# Supplementary Materials

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# 1 The BOIN Design - Full Results

**Scenario 1**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.5 | 2.3 | 2.6 |
| $d_2^A$ | 2.4 | 3.0 | 4.8 |
| $d_3^A$ | 2.9 | 5.1 | **9.0** |

**Scenario 2**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.7 | 2.5 | 3.9 |
| $d_2^A$ | 2.5 | 4.3 | **5.8** |
| $d_3^A$ | 3.7 | **5.7** | 3.7 |

**Scenario 3**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.3 | 1.9 | 2.9 |
| $d_2^A$ | 2.4 | 3.3 | 9.0 |
| $d_3^A$ | 3.1 | **5.0** | 5.1 |

**Scenario 4**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.6 | 2.4 | 4.2 |
| $d_2^A$ | 2.5 | 5.0 | **7.4** |
| $d_3^A$ | 4.6 | 4.6 | 2.3 |

**Scenario 5**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.6 | 3.0 | 8.6 |
| $d_2^A$ | 5.3 | **6.8** | 4.2 |
| $d_3^A$ | 2.5 | 1.5 | 0.5 |

**Scenario 6**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 4.5 | 4.4 | **4.7** |
| $d_2^A$ | 4.2 | **5.9** | 2.7 |
| $d_3^A$ | **4.7** | 3.0 | 0.6 |

**Scenario 7**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 4.8 | 5.5 | 2.7 |
| $d_2^A$ | 4.7 | **6.7** | 1.9 |
| $d_3^A$ | **5.5** | 2.6 | 0.4 |

**Scenario 8**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.6 | 2.7 | 3.7 |
| $d_2^A$ | 3.2 | 5.8 | **7.2** |
| $d_3^A$ | **4.1** | 3.4 | 1.8 |

**Scenario 9**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 5.6 | 6.4 | **7.4** |
| $d_2^A$ | **5.6** | 4.2 | 1.6 |
| $d_3^A$ | 2.5 | 1.2 | 0.3 |

**Scenario 10**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 8.9 | **7.2** | 2.5 |
| $d_2^A$ | **7.6** | 3.0 | 0.5 |
| $d_3^A$ | 2.6 | 0.6 | 0.1 |

**Scenario 11**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 4.1 | 3.6 | 13.4 |
| $d_2^A$ | **6.4** | 4.1 | 1.6 |
| $d_3^A$ | 2.0 | 0.7 | 0.1 |

**Scenario 12**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 12.1 | **8.1** | 3.0 |
| $d_2^A$ | 4.6 | 1.7 | 0.3 |
| $d_3^A$ | 0.6 | 0.1 | 0.0 |

**Scenario 13**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | **13.7** | 3.8 | 0.8 |
| $d_2^A$ | 3.8 | 0.8 | 0.2 |
| $d_3^A$ | 0.8 | 0.2 | 0.0 |

**Scenario 14**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 8.8 | 1.4 | 0.1 |
| $d_2^A$ | 1.3 | 0.3 | 0.0 |
| $d_3^A$ | 0.2 | 0.0 | 0.0 |

**Scenario 15**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 4.2 | 2.1 | 1.5 |
| $d_2^A$ | 2.1 | 2.0 | 2.1 |
| $d_3^A$ | 1.8 | 2.4 | 16.5 |

Table 1: Mean number of patients treated at each combination for the BOIN design.

**Scenario 1**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.4 | 7.4 |
| $d_2^A$ | 0.6 | 2.9 | 19.2 |
| $d_3^A$ | 8.7 | 20.8 | **39.0** |

**Scenario 2**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.3 | 0.8 | 15.2 |
| $d_2^A$ | 1.6 | 10.0 | **24.4** |
| $d_3^A$ | 13.4 | **24.4** | 9.2 |

**Scenario 3**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.2 | 8.9 |
| $d_2^A$ | 0.6 | 4.2 | 44.0 |
| $d_3^A$ | 10.9 | **20.4** | 10.6 |

**Scenario 4**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.8 | 16.9 |
| $d_2^A$ | 1.5 | 15.6 | **32.8** |
| $d_3^A$ | 20.4 | 10.2 | 0.8 |

**Scenario 5**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.6 | 3.1 | 37.9 |
| $d_2^A$ | 14.4 | **25.8** | 10.6 |
| $d_3^A$ | 5.4 | 1.9 | 0.1 |

**Scenario 6**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.9 | 10.1 | **18.6** |
| $d_2^A$ | 9.9 | **22.1** | 7.2 |
| $d_3^A$ | **18.9** | 8.1 | 0.2 |

**Scenario 7**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 1.6 | 15.9 | 6.7 |
| $d_2^A$ | 10.5 | **29.8** | 3.1 |
| $d_3^A$ | **22.7** | 5.0 | 0.4 |

**Scenario 8**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 1.9 | 14.6 |
| $d_2^A$ | 4.6 | 19.4 | **33.0** |
| $d_3^A$ | **14.9** | 8.5 | 1.9 |

**Scenario 9**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.8 | 20.1 | **30.9** |
| $d_2^A$ | **16.6** | 12.1 | 3.0 |
| $d_3^A$ | 7.2 | 2.4 | 0.0 |

**Scenario 10**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 16.8 | **24.6** | 6.2 |
| $d_2^A$ | **27.4** | 7.1 | 1.0 |
| $d_3^A$ | 6.3 | 0.8 | 0.0 |

**Scenario 11**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 1.4 | 4.0 | 60.0 |
| $d_2^A$ | **20.4** | 8.8 | 0.8 |
| $d_3^A$ | 4.0 | 0.4 | 0.0 |

**Scenario 12**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 31.6 | **31.1** | 8.0 |
| $d_2^A$ | 8.8 | 2.2 | 0.3 |
| $d_3^A$ | 0.2 | 0.0 | 0.0 |

**Scenario 13**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | **37.1** | 8.6 | 1.1 |
| $d_2^A$ | 8.1 | 1.6 | 0.1 |
| $d_3^A$ | 1.1 | 0.1 | 0.0 |

**Scenario 14**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 10.4 | 1.6 | 0.0 |
| $d_2^A$ | 1.5 | 0.3 | 0.0 |
| $d_3^A$ | 0.2 | 0.0 | 0.0 |

**Scenario 15**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.1 | 0.1 | 3.0 |
| $d_2^A$ | 0.0 | 0.2 | 3.0 |
| $d_3^A$ | 3.8 | 3.6 | 82.2 |

Table 2: Proportion each combination was selected for the BOIN design.

# 2 The Keyboard Design - Full Results

**Scenario 1**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.6 | 2.5 | 2.1 |
| $d_2^A$ | 2.3 | 3.2 | 4.8 |
| $d_3^A$ | 2.0 | 4.4 | **10.7** |

**Scenario 2**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.7 | 2.5 | 2.9 |
| $d_2^A$ | 2.7 | 4.4 | **5.9** |
| $d_3^A$ | 3.2 | **5.8** | 4.5 |

**Scenario 3**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.3 | 1.9 | 2.2 |
| $d_2^A$ | 2.6 | 3.6 | 7.3 |
| $d_3^A$ | 2.9 | **6.0** | 6.2 |

**Scenario 4**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.6 | 2.4 | 3.0 |
| $d_2^A$ | 2.8 | 5.2 | **7.2** |
| $d_3^A$ | 4.6 | 4.6 | 2.3 |

**Scenario 5**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.7 | 2.7 | 5.8 |
| $d_2^A$ | 6.1 | **7.3** | 4.7 |
| $d_3^A$ | 3.0 | 2.0 | 0.7 |

**Scenario 6**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 4.5 | 4.5 | **4.5** |
| $d_2^A$ | 4.2 | **6.2** | 3.1 |
| $d_3^A$ | **4.1** | 2.9 | 0.8 |

**Scenario 7**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 4.9 | 5.5 | 2.7 |
| $d_2^A$ | 4.5 | **7.1** | 2.2 |
| $d_3^A$ | **4.4** | 2.8 | 0.5 |

**Scenario 8**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.6 | 2.7 | 3.4 |
| $d_2^A$ | 3.3 | 5.5 | **6.9** |
| $d_3^A$ | **4.1** | 4.1 | 2.2 |

**Scenario 9**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 5.7 | 5.8 | **6.3** |
| $d_2^A$ | **6.4** | 4.8 | 1.8 |
| $d_3^A$ | 2.4 | 1.2 | 0.3 |

**Scenario 10**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 8.3 | **7.5** | 2.6 |
| $d_2^A$ | **7.4** | 3.5 | 0.7 |
| $d_3^A$ | 2.6 | 0.6 | 0.1 |

**Scenario 11**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 4.6 | 3.5 | 8.8 |
| $d_2^A$ | **8.0** | 5.5 | 2.1 |
| $d_3^A$ | 2.6 | 0.8 | 0.1 |

**Scenario 12**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 11.2 | **8.0** | 2.9 |
| $d_2^A$ | 5.6 | 2.1 | 0.4 |
| $d_3^A$ | 0.7 | 0.1 | 0.0 |

**Scenario 13**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | **14.0** | 4.1 | 0.7 |
| $d_2^A$ | 4.2 | 0.8 | 0.1 |
| $d_3^A$ | 0.7 | 0.1 | 0.0 |

**Scenario 14**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 9.5 | 1.2 | 0.2 |
| $d_2^A$ | 1.4 | 0.2 | 0.0 |
| $d_3^A$ | 0.2 | 0.0 | 0.0 |

**Scenario 15**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 4.2 | 2.1 | 1.1 |
| $d_2^A$ | 2.2 | 2.2 | 2.1 |
| $d_3^A$ | 1.4 | 2.2 | 17.3 |

Table 3: Mean number of patients treated at each combination for the Keyboard design.

**Scenario 1**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.4 | 5.1 |
| $d_2^A$ | 0.3 | 2.3 | 19.4 |
| $d_3^A$ | 5.4 | 16.8 | **49.5** |

**Scenario 2**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.1 | 0.9 | 10.5 |
| $d_2^A$ | 0.8 | 9.5 | **27.5** |
| $d_3^A$ | 11.2 | **25.9** | 12.7 |

**Scenario 3**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.1 | 5.8 |
| $d_2^A$ | 0.5 | 5.0 | 37.0 |
| $d_3^A$ | 9.0 | **27.4** | 15.2 |

**Scenario 4**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.6 | 11.3 |
| $d_2^A$ | 1.3 | 16.1 | **35.4** |
| $d_3^A$ | 21.3 | 11.8 | 1.3 |

**Scenario 5**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.1 | 1.9 | 27.0 |
| $d_2^A$ | 15.9 | **30.6** | 13.8 |
| $d_3^A$ | 7.5 | 2.9 | 0.2 |

**Scenario 6**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.6 | 8.3 | **18.8** |
| $d_2^A$ | 8.2 | **24.0** | 9.9 |
| $d_3^A$ | **16.8** | 9.3 | 0.6 |

**Scenario 7**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 1.0 | 15.2 | 7.7 |
| $d_2^A$ | 8.3 | **31.4** | 5.5 |
| $d_3^A$ | **19.8** | 6.3 | 0.4 |

**Scenario 8**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 1.2 | 12.6 |
| $d_2^A$ | 2.1 | 16.8 | **35.9** |
| $d_3^A$ | **16.8** | 11.8 | 2.1 |

**Scenario 9**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 2.4 | 15.7 | **29.9** |
| $d_2^A$ | **18.8** | 15.0 | 2.9 |
| $d_3^A$ | 8.5 | 2.8 | 0.3 |

**Scenario 10**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 11.8 | **27.5** | 7.8 |
| $d_2^A$ | **26.4** | 8.8 | 1.2 |
| $d_3^A$ | 7.3 | 0.8 | 0.0 |

**Scenario 11**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 1.1 | 3.6 | 46.9 |
| $d_2^A$ | **26.1** | 13.5 | 1.0 |
| $d_3^A$ | 7.4 | 0.4 | 0.0 |

**Scenario 12**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 25.3 | **32.6** | 10.1 |
| $d_2^A$ | 11.5 | 3.8 | 0.2 |
| $d_3^A$ | 0.5 | 0.2 | 0.0 |

**Scenario 13**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | **37.4** | 8.9 | 1.5 |
| $d_2^A$ | 9.2 | 1.1 | 0.0 |
| $d_3^A$ | 1.2 | 0.2 | 0.0 |

**Scenario 14**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 11.8 | 1.1 | 0.2 |
| $d_2^A$ | 1.3 | 0.2 | 0.0 |
| $d_3^A$ | 0.1 | 0.0 | 0.0 |

**Scenario 15**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.2 | 1.0 |
| $d_2^A$ | 0.2 | 0.5 | 2.1 |
| $d_3^A$ | 1.7 | 2.2 | 88.8 |

Table 4: Proportion each combination was selected for the Keyboard design.

# 3 The PIPE Design - Full Results

**Scenario 1**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.1 | 1.8 | 3.8 |
| $d_2^A$ | 1.8 | 4.6 | 6.4 |
| $d_3^A$ | 4.1 | 46.5 | **3.9** |

**Scenario 2**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.1 | 2.1 | 5.7 |
| $d_2^A$ | 2.2 | 6.1 | **5.4** |
| $d_3^A$ | 5.4 | **5.1** | 1.0 |

**Scenario 3**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.0 | 1.8 | 4.4 |
| $d_2^A$ | 1.8 | 5.4 | 7.4 |
| $d_3^A$ | 4.5 | **5.9** | 1.7 |

**Scenario 4**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.0 | 2.1 | 6.0 |
| $d_2^A$ | 2.3 | 6.8 | **5.4** |
| $d_3^A$ | 6.0 | 4.0 | 0.4 |

**Scenario 5**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.0 | 3.6 | 9.9 |
| $d_2^A$ | 3.8 | **7.2** | 2.9 |
| $d_3^A$ | 4.2 | 1.3 | 0.0 |

**Scenario 6**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.5 | 4.2 | **6.1** |
| $d_2^A$ | 4.2 | **7.1** | 2.2 |
| $d_3^A$ | **6.3** | 2.2 | 0.1 |

**Scenario 7**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.6 | 5.2 | 4.7 |
| $d_2^A$ | 5.2 | **7.3** | 1.2 |
| $d_3^A$ | **7.0** | 1.7 | 0.1 |

**Scenario 8**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.0 | 2.4 | 6.2 |
| $d_2^A$ | 2.6 | 7.5 | **4.9** |
| $d_3^A$ | **5.7** | 3.2 | 0.3 |

**Scenario 9**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 4.1 | 6.8 | **7.4** |
| $d_2^A$ | **5.4** | 5.5 | 1.2 |
| $d_3^A$ | 4.5 | 1.0 | 0.0 |

**Scenario 10**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 7.3 | **7.6** | 4.1 |
| $d_2^A$ | **7.7** | 4.1 | 0.5 |
| $d_3^A$ | 4.0 | 0.5 | 0.0 |

**Scenario 11**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.1 | 4.2 | 13.7 |
| $d_2^A$ | **4.3** | 5.1 | 1.6 |
| $d_3^A$ | 3.4 | 0.6 | 0.0 |

**Scenario 12**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 10.4 | **9.3** | 4.2 |
| $d_2^A$ | 5.8 | 2.9 | 0.3 |
| $d_3^A$ | 1.8 | 0.2 | 0.0 |

**Scenario 13**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | **14.1** | 5.6 | 2.1 |
| $d_2^A$ | 5.5 | 2.2 | 0.2 |
| $d_3^A$ | 2.0 | 0.2 | 0.0 |

**Scenario 14**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 12.0 | 3.7 | 1.0 |
| $d_2^A$ | 3.7 | 1.2 | 0.1 |
| $d_3^A$ | 1.0 | 0.1 | 0.0 |

**Scenario 15**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.2 | 1.7 | 2.3 |
| $d_2^A$ | 1.5 | 2.7 | 5.0 |
| $d_3^A$ | 2.0 | 5.0 | 12.5 |

Table 5: Mean number of patients treated at each combination for the PIPE design.

**Scenario 1**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.2 | 0.8 | 13.4 |
| $d_2^A$ | 0.7 | 6.0 | 26.8 |
| $d_3^A$ | 13.1 | 24.4 | **13.3** |

**Scenario 2**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.2 | 1.4 | 22.7 |
| $d_2^A$ | 3.4 | 12.8 | **18.9** |
| $d_3^A$ | 21.9 | **16.4** | 1.3 |

**Scenario 3**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.2 | 13.7 |
| $d_2^A$ | 1.6 | 8.2 | 31.1 |
| $d_3^A$ | 22.1 | **19.5** | 2.4 |

**Scenario 4**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 1.6 | 23.9 |
| $d_2^A$ | 2.9 | 17.5 | **19.4** |
| $d_3^A$ | 26.9 | 6.7 | 0.2 |

**Scenario 5**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 4.4 | 40.1 |
| $d_2^A$ | 17.9 | **19.9** | 4.8 |
| $d_3^A$ | 11.2 | 0.7 | 0.0 |

**Scenario 6**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 1.8 | 14.3 | **20.1** |
| $d_2^A$ | 13.6 | **19.2** | 3.4 |
| $d_3^A$ | **22.8** | 3.5 | 0.0 |

**Scenario 7**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 2.5 | 21.4 | 10.6 |
| $d_2^A$ | 18.5 | **20.1** | 1.0 |
| $d_3^A$ | **23.3** | 1.6 | 0.0 |

**Scenario 8**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 4.2 | 25.1 |
| $d_2^A$ | 5.6 | 19.4 | **16.6** |
| $d_3^A$ | **23.2** | 4.5 | 0.1 |

**Scenario 9**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 6.3 | 28.6 | **24.6** |
| $d_2^A$ | **17.8** | 8.2 | 0.9 |
| $d_3^A$ | 11.7 | 1.0 | 0.0 |

**Scenario 10**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 27.9 | **25.1** | 6.0 |
| $d_2^A$ | **26.6** | 4.5 | 0.2 |
| $d_3^A$ | 6.2 | 0.3 | 0.0 |

**Scenario 11**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.2 | 4.0 | 56.6 |
| $d_2^A$ | **23.9** | 6.3 | 0.4 |
| $d_3^A$ | 8.3 | 0.3 | 0.0 |

**Scenario 12**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 41.6 | **32.2** | 4.9 |
| $d_2^A$ | 7.6 | 1.8 | 0.0 |
| $d_3^A$ | 0.6 | 0.0 | 0.0 |

**Scenario 13**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | **38.0** | 7.5 | 1.9 |
| $d_2^A$ | 6.5 | 1.4 | 0.0 |
| $d_3^A$ | 2.0 | 0.1 | 0.0 |

**Scenario 14**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 8.7 | 2.4 | 0.6 |
| $d_2^A$ | 2.1 | 0.4 | 0.0 |
| $d_3^A$ | 0.4 | 0.0 | 0.0 |

**Scenario 15**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.2 | 0.2 | 5.2 |
| $d_2^A$ | 0.2 | 0.4 | 8.6 |
| $d_3^A$ | 4.6 | 8.4 | 70.3 |

Table 6: Proportion each combination was selected for the Keyboard design.

# 4 The Surface-Free Design - Full Results

**Scenario 1**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.0 | 1.9 | 2.3 |
| $d_2^A$ | 1.8 | 3.3 | 5.3 |
| $d_3^A$ | 2.4 | 5.2 | **10.6** |

**Scenario 2**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.0 | 2.1 | 3.2 |
| $d_2^A$ | 2.0 | 4.8 | **6.7** |
| $d_3^A$ | 3.6 | **6.2** | 4.3 |

**Scenario 3**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.0 | 1.7 | 2.2 |
| $d_2^A$ | 1.9 | 3.6 | 7.3 |
| $d_3^A$ | 3.3 | **6.5** | 6.3 |

**Scenario 4**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.1 | 2.1 | 3.6 |
| $d_2^A$ | 2.2 | 5.6 | **7.4** |
| $d_3^A$ | 4.3 | 5.9 | 1.9 |

**Scenario 5**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.0 | 2.4 | 5.7 |
| $d_2^A$ | 4.7 | **8.5** | 5.2 |
| $d_3^A$ | 3.9 | 2.2 | 0.4 |

**Scenario 6**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.3 | 4.0 | **4.9** |
| $d_2^A$ | 4.0 | **7.9** | 3.3 |
| $d_3^A$ | **4.7** | 3.3 | 0.5 |

**Scenario 7**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.4 | 5.1 | 4.0 |
| $d_2^A$ | 4.3 | **8.3** | 2.0 |
| $d_3^A$ | **5.5** | 3.0 | 0.3 |

**Scenario 8**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.1 | 2.1 | 3.8 |
| $d_2^A$ | 2.4 | 6.3 | **7.2** |
| $d_3^A$ | **4.4** | 4.481 | 1.8 |

**Scenario 9**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.8 | 6.0 | **6.9** |
| $d_2^A$ | **6.3** | 6.3 | 1.8 |
| $d_3^A$ | 3.2 | 1.4 | 0.2 |

**Scenario 10**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 5.8 | **8.4** | 3.5 |
| $d_2^A$ | **8.5** | 4.4 | 0.6 |
| $d_3^A$ | 3.3 | 0.5 | 0.1 |

**Scenario 11**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.1 | 3.3 | 9.7 |
| $d_2^A$ | **6.7** | 6.9 | 2.1 |
| $d_3^A$ | 3.0 | 1.0 | 0.1 |

**Scenario 12**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 8.6 | **10.1** | 4.1 |
| $d_2^A$ | 6.9 | 2.6 | 0.4 |
| $d_3^A$ | 1.2 | 0.1 | 0.0 |

**Scenario 13**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | **12.3** | 5.8 | 1.2 |
| $d_2^A$ | 6.2 | 1.3 | 0.2 |
| $d_3^A$ | 1.3 | 0.1 | 0.0 |

**Scenario 14**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 9.6 | 3.2 | 0.4 |
| $d_2^A$ | 3.0 | 0.5 | 0.0 |
| $d_3^A$ | 0.5 | 0.0 | 0.0 |

**Scenario 15**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.2 | 1.9 | 1.6 |
| $d_2^A$ | 1.9 | 2.5 | 2.8 |
| $d_3^A$ | 1.7 | 2.9 | 17.4 |

Table 7: Mean number of patients treated at each combination for the Surface-Free design.

**Scenario 1**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.6 | 4.0 |
| $d_2^A$ | 0.4 | 1.8 | 13.1 |
| $d_3^A$ | 5.7 | 14.1 | **60.3** |

**Scenario 2**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 1.2 | 10.2 |
| $d_2^A$ | 1.8 | 7.6 | **25.5** |
| $d_3^A$ | 12.0 | **23.8** | 17.9 |

**Scenario 3**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.9 | 4.8 |
| $d_2^A$ | 0.8 | 2.8 | 25.4 |
| $d_3^A$ | 16.1 | **22.4** | 26.8 |

**Scenario 4**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 2.5 | 10.4 |
| $d_2^A$ | 2.0 | 13.5 | **30.1** |
| $d_3^A$ | 18.0 | 19.1 | 4.5 |

**Scenario 5**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 8.2 | 15.9 |
| $d_2^A$ | 19.2 | **29.8** | 19.0 |
| $d_3^A$ | 10.9 | 3.4 | 0.2 |

**Scenario 6**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 8.2 | **15.9** |
| $d_2^A$ | 7.8 | **28.2** | 11.4 |
| $d_3^A$ | **17.4** | 9.4 | 0.9 |

**Scenario 7**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.2 | 16.1 | 11.1 |
| $d_2^A$ | 7.6 | **30.3** | 4.3 |
| $d_3^A$ | **21.4** | 8.1 | 0.3 |

**Scenario 8**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 2.2 | 10.6 |
| $d_2^A$ | 2.1 | 14.7 | **30.9** |
| $d_3^A$ | **20.9** | 14.2 | 4.5 |

**Scenario 9**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.6 | 12.2 | **28.0** |
| $d_2^A$ | **24.5** | 17.2 | 5.0 |
| $d_3^A$ | 9.3 | 2.4 | 0.2 |

**Scenario 10**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 6.1 | **30.3** | 10.6 |
| $d_2^A$ | **28.9** | 9.3 | 0.8 |
| $d_3^A$ | 9.8 | 0.7 | 0.0 |

**Scenario 11**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 1.6 | 18.2 |
| $d_2^A$ | **54.1** | 16.9 | 2.6 |
| $d_3^A$ | 5.2 | 1.1 | 0.0 |

**Scenario 12**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 16.4 | **37.0** | 13.9 |
| $d_2^A$ | 17.4 | 3.0 | 0.0 |
| $d_3^A$ | 1.6 | 0.0 | 0.0 |

**Scenario 13**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | **27.5** | 11.6 | 1.8 |
| $d_2^A$ | 13.2 | 1.8 | 0.1 |
| $d_3^A$ | 2.4 | 0.2 | 0.0 |

**Scenario 14**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 6.7 | 3.2 | 0.2 |
| $d_2^A$ | 3.0 | 0.2 | 0.0 |
| $d_3^A$ | 0.4 | 0.0 | 0.0 |

**Scenario 15**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.2 | 1.1 |
| $d_2^A$ | 0.2 | 0.3 | 1.2 |
| $d_3^A$ | 1.2 | 1.7 | 93.7 |

Table 8: Proportion each combination was selected for the Surface-Free design.

# 5 The BLRM - Full Results

**Scenario 1**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.1 | 1.9 | 2.1 |
| $d_2^A$ | 2.0 | 2.4 | 6.1 |
| $d_3^A$ | 2.1 | 6.2 | **10.1** |

**Scenario 2**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.1 | 2.3 | 2.9 |
| $d_2^A$ | 2.4 | 5.3 | **7.1** |
| $d_3^A$ | 2.9 | **6.2** | 3.8 |

**Scenario 3**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.0 | 1.6 | 2.0 |
| $d_2^A$ | 2.2 | 3.0 | 8.2 |
| $d_3^A$ | 3.0 | **6.9** | 6.1 |

**Scenario 4**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.1 | 2.2 | 2.8 |
| $d_2^A$ | 2.8 | 7.4 | **7.5** |
| $d_3^A$ | 3.5 | 4.8 | 1.9 |

**Scenario 5**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.3 | 3.1 | 4.7 |
| $d_2^A$ | 5.3 | **9.0** | 5.8 |
| $d_3^A$ | 2.1 | 1.4 | 0.9 |

**Scenario 6**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.6 | 5.0 | **3.0** |
| $d_2^A$ | 4.8 | **9.6** | 3.2 |
| $d_3^A$ | **2.9** | 3.0 | 0.7 |

**Scenario 7**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.9 | 5.6 | 2.1 |
| $d_2^A$ | 5.3 | **10.4** | 1.6 |
| $d_3^A$ | **3.2** | 3.1 | 0.5 |

**Scenario 8**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.1 | 2.6 | 3.0 |
| $d_2^A$ | 3.1 | 7.9 | **7.5** |
| $d_3^A$ | **3.2** | 4.0 | 1.8 |

**Scenario 9**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 5.1 | 7.5 | **4.1** |
| $d_2^A$ | **5.9** | 7.3 | 2.4 |
| $d_3^A$ | 1.8 | 1.3 | 0.4 |

**Scenario 10**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 8.7 | **7.8** | 1.7 |
| $d_2^A$ | **8.1** | 5.5 | 0.8 |
| $d_3^A$ | 1.7 | 0.8 | 0.1 |

**Scenario 11**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 4.1 | **5.0** | 7.1 |
| $d_2^A$ | **6.5** | 6.2 | 4.0 |
| $d_3^A$ | 1.8 | 0.8 | 0.4 |

**Scenario 12**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 12.5 | **9.1** | 1.8 |
| $d_2^A$ | 5.2 | 3.3 | 0.6 |
| $d_3^A$ | 0.7 | 0.2 | 0.1 |

**Scenario 13**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | **14.6** | 5.1 | 0.7 |
| $d_2^A$ | 5.1 | 2.1 | 0.2 |
| $d_3^A$ | 0.7 | 0.3 | 0.1 |

**Scenario 14**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 14.6 | 5.1 | 0.7 |
| $d_2^A$ | 5.1 | 1.1 | 0.1 |
| $d_3^A$ | 0.7 | 0.1 | 0.0 |

**Scenario 15**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 3.1 | 1.8 | 1.5 |
| $d_2^A$ | 1.8 | 1.5 | 3.0 |
| $d_3^A$ | 1.4 | 2.9 | 18.7 |

Table 9: Mean number of patients treated at each combination for the BLRM.

**Scenario 1**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.2 | 1.1 |
| $d_2^A$ | 0.4 | 6.0 | 20.9 |
| $d_3^A$ | 2.0 | 21.3 | **48.0** |

**Scenario 2**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.7 | 4.3 |
| $d_2^A$ | 0.9 | 20.1 | **32.2** |
| $d_3^A$ | 5.7 | **27.1** | 9.0 |

**Scenario 3**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.0 | 0.4 |
| $d_2^A$ | 0.4 | 7.5 | 32.2 |
| $d_3^A$ | 4.9 | **31.9** | 22.6 |

**Scenario 4**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.6 | 3.6 |
| $d_2^A$ | 0.8 | 28.9 | **34.7** |
| $d_3^A$ | 9.2 | 20.4 | 1.8 |

**Scenario 5**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.8 | 9.8 |
| $d_2^A$ | 13.9 | **48.6** | 21.7 |
| $d_3^A$ | 2.7 | 1.5 | 0.1 |

**Scenario 6**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.4 | 8.0 | **7.8** |
| $d_2^A$ | 7.5 | **52.1** | 8.2 |
| $d_3^A$ | **7.8** | 7.3 | 0.2 |

**Scenario 7**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.4 | 13.1 | 3.2 |
| $d_2^A$ | 9.2 | **54.4** | 2.2 |
| $d_3^A$ | **9.5** | 6.5 | 0.1 |

**Scenario 8**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 1.1 | 5.5 |
| $d_2^A$ | 1.4 | 31.2 | **34.0** |
| $d_3^A$ | **10.1** | 14.0 | 2.5 |

**Scenario 9**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 1.1 | 16.6 | **14.5** |
| $d_2^A$ | **24.4** | 341 | 4.2 |
| $d_3^A$ | 2.4 | 1.6 | 0.1 |

**Scenario 10**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 10.1 | **31.9** | 2.5 |
| $d_2^A$ | **31.4** | 16.6 | 0.3 |
| $d_3^A$ | 2.0 | 0.2 | 0.0 |

**Scenario 11**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 2.0 | 15.3 |
| $d_2^A$ | **32.8** | 33.7 | 14.1 |
| $d_3^A$ | 1.2 | 0.1 | 0.0 |

**Scenario 12**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 23.1 | **37.0** | 2.8 |
| $d_2^A$ | 15.4 | 6.3 | 0.2 |
| $d_3^A$ | 0.0 | 0.0 | 0.0 |

**Scenario 13**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | **31.2** | 11.2 | 0.4 |
| $d_2^A$ | 11.3 | 1.9 | 0.0 |
| $d_3^A$ | 0.2 | 0.1 | 0.0 |

**Scenario 14**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 8.0 | 1.9 | 0.1 |
| $d_2^A$ | 2.2 | 0.3 | 0.0 |
| $d_3^A$ | 0.0 | 0.0 | 0.0 |

**Scenario 15**

| | $d_1^B$ | $d_2^B$ | $d_3^B$ |
|---|---|---|---|
| $d_1^A$ | 0.0 | 0.2 | 0.6 |
| $d_2^A$ | 0.2 | 2.0 | 4.2 |
| $d_3^A$ | 0.3 | 3.7 | 88.5 |

Table 10: Proportion each combination was selected for the BLRM.

# 6 Operating Characteristics

| | PCS | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | Mean |
| BOIN | 39.0 | 48.8 | 20.4 | 32.8 | 25.8 | 59.6 | 52.5 | 47.9 | 47.5 | 52.0 | 20.4 | 31.1 | 37.1 | 0.0 | 0.0 | 34.3 |
| KEY | 49.5 | 53.4 | 27.4 | 35.4 | 30.6 | 59.5 | 51.2 | 52.6 | 48.7 | 53.9 | 26.1 | 32.6 | 37.4 | 0.0 | 0.0 | 37.2 |
| PIPE | 13.4 | 35.2 | 19.5 | 19.4 | 19.9 | 62.1 | 43.4 | 39.8 | 42.4 | 51.7 | 23.9 | 32.2 | 38.0 | 0.0 | 0.0 | 29.4 |
| SFD | 60.3 | 49.2 | 22.4 | 30.1 | 29.8 | 61.6 | 51.8 | 51.8 | 52.5 | 59.2 | 54.1 | 37.0 | 27.5 | 0.0 | 0.0 | 39.1 |
| BLRM | 48.0 | 59.3 | 31.9 | 34.7 | 48.6 | 67.7 | 63.9 | 44.0 | 38.9 | 63.4 | 32.8 | 37.0 | 31.2 | 0.0 | 0.0 | 40.1 |
| | PAS | | | | | | | | | | | | | | | |
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | Mean |
| BOIN | 79.0 | 72.2 | 75.3 | 68.8 | 40.2 | 59.6 | 68.5 | 81.8 | 47.5 | 52.0 | 20.4 | 62.6 | 37.1 | 0.0 | 0.0 | 51.0 |
| KEY | 85.7 | 72.3 | 73.4 | 72.8 | 46.5 | 59.6 | 66.4 | 82.1 | 48.7 | 53.9 | 26.1 | 57.9 | 37.4 | 0.0 | 0.0 | 52.2 |
| PIPE | 64.5 | 70.0 | 72.8 | 63.8 | 37.8 | 62.1 | 64.8 | 84.2 | 42.4 | 51.7 | 23.9 | 73.9 | 38.0 | 0.0 | 0.0 | 50.0 |
| SFD | 87.5 | 68.8 | 64.0 | 61.5 | 49.0 | 61.6 | 67.8 | 77.0 | 52.5 | 59.2 | 54.1 | 53.3 | 27.5 | 0.0 | 0.0 | 52.3 |
| BLRM | 90.2 | 85.0 | 69.0 | 72.8 | 62.5 | 67.7 | 77.0 | 80.8 | 27.9 | 63.4 | 32.8 | 60.1 | 31.2 | 0.0 | 0.0 | 54.7 |
| | Proportion of overly toxic selections | | | | | | | | | | | | | | | |
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | Mean |
| BOIN | 0.0 | 9.2 | 10.7 | 11.0 | 18.1 | 15.6 | 15.2 | 10.4 | 24.8 | 21.5 | 13.9 | 19.6 | 20.8 | 14.2 | 0.0 | 13.7 |
| KEY | 0.0 | 12.7 | 15.2 | 13.1 | 24.4 | 19.6 | 19.9 | 13.9 | 29.5 | 25.9 | 22.3 | 26.3 | 22.1 | 14.7 | 0.0 | 17.3 |
| PIPE | 0.0 | 1.3 | 2.4 | 6.8 | 16.8 | 6.9 | 13.2 | 4.6 | 21.7 | 17.2 | 15.2 | 15.0 | 19.6 | 14.8 | 0.0 | 10.4 |
| SFD | 0.0 | 17.9 | 26.8 | 23.6 | 33.4 | 21.8 | 23.9 | 18.6 | 34.1 | 31.4 | 25.9 | 36.1 | 30.9 | 13.8 | 0.0 | 22.5 |
| BLRM | 0.0 | 9.0 | 22.6 | 22.2 | 26.0 | 15.8 | 12.1 | 16.4 | 42.5 | 21.7 | 49.1 | 24.9 | 25.2 | 12.6 | 0.0 | 20.0 |
| | Proportion of trials in which no combination was selected | | | | | | | | | | | | | | | |
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | Mean |
| BOIN | 0.0 | 9.2 | 10.7 | 11.0 | 18.1 | 15.6 | 15.2 | 10.4 | 24.8 | 21.5 | 13.9 | 19.6 | 20.8 | 14.2 | 0.0 | 13.7 |
| KEY | 0.0 | 12.7 | 15.2 | 13.1 | 24.4 | 19.6 | 19.9 | 13.9 | 29.5 | 25.9 | 22.3 | 26.3 | 22.1 | 14.7 | 0.0 | 17.3 |
| PIPE | 0.0 | 1.3 | 2.4 | 6.8 | 16.8 | 6.9 | 13.2 | 4.6 | 21.7 | 17.2 | 15.2 | 15.0 | 19.6 | 14.8 | 0.0 | 10.4 |
| SFD | 0.0 | 17.9 | 26.8 | 23.6 | 33.4 | 21.8 | 23.9 | 18.6 | 34.1 | 31.4 | 25.9 | 36.1 | 30.9 | 13.8 | 0.0 | 22.5 |
| BLRM | 0.0 | 9.0 | 22.6 | 22.2 | 26.0 | 15.8 | 12.1 | 16.4 | 42.5 | 21.7 | 49.1 | 24.9 | 25.2 | 12.6 | 0.0 | 20.0 |

Table 11: Proportions of correct, acceptable, overly toxic and zero selections.

| | PCE | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | Mean |
| BOIN | 39.0 | 48.8 | 20.4 | 32.8 | 25.8 | 59.6 | 52.5 | 47.9 | 47.5 | 52.0 | 20.4 | 31.1 | 37.1 | 0.0 | 0.0 | 34.3 |
| KEY | 49.5 | 53.4 | 27.4 | 35.4 | 30.6 | 59.5 | 51.2 | 52.6 | 48.7 | 53.9 | 26.1 | 32.6 | 37.4 | 0.0 | 0.0 | 37.2 |
| PIPE | 13.4 | 35.2 | 19.5 | 19.4 | 19.9 | 62.1 | 43.4 | 39.8 | 42.4 | 51.7 | 23.9 | 32.2 | 38.0 | 0.0 | 0.0 | 29.4 |
| SFD | 60.3 | 49.2 | 22.4 | 30.1 | 29.8 | 61.6 | 51.8 | 51.8 | 52.5 | 59.2 | 54.1 | 37.0 | 27.5 | 0.0 | 0.0 | 39.1 |
| BLRM | 48.0 | 59.3 | 31.9 | 34.7 | 48.6 | 67.7 | 63.9 | 44.0 | 38.9 | 63.4 | 32.8 | 37.0 | 31.2 | 0.0 | 0.0 | 40.1 |
| | PAE | | | | | | | | | | | | | | | |
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | Mean |
| BOIN | 79.0 | 72.2 | 75.3 | 68.8 | 40.2 | 59.6 | 68.5 | 81.8 | 47.5 | 52.0 | 20.4 | 62.6 | 37.1 | 0.0 | 0.0 | 51.0 |
| KEY | 85.7 | 72.3 | 73.4 | 72.8 | 46.5 | 59.6 | 66.4 | 82.1 | 48.7 | 53.9 | 26.1 | 57.9 | 37.4 | 0.0 | 0.0 | 52.2 |
| PIPE | 64.5 | 70.0 | 72.8 | 63.8 | 37.8 | 62.1 | 64.8 | 84.2 | 42.4 | 51.7 | 23.9 | 73.9 | 38.0 | 0.0 | 0.0 | 50.0 |
| SFD | 87.5 | 68.8 | 64.0 | 61.5 | 49.0 | 61.6 | 67.8 | 77.0 | 52.5 | 59.2 | 54.1 | 53.3 | 27.5 | 0.0 | 0.0 | 52.3 |
| BLRM | 90.2 | 85.0 | 69.0 | 72.8 | 62.5 | 67.7 | 77.0 | 80.8 | 27.9 | 63.4 | 32.8 | 60.1 | 31.2 | 0.0 | 0.0 | 54.7 |
| | Proportion of patients treated at overly toxic combinations | | | | | | | | | | | | | | | |
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | Mean |
| BOIN | 0.0 | 9.2 | 10.7 | 11.0 | 18.1 | 15.6 | 15.2 | 10.4 | 24.8 | 21.5 | 13.9 | 19.6 | 20.8 | 14.2 | 0.0 | 13.7 |
| KEY | 0.0 | 12.7 | 15.2 | 13.1 | 24.4 | 19.6 | 19.9 | 13.9 | 29.5 | 25.9 | 22.3 | 26.3 | 22.1 | 14.7 | 0.0 | 17.3 |
| PIPE | 0.0 | 1.3 | 2.4 | 6.8 | 16.8 | 6.9 | 13.2 | 4.6 | 21.7 | 17.2 | 15.2 | 15.0 | 19.6 | 14.8 | 0.0 | 10.4 |
| SFD | 0.0 | 17.9 | 26.8 | 23.6 | 33.4 | 21.8 | 23.9 | 18.6 | 34.1 | 31.4 | 25.9 | 36.1 | 30.9 | 13.8 | 0.0 | 22.5 |
| BLRM | 0.0 | 9.0 | 22.6 | 22.2 | 26.0 | 15.8 | 12.1 | 16.4 | 42.5 | 21.7 | 49.1 | 24.9 | 25.2 | 12.6 | 0.0 | 20.0 |

Table 12: Proportions of correct, acceptable and overly toxic experimentation.

| | Mean number of patients treated per trial | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | Mean |
| BOIN | 35.7 | 35.8 | 36.0 | 35.7 | 36.0 | 34.8 | 34.6 | 35.6 | 34.8 | 32.9 | 36.0 | 30.5 | 24.0 | 12.2 | 34.7 | 32.6 |
| KEY | 35.7 | 35.7 | 36.0 | 35.7 | 36.0 | 34.8 | 34.6 | 35.7 | 34.8 | 33.3 | 36.0 | 31.1 | 24.7 | 12.5 | 34.9 | 32.8 |
| PIPE | 36.0 | 36.0 | 36.0 | 36.0 | 36.0 | 35.9 | 35.9 | 36.0 | 36.0 | 35.7 | 36.0 | 34.9 | 31.9 | 22.7 | 36.0 | 34.7 |
| SFD | 36.0 | 36.0 | 36.0 | 36.0 | 36.0 | 35.8 | 35.9 | 36.0 | 35.9 | 35.3 | 36.0 | 34.0 | 28.3 | 17.3 | 35.9 | 34.0 |
| BLRM | 36.0 | 36.0 | 36.0 | 36.0 | 35.8 | 35.9 | 35.7 | 36.1 | 35.8 | 35.2 | 35.9 | 33.4 | 28.9 | 18.5 | 36.0 | 34.1 |

| | Mean number of toxic responses observed per trial | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | Mean |
| BOIN | 6.7 | 8.0 | 7.4 | 8.3 | 8.8 | 9.3 | 9.7 | 8.6 | 9.7 | 10.1 | 7.8 | 9.8 | 8.8 | 5.8 | 3.5 | 8.2 |
| KEY | 6.9 | 8.2 | 7.9 | 8.7 | 9.5 | 9.5 | 9.8 | 8.9 | 9.9 | 10.4 | 8.9 | 10.2 | 9.1 | 5.9 | 3.5 | 8.5 |
| PIPE | 6.1 | 7.3 | 6.5 | 7.7 | 8.6 | 9.5 | 10.1 | 8.2 | 10.3 | 11.7 | 8.1 | 12.3 | 12.7 | 10.9 | 3.6 | 8.9 |
| SFD | 7.0 | 8.5 | 8.1 | 9.0 | 10.0 | 10.1 | 10.6 | 9.2 | 10.9 | 11.7 | 9.6 | 12.0 | 11.1 | 8.3 | 3.6 | 9.3 |
| BLRM | 7.0 | 8.5 | 8.0 | 8.8 | 9.7 | 9.7 | 9.9 | 8.9 | 10.4 | 11.0 | 9.8 | 11.1 | 10.9 | 8.8 | 3.6 | 9.1 |

Table 13: Mean numbers of patients and toxic responses.