A Partially Optimized Bayesian Phase II Design

pob2ef

1 Overview

The `pob2ef` package implements a Bayesian single-arm phase II design for a binary efficacy endpoint. The method distinguishes an unacceptable response-rate benchmark p_0 from a clinically desirable target p_1, where $p_1 > p_0$. It permits efficacy and futility stopping while intentionally retaining a final grey-zone result when the evidence is intermediate.

2 Posterior decision rules

At a planned analysis after n evaluable participants, let D_n denote the observed response data. The design declares futility when

$$\Pr(\theta > p_0 \mid D_n) < C_F(n),$$

and declares superiority when

$$\Pr(\theta > p_1 \mid D_n) > C_E(n).$$

The boundary family is

$$C_F(n) = \lambda_1 (n/N)^{\gamma}, \qquad C_E(n) = 1 - \lambda_2 (n/N)^{\eta},$$

with tuning-parameter constraints

$$0 < \lambda_1 \leq 0.5, \qquad 0 < \lambda_2 < 0.5, \qquad \gamma, \eta \geq 0.$$

If neither rule is met at an interim analysis, accrual continues. If neither rule is met at the final analysis, the outcome is a grey-zone result. The grey zone is an intentional evidence category; it is not silently reclassified as a futility conclusion.

3 Constrained partial optimization

Candidate boundary settings must satisfy the two prespecified error constraints

$$\Pr_{p_0}(\text{superiority}) \leq \alpha, \qquad \Pr_{p_1}(\text{futility}) \leq \beta.$$

Among feasible candidates, `pob2ef` first minimizes the final grey-zone probability at p_1, then uses expected sample size at p_0 as a tie-breaker. Thus, error control is mandatory and grey-zone minimization is the optimization objective among designs meeting those constraints.

4 Selecting a design

The following small grid illustrates the workflow. In practice, users should specify a grid appropriate for the planned sample size and analysis schedule.

```
design <- select_design(
  n_max = 20,
  looks = c(10, 20),
  p0 = 0.20,
  p1 = 0.40,
  alpha = 0.10,
  beta = 0.20,
  lambda1_grid = 0.50,
  lambda2_grid = 0.20,
  gamma_grid = 0,
  eta_grid = 0
)

design$selected
```

```
  lambda1 lambda2 gamma eta type1_error type2_error grey_zone_probability_p1
1     0.5     0.2     0   0 0.007994491  0.05326348                0.6519206
  expected_sample_size_p0 expected_sample_size_p1 superiority_probability_p1
1                16.17821                17.87404                    0.294816
  feasible
1     TRUE
```

5 Decision table and operating characteristics

The response-count table gives the action for every possible cumulative number of responses at each look.

```
actions <- decision_table(design)
actions[actions$sample_size == 20, c("responses", "action")]
```

```
   responses      action
12         0    futility
13         1    futility
14         2    futility
15         3    futility
16         4   grey_zone
17         5   grey_zone
18         6   grey_zone
19         7   grey_zone
20         8   grey_zone
21         9   grey_zone
22        10 superiority
23        11 superiority
24        12 superiority
25        13 superiority
26        14 superiority
27        15 superiority
28        16 superiority
29        17 superiority
```

```
30        18 superiority
31        19 superiority
32        20 superiority
```

Exact trial-path enumeration is used during design selection. Simulation can then be used to examine operating characteristics across additional scenarios.

```
simulation <- simulate_design(
  design,
  true_rates = c(0.20, 0.30, 0.40),
  n_sim = 500,
  seed = 2026
)

simulation$results

  true_rate superiority_probability futility_probability grey_zone_probability
1       0.2                   0.004                0.514                 0.482
2       0.3                   0.094                0.166                 0.740
3       0.4                   0.312                0.042                 0.646
  expected_sample_size superiority_mcse futility_mcse grey_zone_mcse
1                16.18      0.002822765   0.022351913     0.02234619
2                18.06      0.013050977   0.016639952     0.01961632
3                17.84      0.020719846   0.008970619     0.02138616
  expected_sample_size_mcse
1                 0.2175082
2                 0.1770183
3                 0.1842191
```