**Scenarios our method doesn't work**

1. when d3 is very close to the maximum allowable threshold for toxicity, our method tend not to select d3 as the optimal dose, k>=2 and k=3 both do not work.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | K=0  (toxicity) | K=1  (no/little efficacy) | K=2  (median efficacy) | K=3  (high efficacy) | CM |
| d1 | 0.15 | 0.6357 | 0.17 | 0.0425 | 1.10 |
| d2 | 0.3 | 0.42 | 0.21 | 0.07 | 1.05 |
| d3 | 0.45 | 0.0275 | 0.11 | 0.4125 | 1.48 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| N=48 | recommendation for d1 | recommendation for d2 | recommendation for d3 | work |
| k>=2 | 0.3035 | 0.4841 | 0.2124 | no |
| k=3 | 0.2198 | 0.4194 | 0.3608 | no |

1. when each dose has same efficacy but different toxicity, k>=2 and k=3 both do not work.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | K=0  (toxicity) | K=1  (no/little efficacy) | K=2  (median efficacy) | K=3  (high efficacy) | CM |
| d1 | 0.1 | 0.5 | 0.2 | 0.2 | 1.5 |
| d2 | 0.2 | 0.4 | 0.2 | 0.2 | 1.4 |
| d3 | 0.3 | 0.3 | 0.2 | 0.2 | 1.3 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| N=48 | recommendation for d1 | recommendation for d2 | recommendation for d3 | work |
| k>=2 | 0.1976 | 0.4217 | 0.3807 | no |
| k=3 | 0.1194 | 0.3200 | 0.5606 | no |

1. k=3 works, k>=2 doesn't work

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | K=0  (toxicity) | K=1  (no/little efficacy) | K=2  (median efficacy) | K=3  (high efficacy) | CM |
| d1 | 0.1 | 0.72 | 0.09 | 0.09 | 1.17 |
| d2 | 0.2 | 0.32 | 0.24 | 0.24 | 1.52 |
| d3 | 0.3 | 0.07 | 0.07 | 0.56 | 1.89 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| N=48 | recommendation for d1 | recommendation for d2 | recommendation for d3 | work |
| k>=2 | 0.1179 | 0.4646 | 0.4175 | no |
| k=3 | 0.1117 | 0.2515 | 0.6368 | yes |

It seems this is caused by the same reason as (b): when k>=2, the success probability of dose 2 and 3 are close (0.48 and 0.63).

if we make the success probability of dose 2 and 3 closer, k>=2 still doesn't work:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | K=0  (toxicity) | K=1  (no/little efficacy) | K=2  (median efficacy) | K=3  (high efficacy) | CM |
| d1 | 0.1 | 0.72 | 0.09 | 0.09 | 1.17 |
| d2 | 0.2 | 0.26 | 0.30 | 0.24 | 1.58 |
| d3 | 0.3 | 0.07 | 0.07 | 0.56 | 1.89 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| N=48 | recommendation for d1 | recommendation for d2 | recommendation for d3 | work |
| k>=2 | 0.1151 | 0.5815 | 0.3034 | no |

if we make the success probability of dose 2 and 3 more different, k>=2 works:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | K=0  (toxicity) | K=1  (no/little efficacy) | K=2  (median efficacy) | K=3  (high efficacy) | CM |
| d1 | 0.1 | 0.72 | 0.09 | 0.09 | 1.17 |
| d2 | 0.2 | 0.4 | 0.16 | 0.24 | 1.44 |
| d3 | 0.3 | 0.07 | 0.07 | 0.56 | 1.89 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| N=48 | recommendation for d1 | recommendation for d2 | recommendation for d3 | work |
| k>=2 | 0.1127 | 0.3497 | 0.5376 | yes |

1. k>=2 works but k=3 doesn't work

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | K=0  (toxicity) | K=1  (no/little efficacy) | K=2  (median efficacy) | K=3  (high efficacy) | CM |
| d1 | 0.1 | 0.72 | 0.09 | 0.09 | 1.17 |
| d2 | 0.2 | 0.35 | 0.05 | 0.4 | 1.65 |
| d3 | 0.3 | 0.05 | 0.25 | 0.4 | 1.75 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| N=48 | recommendation for d1 | recommendation for d2 | recommendation for d3 | work |
| k>=2 | 0.1135 | 0.4219 | 0.4646 | yes |
| k=3 | 0.1140 | 0.4886 | 0.3974 | no |

**Summary**

When the success probability is close and toxicity probability has big difference, our method tend to make mistakes.

When the toxicity probability is close to the maximum allowable toxicity, our method tend to make msitakes.