### Supplemental materials

In the “simple” scenario, the repeated treatment cycles can be modeled as a simple Markov chain with absorbing state (patient responds), as well as transition probabilities and . Here, is the current treatment cycle, and is the probability of responding to the th treatment, which is held constant across all treatment cycles.

In this scenario, the formula to calculate the cumulative response after treatment cycles reduces to:

|  |  |
| --- | --- |
|  | (1) |

The number of “excess” treatment can be obtained using this formula:

|  |  |
| --- | --- |
|  | (2) |

If we additionally consider “decay” of the treatment response (e.g., response rates decrease by 10% with each additional treatment attempt), we obtain the following formula for the cumulative response:

|  |  |
| --- | --- |
|  | (3) |

where is the cumulative treatment response, is the response rate of treatments, encodes the proportional “decay” with each treatment cycle, and is the total number of treatment cycles.

Reference:

Blitzstein, J.K., & Hwang, J. (2019). Introduction to Probability, Second Edition (2nd ed.). Chapman and Hall/CRC. https://doi.org/10.1201/9780429428357

Overview of the scenarios

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | *Cycles* | *Total Txs* | *Excess Txs* | *Mean Txs* |  | *Reduction excess Txs* |
| A. MAIN SCENARIOS |  |  |  |  |  |  |
| A.1. Simple scenario (42% response, no decline) | 9 | 237 | 137 | 2.31 |  |  |
| A.2. Realistic scenario (50% response, 10% decline) | 14 | 230 | 130 | 2.67 |  | Benchmark |
| A.3. Higher response 1st treatment (57%, 10% decline) | 13 | 210 | 110 | 2.48 |  | 15% (20/130) |
| A.4. Higher response in all treatments (7%; 10% decline) | 10 | 193 | 93 | 2.11 |  | 28% (37/130) |
| A.5. Higher response 3rd treatment (50%) | 13 | 221 | 121 | 2.48 |  | 7% (9/130) |
| A.6. Double effect size for first treatment (64%; 10% decline) | 11 | 185 | 85 | 2.17 |  | 35% (45/130) |
| A.7. Double response in all treatments (14%; 10% decline) | 7 | 165 | 65 | 1.72 |  | 50% (65/130) |
| B. SENSITIVITY ANALYSES (response to 1st treatment is 60%) |  |  |  |  |  |  |
| B.1. Realistic scenario (60% response, 10% decline) | 9 | 179 | 79 | 1.92 |  | Benchmark |
| B.2. Higher response 1st treatment (67%, 10% decline) | 8 | 166 | 66 | 1.83 |  | 16% (13/79) |
| B.3. Higher response in all treatments (7%; 10% decline) | 7 | 158 | 58 | 1.66 |  | 27% (21/79) |
| B.4. Higher response 3rd treatment (60%) | 8 | 175 | 75 | 1.84 |  | 5% (4/79) |
| C. SENSITIVITY ANALYSES (decline is 5%) |  |  |  |  |  |  |
| C.1. Realistic scenario (50% response, 5% decline) | 9 | 209 | 109 | 2.15 |  | Benchmark |
| C.2. Higher response 1st treatment (57%, 5% decline) | 9 | 195 | 95 | 2.09 |  | 13% (14/109) |
| C.3. Higher response in all treatments (7%; 5% decline) | 7 | 182 | 82 | 1.85 |  | 25% (27/109) |
| C.4. Higher response 3rd treatment (50%) | 9 | 206 | 106 | 2.11 |  | 3% (3/109) |
|  |  |  |  |  |  |  |

Abbreviations: Txs: treatments.