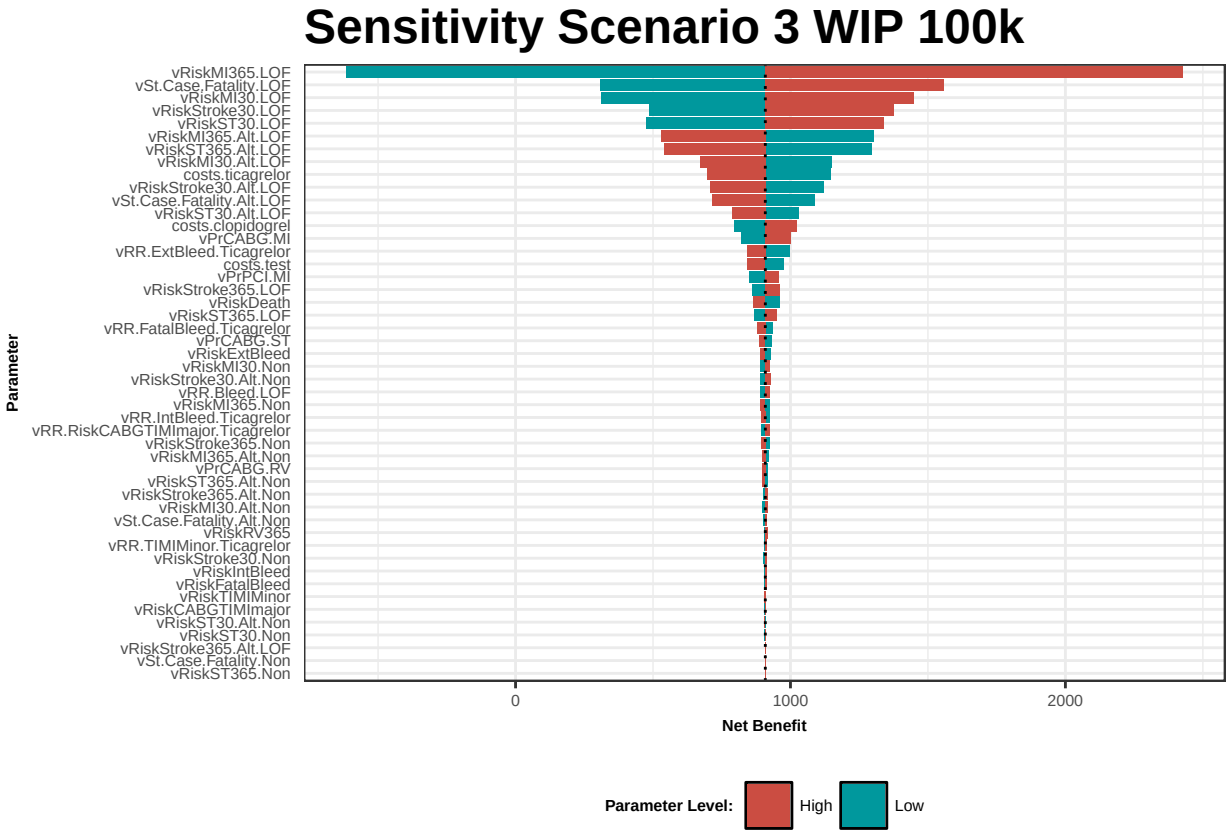
These are made with the standard linear regression across factors.

Sensitivity Scenario 1 WIP 100k



Sensitivity Scenario 2 WIP 100k

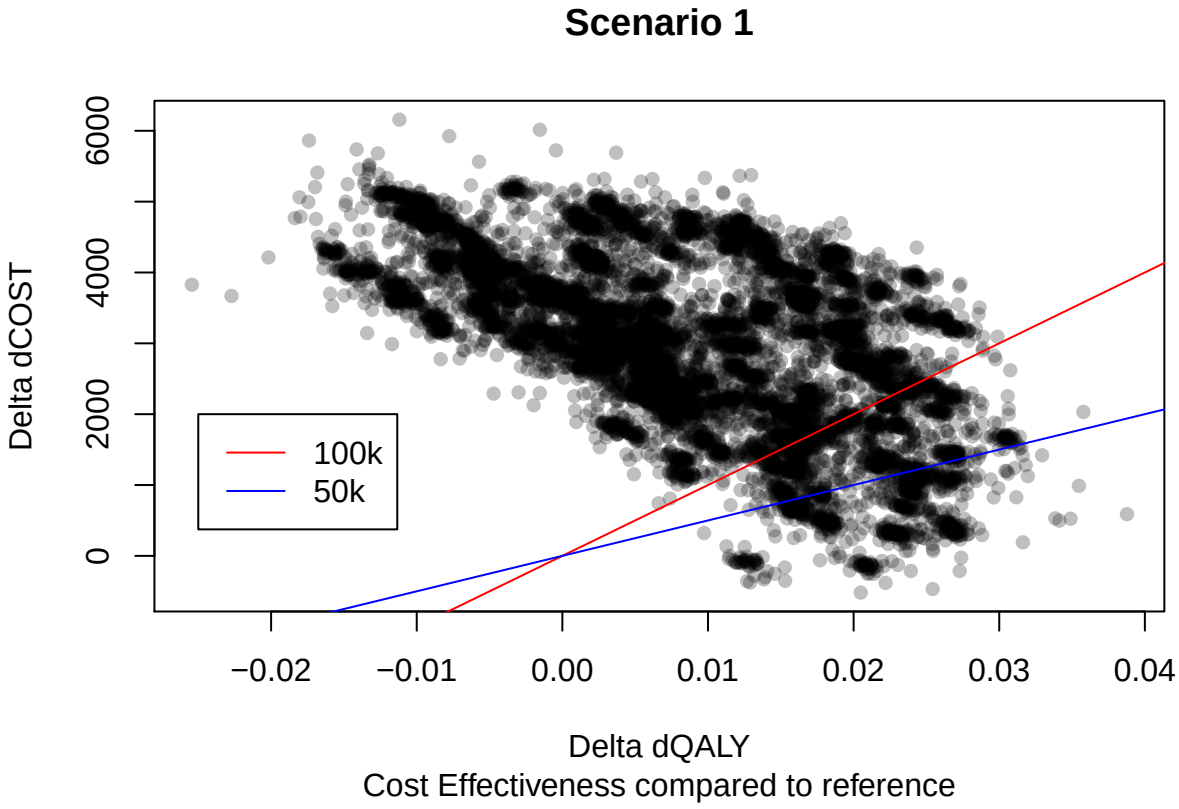


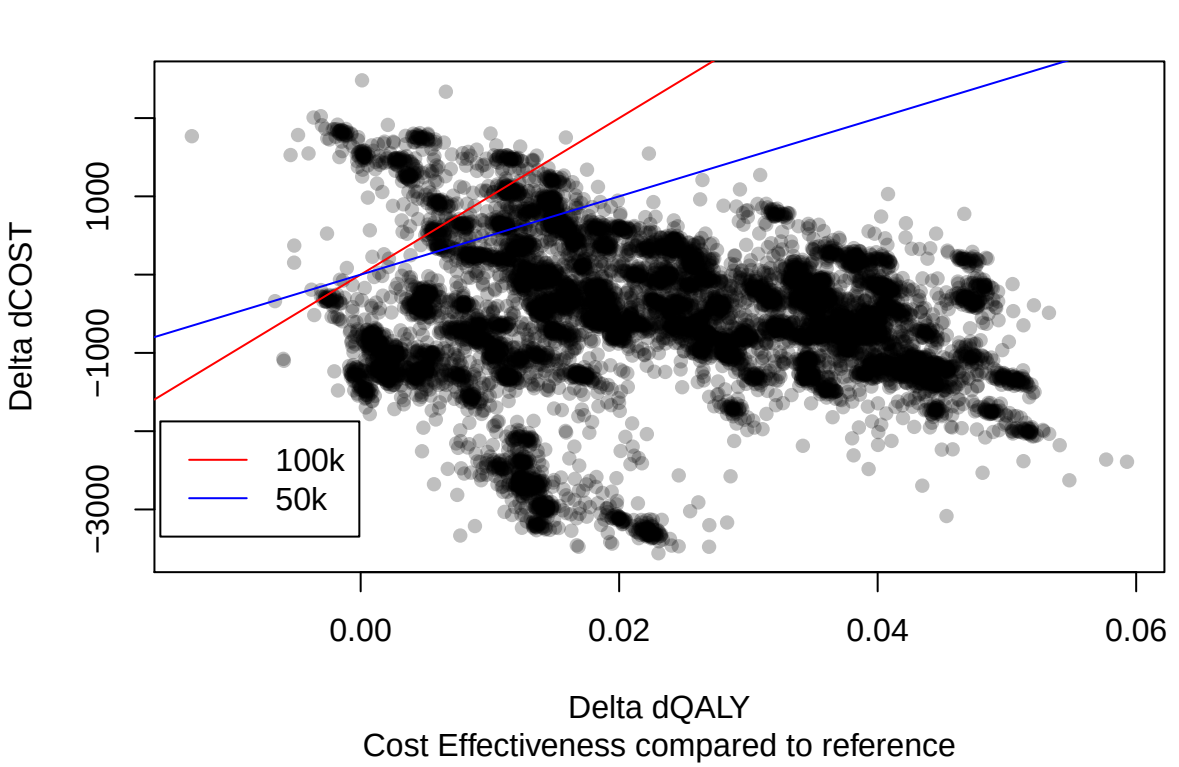


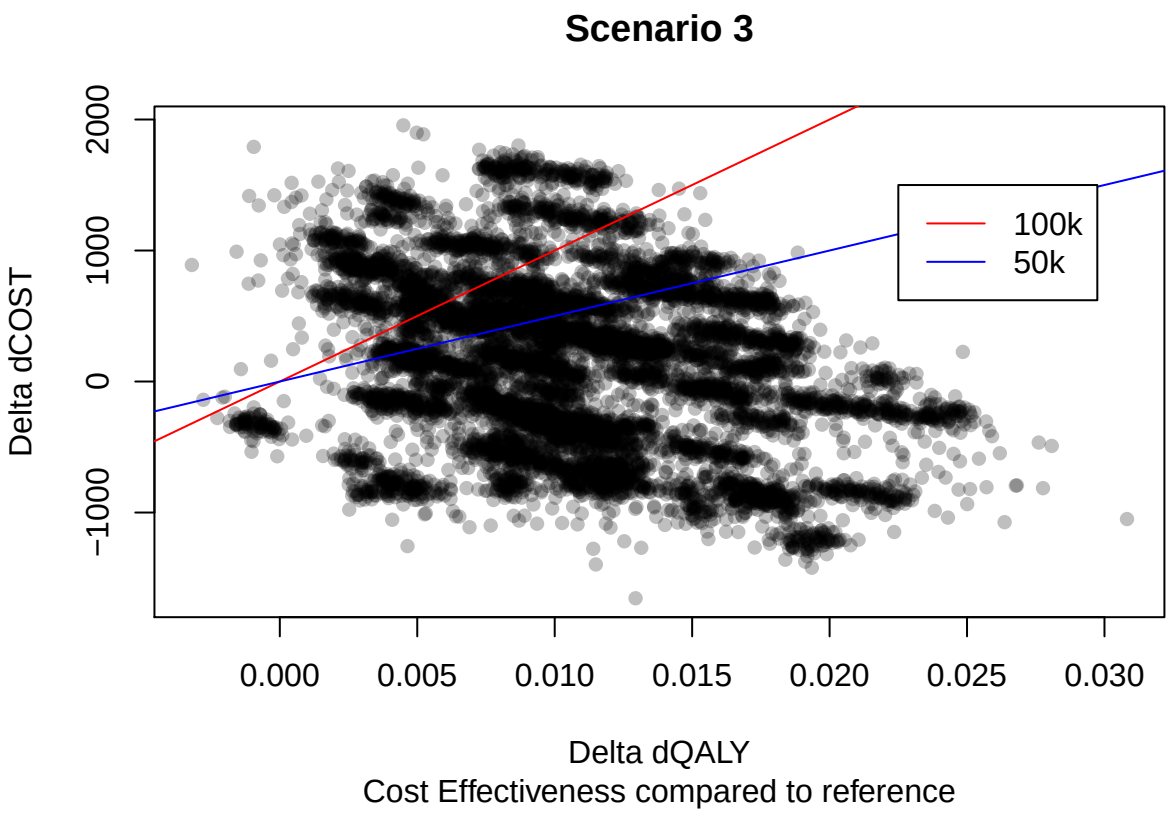
Percent of Runs Greater than Zero

- 18.06% of scenario 1 net monetary benefits are greater than zero at a williness to pay threshold of $100k.
- 95.78% of scenario 2 net monetary benefits are greater than zero at a williness to pay threshold of $100k.
- 83.11% of scenario 3 net monetary benefits are greater than zero at a williness to pay threshold of $100k.
- 7.71% of scenario 1 net monetary benefits are greater than zero at a williness to pay threshold of $50k.
- 91.16% of scenario 2 net monetary benefits are greater than zero at a williness to pay threshold of $50k.
- 67.76% of scenario 3 net monetary benefits are greater than zero at a williness to pay threshold of $50k.

Delta Plots


Scenario 1
Delta dCOST
6000
4000
2000
0
100k
50k
−0.02
−0.01
0.00
0.01
0.02
0.03
0.04
Delta dQALY
Cost Effectiveness compared to reference


Scenario 2
Delta dCOST
1000
−1000
−3000
100k
50k
0.00
0.02
0.04
0.06
Delta dQALY
Cost Effectiveness compared to reference


Scenario 3
Delta dCOST
2000
1000
0
−1000
0.000
0.005
0.010
0.015
0.020
0.025
0.030
100k
50k
Delta dQALY
Cost Effectiveness compared to reference

Saltelli Method Results 100k WTP Scenario 2

Table 2: Saltelli Ranking for Direct Contribution to Variance

Variable	Single
vRiskDeath	16.98
vRiskStroke30.Alt.Non	7.68
vRiskMI30.Alt.Non	5.07
vRiskStroke30.LOF	4.26
vRiskST30.Alt.Non	3.83
vRiskStroke30.Non	3.46
vSt.Case.Fatality.LOF	3.25
vRiskMI365.LOF	2.88
vRiskStroke30.Alt.LOF	2.65
vRiskST30.LOF	2.61
vRiskExtBleed	2.44
vRiskMI30.LOF	2.26
vRiskMI30.Non	2.04
vRiskST365.Non	1.83
costs.ticagrelor	1.76
vRiskMI365.Non	1.65
costs.clopidogrel	1.5
vRiskMI365.Alt.Non	1.48
vPrCABG.ST	1.46
vRR.IntBleed.Ticagrelor	1.41
vRiskCABGTIMImajor	1.35
vRiskMI30.Alt.LOF	1.34
vRR.RiskCABGTIMImajor.Ticagrelor	1.26
vRiskST30.Non	1.22
vRiskStroke365.Non	1.22
vRiskStroke365.Alt.LOF	1.19
vRR.FatalBleed.Ticagrelor	1.18
vSt.Case.Fatality.Alt.Non	1.16
costs.test	1.13
vRR.TIMIMinor.Ticagrelor	1.12
vPrPCI.MI	1.1
vRiskRV365	1.1
vRiskTIMIMinor	1.08
vRR.ExtBleed.Ticagrelor	1.08
vRiskST30.Alt.LOF	1.05
vRiskST365.LOF	1.02
vSt.Case.Fatality.Alt.LOF	1
vRiskStroke365.Alt.Non	0.98
vPrCABG.MI	0.95
vPrCABG.RV	0.95
vRR.Bleed.LOF	0.93
vRiskST365.Alt.LOF	0.91
vRiskIntBleed	0.9
vRiskST365.Alt.Non	0.89
vSt.Case.Fatality.Non	0.87
vRiskMI365.Alt.LOF	0.85
vRiskFatalBleed	0.85
vRiskStroke365.LOF	0.81

Scaled to 100%

Table 3: Saltelli Ranking Including All Interactions to Variance	
Variable	**Total**
vRiskDeath	38.79
vRiskStroke30.Alt.Non	15.17
vRiskMI30.Alt.Non	10.98
vRiskStroke30.LOF	7.53
vRiskStroke30.Non	7.49
vRiskST30.Alt.Non	7.02
vRiskStroke30.Alt.LOF	5.01
vRiskST30.LOF	5
vRiskMI365.Non	4.96
vRiskMI30.LOF	4.87
vRiskRV365	4.71
vRiskExtBleed	4.63
vRiskMI365.LOF	3.76
vRiskMI30.Non	3.11
vRiskMI30.Alt.LOF	2.98
vPrCABG.RV	2.98
vRiskST365.Non	2.74
vRiskST365.Alt.LOF	2.14
vSt.Case.Fatality.Non	2.08
vPrPCI.MI	1.93
vRiskMI365.Alt.LOF	1.89
vRiskST30.Alt.LOF	1.86
vRiskST30.Non	1.78
vSt.Case.Fatality.Alt.LOF	1.74
vRiskStroke365.LOF	1.74
vRiskStroke365.Alt.Non	1.61
vRiskST365.Alt.Non	1.55
vRiskIntBleed	1.48
vRR.ExtBleed.Ticagrelor	1.48
costs.clopidogrel	1.38
vRiskST365.LOF	1.36
costs.ticagrelor	1.32
vRiskStroke365.Alt.LOF	1.21
vRiskFatalBleed	1.19
vPrCABG.MI	1.13
vRiskTIMIMinor	1.12
vRR.Bleed.LOF	1.04
vRR.FatalBleed.Ticagrelor	1.02
vRiskMI365.Alt.Non	1
vRiskCABGTIMImajor	0.94
vRiskStroke365.Non	0.93
vSt.Case.Fatality.LOF	0.9
vRR.RiskCABGTIMImajor.Ticagrelor	0.85
costs.test	0.85
vPrCABG.ST	0.76
vRR.TIMIMinor.Ticagrelor	0.75
vSt.Case.Fatality.Alt.Non	0.69
vRR.IntBleed.Ticagrelor	0

Total exceeds 100% since variance contribution occurs in multiple terms via interaction

Saltelli Method Results 100k WTP Scenario 3

Table 4: Saltelli Ranking for Direct Contribution to Variance

Variable	Single
vRiskMI365.LOF	46.83
vRiskStroke30.LOF	7.95
vSt.Case.Fatality.LOF	7.47
vRiskST30.LOF	7.06
vRiskST365.Alt.LOF	3.72
costs.ticagrelor	3.36
vRiskMI365.Alt.LOF	3.12
vRiskStroke30.Alt.LOF	2.33
costs.clopidogrel	1.97
vPrPCI.MI	1.53
vRiskMI365.Alt.Non	1.32
vRR.IntBleed.Ticagrelor	1.32
vRR.RiskCABGTIMImajor.Ticagrelor	1.05
vSt.Case.Fatality.Non	0.95
vRR.TIMIMinor.Ticagrelor	0.94
vRiskMI30.Non	0.8
vRiskCABGTIMImajor	0.73
vRiskStroke365.Non	0.57
vPrCABG.ST	0.55
vRiskST30.Non	0.51
vRiskStroke30.Alt.Non	0.49
vRR.FatalBleed.Ticagrelor	0.49
vRiskST365.Alt.Non	0.43
vRiskStroke365.Alt.LOF	0.42
vRiskST365.Non	0.41
vRiskStroke30.Non	0.41
vRiskTIMIMinor	0.4
vRiskST365.LOF	0.39
vRiskST30.Alt.Non	0.34
vRR.ExtBleed.Ticagrelor	0.31
vPrCABG.RV	0.29
costs.test	0.29
vRiskStroke365.Alt.Non	0.27
vRiskExtBleed	0.24
vRiskFatalBleed	0.22
vRiskMI30.Alt.Non	0.21
vRiskST30.Alt.LOF	0.2
vSt.Case.Fatality.Alt.Non	0.05
vRiskStroke365.LOF	0.04
vRiskIntBleed	0.03
vSt.Case.Fatality.Alt.LOF	0
vRiskMI365.Non	0
vRiskMI30.LOF	0
vRiskMI30.Alt.LOF	0
vPrCABG.MI	0
vRiskDeath	0
vRiskRV365	0
vRR.Bleed.LOF	0

Scaled to 100%

Table 5: Saltelli Ranking Including All Interactions to Variance	
Variable	**Total**
vRiskMI365.LOF	67.14
vRiskStroke30.LOF	17.88
vRiskST30.LOF	16.58
vRiskMI365.Alt.LOF	10.21
vRiskST365.Alt.LOF	9.31
costs.ticagrelor	9.08
vSt.Case.Fatality.LOF	7.54
vRiskStroke30.Alt.LOF	7.52
costs.clopidogrel	6.19
vRiskST365.Non	5.34
vRiskStroke365.LOF	5.3
vPrCABG.RV	5.19
costs.test	5.16
vRiskStroke365.Alt.LOF	5.14
vRiskTIMIMinor	5.14
vRiskST30.Alt.Non	5.12
vRiskStroke365.Non	5.05
vRiskStroke365.Alt.Non	5.01
vRiskMI365.Non	4.99
vRiskMI30.Alt.Non	4.94
vRiskDeath	4.7
vRiskST365.LOF	4.69
vRiskST365.Alt.Non	4.63
vRiskST30.Alt.LOF	4.63
vRR.RiskCABGTIMImajor.Ticagrelor	4.6
vRiskRV365	4.49
vRiskIntBleed	4.44
vRiskExtBleed	4.4
vRR.ExtBleed.Ticagrelor	4.38
vSt.Case.Fatality.Non	4.31
vRiskStroke30.Non	4.26
vPrPCI.MI	4.23
vRiskFatalBleed	4.22
vPrCABG.ST	4.19
vRiskStroke30.Alt.Non	3.98
vRiskST30.Non	3.93
vRR.FatalBleed.Ticagrelor	3.93
vRiskCABGTIMImajor	3.91
vRiskMI30.Non	3.88
vRR.Bleed.LOF	3.81
vRiskMI365.Alt.Non	3.57
vPrCABG.MI	3.52
vSt.Case.Fatality.Alt.Non	3.49
vRR.TIMIMinor.Ticagrelor	3.49
vSt.Case.Fatality.Alt.LOF	2.91
vRiskMI30.Alt.LOF	2.78
vRR.IntBleed.Ticagrelor	2.3
vRiskMI30.LOF	0

Total exceeds 100% since variance contribution occurs in multiple terms via interaction 3