Endpoints in Subscreen Package Subgroup Analysis

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The subscreen package example uses **two survival endpoints** for comprehensive subgroup analysis of treatment effects.

1 Primary Endpoints

1.1 PFS (Progression-Free Survival)

```
template.event.pfs <- sample(c(0, 1), dim(pbcdat)[1], replace = TRUE)
template.timepfs <- sample(1:5000, dim(pbcdat)[1], replace = TRUE)
```

- **Event**: `event.pfs` (0 = no progression/death, 1 = progression/death)
- **Time**: `timepfs` (time to progression or death)
- **Source**: Randomly generated for demonstration
- **Range**: 1-5000 time units

1.2 OS (Overall Survival)

```
template.event.os <- pbcdat$event  # Original PBC event data
template.timeos <- pbcdat$time     # Original PBC time data
```

- **Event**: `event.os` (0 = alive, 1 = death)
- **Time**: `timeos` (time to death)
- **Source**: Original PBC dataset (real survival data)
- **Purpose**: Realistic survival analysis

2 Endpoint Usage in Analysis

2.1 Hazard Ratio Calculation

```r
hazardratio <- function(D) {
  # PFS hazard ratio
  HRpfs <- tryCatch(
    exp(coxph(Surv(D$timepfs, D$event.pfs) ~ D$trt)$coefficients[[1]]),
    warning = function(w) {NA}
  )

  # OS hazard ratio
  HRos <- tryCatch(
    exp(coxph(Surv(D$timeos, D$event.os) ~ D$trt)$coefficients[[1]]),
    warning = function(w) {NA}
  )

  data.frame(HR.pfs = round(1/HRpfs, 2), HR.os = round(1/HRos, 2))
}
```

2.2 Funnel Plot Specification

```r
results_factorial_complement_true <- subscreenfunnel(
  data = pbcdat,
  H = results_factorial_complement_true1,
  eval_function = hazardratio,
  endpoints = c("timepfs", "event.pfs", "timeos", "event.os")
)
```

3 Endpoint Summary

Endpoint	Event Variable	Time Variable	Data Source	Purpose
PFS	`event.pfs`	`timepfs`	Synthetic	Demonstration
OS	`event.os`	`timeos`	Original PBC	Realistic analysis

4 Clinical Interpretation

4.1 Hazard Ratio Interpretation

For each subgroup, the analysis calculates hazard ratios where:

- **HR < 1**: Treatment benefit (reduces risk)
- **HR > 1**: Treatment harm (increases risk)
- **HR $= 1$**: No treatment effect

4.2 Dual-Endpoint Advantages

Using both PFS and OS endpoints allows:

1. **Consistency assessment**: Compare treatment effects across outcomes
2. **Differential effects**: Identify subgroups benefiting for one endpoint only

3. **Methodological demonstration**: Show multi-endpoint handling

4. **Clinical realism**: Reflect actual trial practice

5 Key Definitions

- **PFS**: Time from treatment start to disease progression or death (whichever occurs first). Common primary endpoint in oncology trials.

- **OS**: Time from treatment start to death from any cause. Gold standard endpoint in survival analysis.

This dual-endpoint approach provides a comprehensive framework for subgroup analysis that mirrors real clinical trial methodology.