Package 'DelayedEffect.Design'

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Title Sample Size and Power Calculations using the APPLE, SEPPLE, 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 either homogeneous across the individual subject, or varies heterogeneously from individual to individual within a certain domain and following a specific pattern. The methods used are described in two references:

1. Xu, Z., Zhen, B., Park, Y., & Zhu, B. (2017) Designing therapeutic cancer vaccine trials with delayed treatment effect <doi:10.1002/sim.7157>.
2. Xu Z, Park Y, Zhen B, Zhu B. 2018) Designing cancer immunotherapy trials with random treatment time-lag effect. Statistics in Medicine. https://doi.org/10.1002/sim.7937

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DelayedEffect.Design *Sample size and power calculations using the APPLE, SEPPLE, APPLE+ and SEPPLE+ methods*

Description

An R package for sample size and power calculation when the treatment time-lag effect is present. The package incorporates two specific assumptions on the lag duration:
1. the lag duration is homogeneous across the individual subject;
2. the lag duration varies heterogeneously from individual to individual within a certain domain and following a specific pattern.

Details

The four new methods in this package for performing the sample size and power calculation 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),
3. Analytic Power calculation method based on generalized Piecewise weighted Log-rank tEst with random treatment time-lag effect (APPLE+),
4. Simulation-based Empirical Power calculation method based on generalized Piecewise weighted Log-rank tEst with random treatment time-lag effect (SEPPLE+).
See the references for details of these methods. Specifically, APPLE and SEPPLE assume the fixed delayed effect scenario where the lag duration is homogeneous across the individual subject, whereas APPLE+ and SEPPLE+ assume the random delayed effect scenario where the lag duration varies heterogeneously from individual to individual or from study to study within a certain domain and following a specific pattern. The functions for computing power corresponding to the above methods are pow.APPLE, pow.SEPPLE, pow.APPLE.plus, pow.SEPPLE.plus and pow.SEPPLE.random.DE. These can be compared to the functions pow.sim.logrk and pow.sim.logrk.rankdom.DE which compute the power using a simulation-based algorithm based on the regular log-rank test ignoring the existence of lag effects. The package also includes the function N.APPLE, N.APPLE.plus to back calculate the sample size given the power and hazard ratio, and the functions HR.APPLE and HR.APPLE.plus to back calculate the hazard ratio given the power and sample size, respectively, using the close-from APPLE and APPLE+ methods.

Author(s)

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References

Xu, Z., Park, Y., Zhen, B. & Zhu, B. (2018). Xu Z, Park Y, Zhen B, Zhu B. (2018) Designing cancer immunotherapy trials with random treatment time-lag effect. Statistics in Medicine. https://doi.org/10.1002/sim.7937

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 Piecewise Weighted Log-rank Test when the treatment time-lag effect is present and the lag duration is homogeneous across the individual subject. This function assumes the standard delayed effect scenario where the treatment effect is not manifested until t1 and remains constant afterwards (i.e. hazard ratio=1 during the lag period [0, t1]).

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	Lag duration or NULL (see details)
p	Proportion of subjects who survive beyond the lag 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)

Zhenzhen Xu <Zhenzhen.Xu@fda.hhs.gov>, Boguang Zhen<Boguang.Zhen@fda.hhs.gov>, Yongsoek Park <yongpark@pitt.edu> and Bin Zhu <bin.zhu@nih.gov>

References

Xu, Z., Park, Y., Zhen, B. & Zhu, B. (2018). Xu Z, Park Y, Zhen B, Zhu B. (2018） Designing cancer immunotherapy trials with random treatment time-lag effect. Statistics in Medicine. https://doi.org/10.1002/sim.7937

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)
```

HR.APPLE.plus *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 Generalized Piecewise Weighted Log-rank Test when the treatment time-lag effect is present and the lag duration varies heterogeneously from individual to individual or from study to study, within a certain domain [tl, tu] and following a specific pattern. This function assumes the random delayed effect scenario where the treatment effect is not manifested before tl, becomes more apparent from tl to tu, and remains constant after tu.

Usage

```
HR.APPLE.plus(lambda1, tl, tu, N, tao, A, beta, ap=0.5, alpha=0.05)
```

Arguments

lambda1	Baseline hazard
tl	Lower bound of lag duration domain
tu	Upper bound of lag duration domain
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 generalized Piecewise weighted Log-rank tEst with random treatment time-lag effect. See the reference for details of this method.

Value

The hazard ratio

Author(s)

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References

Xu, Z., Park, Y., Zhen, B. & Zhu, B. (2018). Xu Z, Park Y, Zhen B, Zhu B. (2018) Designing cancer immunotherapy trials with random treatment time-lag effect. Statistics in Medicine. https://doi.org/10.1002/sim.7937

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.plus, N.APPLE.plus

Examples

```
lambda1 <- 0.001982
tl      <- 30
tu      <- 30*11
N       <- 200
tao     <- 365*3
A       <- 365
beta    <- 0.2
HR.APPLE.plus(lambda1, tl, tu, 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 close-form APPLE method based on Piecewise Weighted Log-rank Test when the treatment time-lag effect is present and the lag duration is homogeneous across the individual subject. This function assumes the standard delayed effect scenario where the treatment effect is not manifested until t1 and remains constant afterwards (i.e. hazard ratio=1 during the lag period [0, t1]).

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	Lag duration or NULL (see details)
p	Proportion of subjects who survive beyond the lag period or NULL (see details)
HR	Post-delay hazard ratio: Post-delay hazard ratio, defined as the post-delay hazard rate of the treatment group compared to that of the control group
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., Park, Y., Zhen, B. & Zhu, B. (2018). Xu Z, Park Y, Zhen B, Zhu B. (2018) Designing cancer immunotherapy trials with random treatment time-lag effect. Statistics in Medicine. https://doi.org/10.1002/sim.7937

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)
```

N.APPLE.plus *APPLE+ sample size computation*

Description

Perform the sample size calculation given the power and post-delay hazard ratio using the close-form APPLE+ method based on Generalized Piecewise Weighted Log-rank Test when the treatment time-lag effect is present and the lag duration varies heterogeneously from individual to indi-vidual or from study to study, within a certain domain [tl, tu] and following a specific pattern. This function assumes the random delayed effect scenario where the treatment effect is not manifested before tl, becomes more apparent from tl to tu, and remains constant after tu.

Usage

```
N.APPLE.plus(lambda1, tl, tu, HR, tao, A, beta, ap=0.5, alpha=0.05)
```

Arguments

lambda1	Baseline hazard
tl	Lower bound of lag duration domain
tu	Upper bound of lag duration domain
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 generalized Piecewise weighted Log-rank tEst with random treatment time-lag effect. See the reference for details of this method.

Value

The sample size

Author(s)

Zhenzhen Xu <Zhenzhen.Xu@fda.hhs.gov>, Boguang Zhen<Boguang.Zhen@fda.hhs.gov>, Yongsoek Park <yongpark@pitt.edu> and Bin Zhu <bin.zhu@nih.gov>

References

Xu, Z., Park, Y., Zhen, B. & Zhu, B. (2018). Xu Z, Park Y, Zhen B, Zhu B. (2018） Designing cancer immunotherapy trials with random treatment time-lag effect. Statistics in Medicine. https://doi.org/10.1002/sim.7937

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.plus, HR.APPLE.plus

Examples

```
lambda1 <- 0.001982
tl      <- 30
tu      <- 30*11
HR      <- 0.55
tao     <- 365*3
A       <- 365
beta    <- 0.2
N.APPLE.plus(lambda1, tl, tu, HR, tao, A, beta)
```

pow.APPLE *APPLE power computation*

Description

Perform the power calculation using the close-form APPLE method based on Piecewise Weighted Log-rank Test when the treatment time-lag effect is present and the lag duration is homogeneous across the individual subject. This function assumes the standard delayed effect scenario where the treatment effect is not manifested until t1 and remains constant afterwards (i.e. hazard ratio=1 during the lag period [0, t1]).

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)

Zhenzhen Xu <Zhenzhen.Xu@fda.hhs.gov>, Boguang Zhen<Boguang.Zhen@fda.hhs.gov>, Yongsoek Park <yongpark@pitt.edu> and Bin Zhu <bin.zhu@nih.gov>

References

Xu, Z., Park, Y., Zhen, B. & Zhu, B. (2018). Xu Z, Park Y, Zhen B, Zhu B. (2018） Designing cancer immunotherapy trials with random treatment time-lag effect. Statistics in Medicine. https://doi.org/10.1002/sim.7937

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.APPLE.plus *APPLE+ power computation*

Description

Perform the power calculation using the close-form APPLE+ method based on Generalized Piecewise Weighted Log-rank Test when the treatment time-lag effect is present and the lag duration varies heterogeneously from individual to individual or from study to study, within a certain domain [tl, tu] and following a specific pattern. This function assumes the random delayed effect scenario where the treatment effect is not manifested before tl, becomes more apparent from tl to tu, and remains constant after tu.

Usage

```
pow.APPLE.plus(lambda1, tl, tu, N, HR, tao, A, ap=0.5, alpha=0.05)
```

Arguments

lambda1	Baseline hazard
tl	Lower bound of delayed duration domain
tu	Upper bound of delayed duration domain
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 generalized Piecewise weighted Log-rank tEst with random treatment time-lag effect. See the reference for details of this method.

Value

The power

Author(s)

Zhenzhen Xu <Zhenzhen.Xu@fda.hhs.gov>, Boguang Zhen<Boguang.Zhen@fda.hhs.gov>, Yongsoek Park <yongpark@pitt.edu> and Bin Zhu <bin.zhu@nih.gov>

References

Xu, Z., Park, Y., Zhen, B. & Zhu, B. (2018). Xu Z, Park Y, Zhen B, Zhu B. (2018） Designing cancer immunotherapy trials with random treatment time-lag effect. Statistics in Medicine. https://doi.org/10.1002/sim.7937

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.plus, HR.APPLE.plus

Examples

```
lambda1 <- 0.001982
tl      <- 30
tu      <- 30*11
N       <- 200
HR      <- 0.55
tao     <- 365*3
A       <- 365
pow.APPLE.plus(lambda1, tl, tu, N, HR, tao, A)
```

---

pow.SEPPLE *SEPPLE power computation*

Description

Perform the power calculation using the numeric SEPPLE method based on Piecewise Weighted Log-rank Test when the treatment time-lag effect is present and the lag duration is homogeneous across the individual subject. This function assumes the standard delayed effect scenario where the treatment effect is not manifested until t1 and remains constant afterwards (i.e. hazard ratio=1 during the lag period [0, t1]).

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)

Zhenzhen Xu <Zhenzhen.Xu@fda.hhs.gov> , Boguang Zhen<Boguang.Zhen@fda.hhs.gov>, Yongsoek Park <yongpark@pitt.edu> and Bin Zhu <bin.zhu@nih.gov>

References

Xu, Z., Park, Y., Zhen, B. & Zhu, B. (2018). Xu Z, Park Y, Zhen B, Zhu B. (2018） Designing cancer immunotherapy trials with random treatment time-lag effect. Statistics in Medicine. https://doi.org/10.1002/sim.7937

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.SEPPLE.plus *SEPPLE+ power computation*

Description

Perform the power calculation using the numeric SEPPLE+ method based on Generalized Piecewise Weighted Log-rank Test when the treatment time-lag effect is present and the lag duration varies heterogeneously from individual to individual or from study to study, within a certain domain [tl, tu] and following a specific pattern. This function assumes the random delayed effect scenario where the treatment effect is not manifested before tl, becomes more apparent from tl to tu, and remains constant after tu.

Usage

```
pow.SEPPLE.plus(lambda1, tl, tu, N, HR, tao, A, dist="uniform",
              shape1=NULL, shape2=NULL, ap=0.5, alpha=0.05, nsim=10000)
```

Arguments

lambda1	Baseline hazard
tl	Lower bound of delayed duration domain
tu	Upper bound of delayed duration domain
N	Sample size
HR	Post-delay hazard ratio
tao	Total study duration
A	Total enrollment duration
dist	One of "uniform", "beta" or "gamma", for the lag distribution
shape1	NULL or a positive parameter value for the beta or gamma distribution.
shape2	NULL or a positive parameter value for the beta or gamma distribution.
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 generalized Piecewise weighted Log-rank tEst with random treatment time-lag effect. See the reference for details of this method.

Value

The power

Author(s)

Zhenzhen Xu <Zhenzhen.Xu@fda.hhs.gov> , Boguang Zhen<Boguang.Zhen@fda.hhs.gov>, Yongsoek Park <yongpark@pitt.edu> and Bin Zhu <bin.zhu@nih.gov>

References

Xu, Z., Park, Y., Zhen, B. & Zhu, B. (2018). Xu Z, Park Y, Zhen B, Zhu B. (2018) Designing cancer immunotherapy trials with random treatment time-lag effect. Statistics in Medicine. https://doi.org/10.1002/sim.7937

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.SEPPLE.random.DE, pow.sim.logrk.random.DE

Examples

```
lambda1 <- 0.001982
tl      <- 30
tu      <- 30*11
N       <- 200
HR      <- 0.55
tao     <- 365*3
A       <- 365
Shape1  <- 5
Shape2  <- 5
pow.SEPPLE.plus(lambda1, tl, tu, N, HR, tao, A, dist="uniform",
              shape1=NULL, shape2=NULL, ap=0.5, alpha=0.05, nsim=10000)
```

`pow.SEPPLE.random.DE` *SEPPLE+ power computation*

Description

Perform the power calculation using the numeric SEPPLE method based on Piecewise Weighted Log-rank Test when the treatment time-lag effect is present and the lag duration varies heterogeneously from individual to individual or from study to study, within a certain domain [tl, tu] and following a specific pattern. The SEPPLE method assumes the fixed delayed effect scenario where the lag duration is homogeneous across the individula subject and the treatment effect is not manifested until a fixed time point t.fixed for all subjects, whereas the underlying truth is the random delayed effect scenario where the lag duration varies heterogeneously and the treatment effect is not manifested until tl, gradually increases from tl to tu, and remains constant after tu. The purpose of this function is to evaluate the property of SEPPLE when applied under a mis-specified delayed effect scenario.

Usage

```
pow.SEPPLE.random.DE(lambda1, tl, tu, N, HR, tao, A, t.fixed, dist="uniform",
              shape1=NULL, shape2=NULL, ap=0.5, alpha=0.05, nsim=10000)
```

Arguments

`lambda1`	Baseline hazard
`tl`	Lower bound of lag duration domain
`tu`	Upper bound of lag duration domain
`N`	Sample size
`HR`	Post-delay hazard ratio
`tao`	Total study duration
`A`	Total enrollment duration
`t.fixed`	Fixed lag duration in SEPPLE
`dist`	One of "uniform", "beta" or "gamma", for the lag distribution
`shape1`	NULL or a positive parameter value for the `beta` or `gamma` distribution.
`shape2`	NULL or a positive parameter value for the `beta` or `gamma` distribution.
`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 generalized Piecewise weighted Log-rank tEst with random treatment time-lag effect. See the reference for details of this method.

Value

The power

Author(s)

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References

Xu, Z., Park, Y., Zhen, B. & Zhu, B. (2018). Xu Z, Park Y, Zhen B, Zhu B. (2018) Designing cancer immunotherapy trials with random treatment time-lag effect. Statistics in Medicine. https://doi.org/10.1002/sim.7937

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.SEPPLE.plus, pow.sim.logrk.random.DE

Examples

```
lambda1 <- 0.001982
tl      <- 30
tu      <- 30*11
N       <- 200
HR      <- 0.55
tao     <- 365*3
A       <- 365
t.fixed <- (tl+tu)/2
Shape1  <- 5
Shape2  <- 5
pow.SEPPLE.random.DE(lambda1, tl, tu, N, HR, tao, A, t.fixed, dist="beta",
                     shape1=shape1, shape2=shape2, ap=0.5, alpha=0.05, nsim=10000)
```

---

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. This function assumes the treatment time-lag effect does not exist whereas the underlying truth is that the treatment effect is not manifested until t1 and remains constant afterwards (i.e. hazard ratio=1 during the lag period [0, t1]). The purpose of this funtion is to evaluate the impact of ignoring the delayed effect on the study power given sample size, under the fixed delayed effect scenario.

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	Lag duration or NULL (see details)
p	Proportion of subjects who survive beyond the lag 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

Author(s)

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References

Xu, Z., Park, Y., Zhen, B. & Zhu, B. (2018). Xu Z, Park Y, Zhen B, Zhu B. (2018) Designing cancer immunotherapy trials with random treatment time-lag effect. Statistics in Medicine. https://doi.org/10.1002/sim.7937

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)
```

---

pow.sim.logrk.random.DE *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 varies heterogeneously from individual to individual or from study to study, within a certain domain [tl, tu] and following a specific pattern. This function assumes the treatment time-lag effect does not exist whereas the underlying truth is that the lag duration varies heterogeneously and the treatment effect is not manifested until tl, gradually increases from tl to tu, and remains constant after tu. The purpose of this funtion is to evaluate the impact of ignoring the delayed effect on the study power given sample size, under the random delayed effect scenario.

Usage

```
pow.sim.logrk.random.DE(lambda1, tl, tu, N, HR, tao, A, dist="uniform",
              shape1=NULL, shape2=NULL, ap=0.5, alpha=0.05, nsim=10000)
```

Arguments

lambda1	Baseline hazard
tl	Lower bound of lag duration domain
tu	Upper bound of lag duration domain
N	Sample size
HR	Post-delay hazard ratio
tao	Total study duration
A	Total enrollment duration
dist	One of "uniform", "beta" or "gamma", for the lag distribution
shape1	NULL or a positive parameter value for the beta or gamma distribution.
shape2	NULL or a positive parameter value for the beta or gamma distribution.
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

The regular log-rank test is used here

Value

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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.SEPPLE.plus, pow.SEPPLE.random.DE

Examples

```
lambda1 <- 0.001982
tl      <- 30
tu      <- 30*11
N       <- 200
HR      <- 0.55
tao     <- 365*3
A       <- 365
Shape1  <- 5
Shape2  <- 5
pow.sim.logrk.random.DE(lambda1, tl, tu, N, HR, tao, A, dist="beta",
       shape1=shape1, shape2=shape2, ap=0.5, alpha=0.05, nsim=10000)
```

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