Package ‘DelayedEffect.Design’

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Title Sample Size and Power Calculations using the APPLE and SEPPLE Methods

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Description Provides sample size and power calculations when the treatment time-lag effect is present and the lag duration is homogeneous across the individual subject. The methods used are described in Xu, Z., Zhen, B., Park, Y., & Zhu, B. (2017) <doi:10.1002/sim.7157>.

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DelayedEffect.Design *Sample size and power calculations using APPLE and SEPPLE*

Description

An R package for sample size and power calculation when the treatment time-lag effect is present and the lag duration is homogeneous across the individual subject using the APPLE and SEPPLE methods based on the piecewise weighted log-rank test. For comparison, this package also performs the power calculation based on the regular log-rank test which ignores the existence of lag effect.

Details

The two new methods in this package for performing the sample size and power calculations are:
1. Analytic Power calculation method based on Piecewise weighted Log-rank tEst (APPLE),
2. Simulation-based Empirical Power calculation method based on Piecewise weighted Log-rank tEst (SEPPLE).
See the reference for details of these methods and the piecewise weighted log-rank test. The functions for computing power corresponding to the above methods are `pow.APPLE` and `pow.SEPPLE`. These can be compared to `pow.sim.logrk`, which computes the power from a simulation-based algorithm using the regular log-rank test which ignores the existence of lag effect.

This package also includes the function `N.APPLE` to back calculate the sample size given the power and hazard ratio, and the function `HR.APPLE` to back calculate the hazard ratio given the power and sample size, respectively, using the close-form APPLE method.

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References

Xu, Z., Zhen, B., Park, Y., & Zhu, B. (2017). Designing therapeutic cancer vaccine trials with delayed treatment effect. Statistics in medicine, 36(4), 592-605.

HR.APPLE *APPLE hazard ratio computation*

Description

Perform the post-delay hazard ratio calculation given power and sample size using the close-form APPLE method based on the piecewise weighted log-rank test when the treatment time-lag effect is present and the lag duration is homogeneous across the individual subject

Usage

```
HR.APPLE(lambda1, t1, p, N, tao, A, beta, ap=0.5, alpha=0.05)
```

Arguments

`lambda1`	Baseline hazard or NULL (see details)
`t1`	Delayed duration or NULL (see details)
`p`	Proportion of subjects who survive beyond the delayed period or NULL (see details)
`N`	Sample size
`tao`	Total study duration
`A`	Total enrollment duration
`beta`	Type II error rate; Power=1-beta
`ap`	Experimental-control allocation ratio. The default is 0.5.
`alpha`	Type I error rate (two-sided). The default is 0.05.

Details

APPLE is an acronym for:
Analytic Power calculation method based on Piecewise weighted Log-rank tEst. See the reference for details of this method.

Out of the three input parameters `lambda1`, `t1` and `p`, only two need to be specified, the remaining one will be computed internally from the formula `lambda1 = -log(p)/t1`. If all three are not NULL, then `lambda1` will be set to `-log(p)/t1` regardless of the user input value.

Value

The hazard ratio

Author(s)

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References

Xu, Z., Zhen, B., Park, Y., & Zhu, B. (2017). Designing therapeutic cancer vaccine trials with delayed treatment effect. Statistics in medicine, 36(4), 592-605.

See Also

`pow.APPLE`, `N.APPLE`

Examples

```
lambda1 <- NULL
t1      <- 183
p       <- 0.7
N       <- 200
tao     <- 365*3
A       <- 365
```

```
beta    <- 0.2
HR.APPLE(lambda1, t1, p, N, tao, A, beta)
```

N.APPLE *APPLE sample size computation*

Description

Perform the sample size calculation given the power and post-delay hazard ratio using the closeform APPLE method based on the piecewise weighted log-rank test when the treatment time-lag effect is present and the lag duration is homogeneous across the individual subject

Usage

```
N.APPLE(lambda1, t1, p, HR, tao, A, beta, ap=0.5, alpha=0.05)
```

Arguments

`lambda1`	Baseline hazard or NULL (see details)
`t1`	Delayed duration or NULL (see details)
`p`	Proportion of subjects who survive beyond the delayed period or NULL (see details)
`HR`	Post-delay hazard ratio
`tao`	Total study duration
`A`	Total enrollment duration
`beta`	Type II error rate; Power=1-beta
`ap`	Experimental-control allocation ratio. The default is 0.5.
`alpha`	Type I error rate (two-sided). The default is 0.05.

Details

APPLE is an acronym for:
Analytic Power calculation method based on Piecewise weighted Log-rank tEst. See the reference for details of this method.

Out of the three input parameters `lambda1`, `t1` and `p`, only two need to be specified, the remaining one will be computed internally from the formula `lambda1 = -log(p)/t1`. If all three are not NULL, then `lambda1` will be set to `-log(p)/t1` regardless of the user input value.

Value

The sample size

Author(s)

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References

Xu, Z., Zhen, B., Park, Y., & Zhu, B. (2017). Designing therapeutic cancer vaccine trials with delayed treatment effect. Statistics in medicine, 36(4), 592-605.

See Also

pow.APPLE, HR.APPLE

Examples

```
lambda1 <- NULL
t1      <- 183
p       <- 0.7
HR      <- 0.55
tao     <- 365*3
A       <- 365
beta    <- 0.2
N.APPLE(lambda1, t1, p, HR, tao, A, beta)
```

---

pow.APPLE *APPLE power computation*

Description

Perform the power calculation using the close-form APPLE method based on the piecewise weighted log-rank test when the treatment time-lag effect is present and the lag duration is homogeneous across the individual subject

Usage

```
pow.APPLE(lambda1, t1, p, N, HR, tao, A, ap=0.5, alpha=0.05)
```

Arguments

lambda1	Baseline hazard or NULL (see details)
t1	Delayed duration or NULL (see details)
p	Proportion of subjects who survive beyond the delayed period or NULL (see details)
N	Sample size
HR	Post-delay hazard ratio
tao	Total study duration
A	Total enrollment duration
ap	Experimental-control allocation ratio. The default is 0.5.
alpha	Type I error rate (two-sided). The default is 0.05.

Details

APPLE is an acronym for:
Analytic Power calculation method based on Piecewise weighted Log-rank tEst. See the reference for details of this method.

Out of the three input parameters `lambda1`, `t1` and `p`, only two need to be specified, the remaining one will be computed internally from the formula `lambda1 = -log(p)/t1`. If all three are not NULL, then `lambda1` will be set to `-log(p)/t1` regardless of the user input value.

Value

The power

Author(s)

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References

Xu, Z., Zhen, B., Park, Y., & Zhu, B. (2017). Designing therapeutic cancer vaccine trials with delayed treatment effect. Statistics in medicine, 36(4), 592-605.

See Also

`N.APPLE`, `HR.APPLE`, `pow.SEPPLE`, `pow.sim.logrk`

Examples

```
lambda1 <- NULL
t1      <- 183
p       <- 0.7
N       <- 200
HR      <- 0.55
tao     <- 365*3
A       <- 365
pow.APPLE(lambda1, t1, p, N, HR, tao, A)
```

`pow.SEPPLE` *SEPPLE power computation*

Description

Perform the power calculation using the numeric SEPPLE method based on the piecewise weighted log-rank test when the treatment time-lag effect is present and the lag duration is homogeneous across the individual subject

Usage

```
pow.SEPPLE(lambda1, t1, p, N, HR, tao, A, ap=0.5, alpha=0.05, nsim=10000)
```

Arguments

`lambda1`	Baseline hazard or NULL (see details)
`t1`	Delayed duration or NULL (see details)
`p`	Proportion of subjects who survive beyond the delayed period or NULL (see details)
`N`	Sample size
`HR`	Post-delay hazard ratio
`tao`	Total study duration
`A`	Total enrollment duration
`ap`	Experimental-control allocation ratio. The default is 0.5.
`alpha`	Type I error rate (two-sided). The default is 0.05.
`nsim`	Number of simulations. The default is 10000.

Details

SEPPLE is an acronym for:
Simulation-based Empirical Power calculation method based on Piecewise weighted Log-rank tEst. See the reference for details of this method.

Out of the three input parameters `lambda1`, `t1` and `p`, only two need to be specified, the remaining one will be computed internally from the formula `lambda1 = -log(p)/t1`. If all three are not NULL, then `lambda1` will be set to `-log(p)/t1` regardless of the user input value.

Value

The power

Author(s)

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References

Xu, Z., Zhen, B., Park, Y., & Zhu, B. (2017). Designing therapeutic cancer vaccine trials with delayed treatment effect. Statistics in medicine, 36(4), 592-605.

See Also

`pow.APPLE`, `pow.sim.logrk`

Examples

```
lambda1 <- NULL
t1      <- 183
p       <- 0.7
N       <- 200
HR      <- 0.55
tao     <- 365*3
A       <- 365
pow.SEPPLE(lambda1, t1, p, N, HR, tao, A, nsim=1000)
```

---

pow.sim.logrk *Simulated log-rank power computation*

Description

Perform the power calculation using a simulation-based method based on the regular log-rank test when the treatment time-lag effect is present and the lag duration is homogeneous across the individual subject

Usage

```
pow.sim.logrk(lambda1, t1, p, N, HR, tao, A, ap=0.5, alpha=0.05, nsim=10000)
```

Arguments

`lambda1`	Baseline hazard or NULL (see details)
`t1`	Delayed duration or NULL (see details)
`p`	Proportion of subjects who survive beyond the delayed period or NULL (see details)
`N`	Sample size
`HR`	Post-delay hazard ratio
`tao`	Total study duration
`A`	Total enrollment duration
`ap`	Experimental-control allocation ratio. The default is 0.5.
`alpha`	Type I error rate (two-sided). The default is 0.05.
`nsim`	Number of simulations. The default is 10000.

Details

Out of the three input parameters `lambda1`, `t1` and `p`, only two need to be specified, the remaining one will be computed internally from the formula `lambda1 = -log(p)/t1`. If all three are not NULL, then `lambda1` will be set to `-log(p)/t1` regardless of the user input value.

Value

The power

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References

Xu, Z., Zhen, B., Park, Y., & Zhu, B. (2017). Designing therapeutic cancer vaccine trials with delayed treatment effect. Statistics in medicine, 36(4), 592-605.

See Also

pow.APPLE, pow.SEPPLE

Examples

```
lambda1 <- NULL
t1      <- 183
p       <- 0.7
N       <- 200
HR      <- 0.55
tao     <- 365*3
A       <- 365
pow.sim.logrk(lambda1, t1, p, N, HR, tao, A, nsim=1000)
```

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