BI476: Biostatistics - Case Studies

Lec05: Power and Sample Size Calculation

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Example

Table : A multi-center two-arm randomized phase III trial

Study design	A multi-center two-arm randomized phase III trial to compare the combination of gemcitabine (吉西它宾) and docetaxel (多西它赛) versus gemcitabine along
Patients	Advanced or metastatic unresectable soft tissue sarcoma (软组织肉瘤)
Primary outcome	progression-free survival
Secondary outcome	overall survival

Why sample size?

- The aim of a clinical trial is to judge the efficacy and/or safety of a new therapy or drug.
- In the planning phase of the study, the calculation of the necessary sample size is crucial in order to obtain a meaningful result.
- The study design, the expected treatment effect in outcome and its variability, power and significance level are factors which determine the sample size.
- It is often difficult to fix these parameters prior to the start of the study, but related papers from the literature can be helpful sources for the unknown quantities.
- For scientific as well as ethical reasons it is necessary to calculate the sample size in advance in order to be able to answer the study question.

Calculation of sample size

Table : Type I error, Type II error, p-value and power

	H_0 is true	H_1 is true
Reject H_0	α(Type I error)	$1-\beta$(power)
Not Reject H_0		β(Type II error)

Power = The probability of rejecting H_0 if H_1 is true.
Power = $f(\alpha$, variation, clinically significant level, Sample size)
Sample size = f(Power, α, variation, clinically significant level)
p-value = the probability of observing this difference if H_0 were true.

An example

Manuscript writeup

Cognitive therapy for the prevention of suiside attempts: a randomized controlled trial.

Brown GK et al. JAMA 2005; 294:463-570.

To test the primary hypothesis that the mean time to the next suicide attempt during the follow-up period is different between treatment groups, a priori power calculations were based on the results of a previous randomized controlled trial with a similar protocol. The current sample size ($N = 120$) provided at least 80% power to detect a hazard ratio of 0.44 in terms of time to next suicide attempt between treatment groups using an assumed repeat attempt rate of 25.8% during the follow-up period and a two-sided α level of 0.05.

1. Comparing means for continuous outcomes

$$Y_{ik} \sim N(\mu_k, \sigma^2); k = 1, 2; i = 1, \ldots, n_k$$

- Testing for equality of two independent means
- Superiority trial of two independent means
- Non-inferiority trial of two independent means
- Equivalance trial of two independent means

1.1 Testing for equality of two means

$$H_0 : \theta = \mu_1 - \mu_2 = 0 \text{ versus } H_1 : \theta \neq 0$$

Procedure

1. The sample mean: $\bar{Y}_k = \frac{1}{n_k} \sum_{i=1}^{n_k} Y_{ik}, k = 1, 2$
2. The pooled-sample variance: $s_n^2 = \frac{1}{n_1+n_2-2} \sum_{k=1}^{2} \sum_{i=1}^{n_k} (Y_{ik} - \bar{Y}_k)^2$
3. The two-sample t-test statistic: $T_n = \frac{\bar{Y}_1 - \bar{Y}_2}{s_n \sqrt{1/n_1 + 1/n_2}}$
4. Under H_0: $T_n \sim t_\nu, \nu = n_1 + n_2 - 2;$
5. Under H_1: $T_n \sim t_\nu(c), c = \frac{\theta}{\sigma \sqrt{1/n_1 + 1/n_2}}$
6. Reject H_0 if $|T_n| \geq t_{\nu,\alpha/2}$

1.1 Testing for equality of two means

Under H_1, the power of the two-sample t-test is given by

$$1-\beta = 1-\mathcal{T}(t_{\nu,\alpha/2}, c) + \mathcal{T}(-t_{\nu,\alpha/2}, c)$$

where $\mathcal{T}(\dot{;}c)$ denotes the cumulative distribution function of the noncentral $t_\nu(c)$ distribution.

We specify the treatment difference to be detected as θ and define

$$Z = \frac{\bar{Y}_1 - \bar{Y}_2 - \theta}{\sigma\sqrt{1/n_1 + 1/n_2}} \sim N(0,1)$$

Now the power is given by

$$\begin{aligned} 1-\beta &= Pr\left(\left|\frac{\bar{Y}_1-\bar{Y}_2}{\sigma\sqrt{1/n_1+1/n_2}}\right| \geq z_{\alpha/2} \middle| H_1\right) \\ &= Pr\left(Z \geq z_{\alpha/2} - \frac{\theta}{\sigma\sqrt{1/n_1+1/n_2}} \middle| H_1\right) \\ &\quad + Pr\left(Z \leq -z_{\alpha/2} - \frac{\theta}{\sigma\sqrt{1/n_1+1/n_2}} \middle| H_1\right) \end{aligned}$$

1.1 Testing for equality of two means

When $\theta > 0$, we can ignore the second term

$$\beta \approx Pr\left(Z \leq z_{\alpha/2} - \frac{\theta}{\sigma\sqrt{1/n_1 + 1/n_2}} \middle| H_1\right)$$

Similarly when $\theta < 0$, we can ignore the first term

$$\beta \approx Pr\left(Z \leq z_{\alpha/2} + \frac{\theta}{\sigma\sqrt{1/n_1 + 1/n_2}} \middle| H_1\right)$$

That is

$$\beta \approx \Phi\left(z_{\alpha/2} - \frac{|\theta|}{\sigma\sqrt{1/n_1 + 1/n_2}}\right)$$

Therefore, sample size can be obtained by solving

$$-z_\beta = z_{\alpha/2} - \frac{|\theta|}{\sigma\sqrt{1/n_1 + 1/n_2}} \Rightarrow \frac{|\theta|}{\sigma\sqrt{1/n_1 + 1/n_2}} = z_{\alpha/2} + z_\beta$$

If $n_1 = n_2 = n$,

$$n = \frac{2\sigma^2(z_{\alpha/2} + z_\beta)^2}{\theta^2}$$

1.1 Exercise: Unbalanced allocation

If the patience allocation ratio between arm 1 and arm 2 is

$$r = n_1/n_2$$

- Calculate the required total sample size.
- Is it larger or smaller than the balanced allocation?
- If we set $\theta = 1, \sigma^2 = 4, \alpha = 0.05$, calculate the required sample size for balanced allocation and unbalanced allocation with $r = 2$, resepectively.
- Draw a figure to illustrate how the powers change with changing allocation by fixing the total sample size to be 200 and $\alpha = 0.05$.

1.2 Superiority Trial

A superiority trial can be formulated as a one-sided test:

$$H_0 : \theta \leq 0 \text{ versus } H_1 : \theta > 0$$

where θ is the preset clinically meaningful difference and we define

$$Z = \frac{\bar{Y}_1 - \bar{Y}_2 - \theta}{\sigma\sqrt{1/n_1 + 1/n_2}}$$

The power is given by

$$\begin{aligned} 1 - \beta &= Pr\left(\frac{\bar{Y}_1 - \bar{Y}_2}{\sigma\sqrt{1/n_1+1/n_2}} \geq z_\alpha \Big| H_1\right) \\ &= Pr\left(Z \geq z_\alpha - \frac{\theta}{\sigma\sqrt{1/n_1+1/n_2}} \Big| H_1\right) \end{aligned}$$

which leads to

$$\frac{\theta}{\sigma\sqrt{1/n_1 + 1/n_2}} = z_\alpha + z_\beta$$

If $n_1 = n_2 = n$, then

$$n = \frac{2\sigma^2(z_\alpha + z_\beta)^2}{\theta^2}$$

1.3 Non-inferiority Trial

A non-inferiority trial can be formulated as a one-sided test:

$$H_0 : \theta \leq -\delta \text{ versus } H_1 : \theta > -\delta$$

where $\delta > 0$ is the noninferiority margin.

H_0 is rejected when

$$\frac{\bar{Y}_1 - \bar{Y}_2 + \delta}{\sigma\sqrt{1/n_1 + 1/n_2}} \geq z_\alpha$$

and define

$$Z = \frac{\bar{Y}_1 - \bar{Y}_2 - \theta}{\sigma\sqrt{1/n_1 + 1/n_2}}$$

and the power is given by

$$\begin{aligned} 1 - \beta &= Pr\left(\frac{\bar{Y}_1 - \bar{Y}_2 + \delta}{\sigma\sqrt{1/n_1+1/n_2}} \geq z_\alpha \middle| H_1\right) \\ &= Pr\left(Z \geq z_\alpha - \frac{\delta+\theta}{\sigma\sqrt{1/n_1+1/n_2}} \middle| H_1\right) \end{aligned}$$

leading to

$$\frac{\theta + \delta}{\sigma\sqrt{1/n_1 + 1/n_2}} = z_\alpha + z_\beta \Rightarrow n = \frac{2\sigma^2(z_\alpha + z_\beta)^2}{(\theta + \delta)^2}$$

1.4 Equivalence Trial

An equivalence trial can be formulated as

$$H_0 : |\theta| \geq \delta \text{ versus } H_1 : |\theta| < \delta$$

The rejection region can be written as

$$z_\alpha - \frac{\delta}{\sigma\sqrt{1/n_1 + 1/n_2}} \leq \frac{\bar{Y}_1 - \bar{Y}_2}{\sigma\sqrt{1/n_1 + 1/n_2}} \leq -z_\alpha + \frac{\delta}{\sigma\sqrt{1/n_1 + 1/n_2}}$$

Let

$$Z = \frac{\bar{Y}_1 - \bar{Y}_2 - \theta}{\sigma\sqrt{1/n_1 + 1/n_2}} \sim N(0, 1)$$

And the power is given by

$$\begin{aligned} 1 - \beta &= Pr\left(z_\alpha - \frac{\delta+\theta}{\sigma\sqrt{1/n_1+1/n_2}} \leq Z \leq -z_\alpha + \frac{\delta-\theta}{\sigma\sqrt{1/n_1+1/n_2}} \Big| H_1\right) \\ &= \Phi\left(-z_\alpha + \frac{\delta-\theta}{\theta\sqrt{1/n_1+1/n_2}}\right) - \Phi\left(z_\alpha - \frac{\delta+\theta}{\sigma\sqrt{1/n_1+1/n_2}}\right) \end{aligned}$$

1.4 Equivalence Trial

In a conservative derivation with no power inflation, we have

$$1 - \beta \approx 2\Phi\left(-z_\alpha + \frac{\delta - |\theta|}{\sigma\sqrt{1/n_1 + 1/n_2}}\right) - 1$$

which leads to

$$\frac{\delta - |\theta|}{\sigma\sqrt{1/n_1 + 1/n_2}} = z_\alpha + z_{\beta/2}$$

If $n_1 = n_2 = n$, then

$$n = \frac{2\sigma^2(z_\alpha + z_{\beta/2})^2}{(\delta - |\theta|)^2}$$

Note: θ is often set to zero in practice.

1.4 Exercise: Bioequivalence trial sample size

In a clinical trial with cardiovascular disease, both the novel and standard therapies target lowering the blood pressure. The study is to establish equivalence of the two treatments in terms of therapeutic effects with an equivalence margin $\delta = 0.2$. The variance of the medical measurements is estiamted to be 1.0 from previous study.

In an equivalence trial often uses the 90% rather than 95% confidence interval.

Then to achieve a power of 90%, how many total sample size do we need?

2. Comparing proportions for binary outcomes

Let Y_{ik} be the binary outcome for subject $i = 1, \ldots, n_k$ in arm $k = 1, 2$:

$$Y_{ik} = \begin{cases} 1, & \text{with probability } p_k, \\ 0, & \text{with probability } 1 - p_k, \end{cases}$$

and the sum in each arm k is

$$\sum_{i=1}^{n_k} Y_{ik} \sim Bin(n_k, p_k)$$

The sample proportion for arm k is

$$\begin{array}{lcl} \bar{Y}_k & = & \frac{1}{n_k} \sum_{i=1}^{n_k} Y_{ik} \\ E(\bar{Y}_k) & = & p_k \\ Var(\bar{Y}_k) & = & p_k(1 - p_k)/n_k \end{array}$$

The difference

$$\theta = p_1 - p_2$$

2.1 Test for the equation of two proportions

$$H_0 : \theta = 0 \text{ versus } H_1 : \theta \neq 0$$

Under H_0, the test statistic

$$T_n = \frac{\bar{Y}_1 - \bar{Y}_2}{\sqrt{\bar{Y}(1 - \bar{Y})(1/n_1 + 1/n_2)}} \sim N(0, 1),$$

where $\bar{Y}$ is the pooled-sample mean:

$$\bar{Y} = \frac{n_1 \bar{Y}_1 + n_2 \bar{Y}_2}{n_1 + n_2}$$

While under the alternative hypothesis,

$$T_n | H_1 \sim N\left(\frac{\theta}{\sqrt{\bar{p}(1 - \bar{p})(1/n_1 + 1/n_2)}}, \frac{p_1(1 - p_1)/n_1 + p_2(1 - p_2)/n_2}{\bar{p}(1 - \bar{p})(1/n_1 + 1/n_2)}\right)$$

2.1 Test for the equation of two proportions

Define the standard normal random variable

$$Z = \frac{\bar{Y}_1 - \bar{Y}_2 - \theta}{\sqrt{p_1(1-p_1)/n_1 + p_2(1-p_2)/n_2}}$$

where θ is the treatment difference to be detected.

The power is therefore

$$\begin{aligned}
1-\beta &= Pr\left(\left|\frac{\bar{Y}_1-\bar{Y}_2}{\sqrt{\bar{p}(1-\bar{p})(1/n_1+1/n_2)}}\right| \geq z_{\alpha/2} \middle| H_1\right) \\
&= Pr\left(Z \geq \frac{z_{\alpha/2}\sqrt{\bar{p}(1-\bar{p})(1/n_1+1/n_2)}-\theta}{\sqrt{p_1(1-p_1)/n_1+p_2(1-p_2)/n_2}} \middle| H_1\right) \\
&\quad + Pr\left(Z \leq \frac{-z_{\alpha/2}\sqrt{\bar{p}(1-\bar{p})(1/n_1+1/n_2)}-\theta}{\sqrt{p_1(1-p_1)/n_1+p_2(1-p_2)/n_2}} \middle| H_1\right)
\end{aligned}$$

2.1 Test for the equality of two proportions

Therefore

$$\beta \approx \Phi\left(\frac{z_{\alpha/2}\sqrt{\bar{p}(1-\bar{p})(1/n_1+1/n_2)}-|\theta|}{\sqrt{p_1(1-p_1)/n_1+p_2(1-p_2)/n_2}}\right),$$

and the sample size can be obtained by solving

$$|\theta| = z_{\alpha/2}\sqrt{\bar{p}(1-\bar{p})(1/n_1+1/n_2)}+z_{\beta}\sqrt{p_1(1-p_1)/n_1+p_2(1-p_2)/n_2}$$

If $n_1 = n_2 = n$, then the sample size

$$n = \frac{\left(z_{\alpha/2}\sqrt{2\bar{p}(1-\bar{p})}+z_{\beta}\sqrt{p_1(1-p_1)+p_2(1-p_2)}\right)^2}{\theta^2}$$

2.2 Sample size with unpooled variance

Under the two-sided hypothesis,

$$T_n = \frac{\bar{Y}_1 - \bar{Y}_2}{\sqrt{\bar{Y}_1(1-\bar{Y}_1)/n_1 + \bar{Y}_2(1-\bar{Y}_2)/n_2}}$$

which can be approximated by

$$T_n \approx \frac{\bar{Y}_1 - \bar{Y}_2}{\sqrt{p_1(1-p_1)/n_1 + p_2(1-p_2)/n_2}}$$

Under H_0,

$$T_n \big| H_0 \sim N(0, 1)$$

and under H_1,

$$T_n \big| H_1 \sim N\left(\frac{\theta}{\sqrt{p_1(1-p_1)/n_1 + p_2(1-p_2)/n_2}}, 1\right)$$

2.2 Sample size with unpooled variance

The power can be calculated as

$$\begin{aligned} 1-\beta &= Pr\left(\left|\frac{\bar{Y}_1-\bar{Y}_2}{\sqrt{p_1(1-p_1)/n_1+p_2(1-p_2)/n_2)}}\right| \geq z_{\alpha/2}\middle|H_1\right) \\ &= Pr\left(Z \geq z_{\alpha/2} - \frac{\theta}{\sqrt{p_1(1-p_1)/n_1+p_2(1-p_2)/n_2}}\middle|H_1\right) \\ &\quad +Pr\left(Z \leq -z_{\alpha/2} - \frac{\theta}{\sqrt{p_1(1-p_1)/n_1+p_2(1-p_2)/n_2}}\middle|H_1\right) \end{aligned}$$

Therefore,

$$\beta \approx \Phi\left(z_{\alpha/2} - \frac{|\theta|}{\sqrt{p_1(1-p_1)/n_1+p_2(1-p_2)/n_2}}\right)$$

and the sample size can be obtained by solving

$$\frac{|\theta|}{\sqrt{p_1(1-p_1)/n_1+p_2(1-p_2)/n_2}} = z_{\alpha/2}+z_\beta$$

If $n_1 = n_2 = n$, then

$$n = \frac{(z_{\alpha/2}+z_\beta)^2}{\theta^2}\left[p_1(1-p_1)+p_2(1-p_2)\right]$$

2.2 Exercise: Sample size estimation

Suppose that the standard treatment has a response rate of 30% for metastatic breast cancer patients, and the new treatment is expected to have an improvemment of 10%.

We set type I error rate of $\alpha = 0.05$ and power 90%. How many patients do we need? Use both the pooled and unpooled variance estimators.

2.3 Superiority Trial

A superiority trial can be formulated as a one-sided hypothesis:

$$H_0 : \theta \leq 0 \text{ versus } H_1 : \theta > 0.$$

Here the power is given by

$$1 - \beta = Pr\left(Z \geq \frac{z_\alpha\sqrt{\bar{p}(1-\bar{p})(1/n_1 + 1/n_2)} - \theta}{\sqrt{p_1(1-p_1)/n_1 + p_2(1-p_2)/n_2}} \Big| H_1\right)$$

where Z is the standard normal variable defined as

$$Z = \frac{\bar{Y}_1 - \bar{Y}_2 - \theta}{\sqrt{p_1(1-p_1)/n_1 + p_2(1-p_2)/n_2}}$$

Therefore, the sample size can be obtained by solving

$$\theta = z_\alpha\sqrt{\bar{p}(1-\bar{p})(1/n_1 + 1/n_2)} + z_\beta\sqrt{p_1(1-p_1)/n_1 + p_2(1-p_2)/n_2}$$

If $n_1 = n_2 = n$, then

$$n = \frac{\left[z_\alpha\sqrt{2\bar{p}(1-\bar{p})} + z_\beta\sqrt{p_1(1-p_1) + p_2(1-p_2)}\right]^2}{\theta^2}$$

2.3 Exercise: Unbalanced allocation for superiority trial for binary outcome

(1) If we do NOT pool two samples for estimating the variance, and the allocation ratio is r. Write down the required total sample size here for a set of given parameters $\{\alpha, \beta, \theta, p_1, p_2, r\}$.

(2) The response rate of a standard chemotherapy for prostate cancer is 20%, and the experimental drug would double the response rate. In a one-sided test, we specify the type I error rate $\alpha = 0.025$ and power 90%. How many samples do we need in such as superirority trial? Compute based on both balanced and unbalanced allocation of $r = 3$ (i.e., $n_1 = 3n_2$).

2.4 Noninferiority Trial

A noninferiority trial can be formulated as a one-sided hypothesis:

$$H_0 : \theta \leq -\delta \text{ versus } H_1 : \theta > \delta.$$

H_0 is rejected at a significance level of α, if

$$\frac{\bar{Y}_1 - \bar{Y}_2 + \delta}{\sqrt{\bar{p}(1-\bar{p})(1/n_1 + 1/n_2)}} \geq z_\alpha.$$

Here the power is given by

$$1 - \beta = Pr\left(Z \geq \frac{z_\alpha \sqrt{\bar{p}(1-\bar{p})(1/n_1 + 1/n_2)} - (\theta + \delta)}{\sqrt{p_1(1-p_1)/n_1 + p_2(1-p_2)/n_2}} \middle| H_1 \right)$$

where Z is the standard normal variable defined as

$$Z = \frac{\bar{Y}_1 - \bar{Y}_2 - \theta}{\sqrt{p_1(1-p_1)/n_1 + p_2(1-p_2)/n_2}}$$

Therefore, the sample size can be obtained by solving

$$\theta + \delta = z_\alpha \sqrt{\bar{p}(1-\bar{p})(1/n_1 + 1/n_2)} + z_\beta \sqrt{p_1(1-p_1)/n_1 + p_2(1-p_2)/n_2}$$

If $n_1 = n_2 = n$, then $n = \frac{\left[z_\alpha \sqrt{2\bar{p}(1-\bar{p})} + z_\beta \sqrt{p_1(1-p_1) + p_2(1-p_2)}\right]^2}{(\theta+\delta)^2}$

2.4 Exercise: Noninferiority trial

We are interested in testing whether a new treatment is noninferior to the standard care, while less toxic and easier to administer. Suppose that the estimated difference of the response rates between the active control and placebo is 20%, with a 95% confidence interval of $[0.16, 0.24]$.

We may set δ as a half of the minimal estimated difference between the active control and placebo (the lower bound of 95%*CI*), that is, $\delta = 0.08$.

For a one-sided test with $\alpha = 0.025$ and power=80%. How to estimate the required sample size?

2.5 Equivalence Trial

An equivalence trial can be formulated as one-sided trial:

$$H_0 : |\theta| \geq \delta \text{ versus } H1 : |\theta| < \delta$$

The null hypothesis is rejected at a significance level of α, if

$$z_\alpha - \frac{\delta}{\sqrt{\bar{p}(1-\bar{p})(1/n_1 + 1/n_2)}} \leq T_n \leq -z_\alpha + \frac{\delta}{\sqrt{\bar{p}(1-\bar{p})(1/n_1 + 1/n_2)}}$$

Under H_1, the power is given by:

$$1 - \beta \approx 2\Phi\left(\frac{-z_\alpha\sqrt{\bar{p}(1-\bar{p})(1/n_1 + 1/n_2)} + \delta - |\theta|}{\sqrt{p_1(1-p_1)/n_1 + p2(1-p_2)/n_2}}\right) - 1$$

Therefore, the sample size can be obtained by solving

$$\delta - |\theta| = z_\alpha\sqrt{\bar{p}(1-\bar{p})(1/n_1 + 1/n_2)} + z_{\beta/1}\sqrt{p_1(1-p_1)/n_1 + p_2(1-p_2)/n_2}$$

If $n_1 = n_2 = n$, then

$$n = \frac{\left[z_{\alpha\sqrt{\bar{p}(1-\bar{p})}} + z_{\beta/2}\sqrt{p_1(1-p_1) + p_2(1-p_2)}\right]^2}{(\delta - |\theta|)^2}$$

Power and sample size analysis in R: `pwr`

function	power calculation for
`pwr.2p.test`	two proportions (equal *n*)
`pwr.2p2n.test`	two proportions (unequal *n*)
`pwr.anova.test`	balanced one-way ANOVA
`pwr.chisq.test`	chi-squared test
`pwr.f2.test`	general linear model
`pwr.p.test`	proportion (one-sample)
`pwr.r.test`	correlation test
`pwr.t.test`	t-tests (one-sample, two-sample, paired)
`pwr.t2n.test`	t-tests (two-samples with unequal *n*)

Exercise: Fill in the sample size table below

Use $\alpha = 0.025$ and two-sided test for calculations.

$p(y = 1 \mid exposed)$	$p(y = 1 \mid nonexposed)$	Power	Sample size
0.1	0.5	0.90	?
0.3	0.5	0.90	?
0.45	0.5	0.90	?
0.2	0.8	0.80	?
0.4	0.8	0.80	?
0.6	0.8	0.80	?
0.2	0.8	0.70	?
0.4	0.8	0.70	?
0.6	0.8	0.70	?

After-class Exercises

(1) In a superiority trial, suppose that the response rate of the standard treatment is 25%, and we expect that of the experimental treatment to be 40%. We set type I error rate $\alpha = 0.025$ and a power of 90%. What is the total sample size if th allocation ratio between the experimental and standard arms is 2:1? Compare the sample size estimation based on the two different formulae (pooled or unpooled). How about the sample size using an allocation ratio of 1:1?

(2) In a noninferiority trial, suppose that the noninferiority margin $\delta = 0.05$, and we take the response rates of both the standard and experimental treatments to be 30%. For a type I error rate of $\alpha = 0.05$ and a power of 90%, what is the total sample size of the trial with an allocation ratio of 3:1?

Power and sample size: Summary

1. Carefully consider and state the null hypothesis to be tested.

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2. Select an appropriate statistical tests:

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    - e.g., paired t-test

Power and sample size: Summary

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2. Select an appropriate statistical tests:
   - e.g., paired t-test
3. Choose a clinically significant effect size.

Power and sample size: Summary

1. Carefully consider and state the null hypothesis to be tested.
2. Select an appropriate statistical tests:
   - e.g., paired t-test
3. Choose a clinically significant effect size.
4. Provide an estimate of the variability.

Power and sample size: Summary

1. Carefully consider and state the null hypothesis to be tested.
2. Select an appropriate statistical tests:
   - e.g., paired t-test
3. Choose a clinically significant effect size.
4. Provide an estimate of the variability.
   - according to previous studies or literature.

Power and sample size: Summary

1. Carefully consider and state the null hypothesis to be tested.
2. Select an appropriate statistical tests:
   - e.g., paired t-test
3. Choose a clinically significant effect size.
4. Provide an estimate of the variability.
   - according to previous studies or literature.
5. Select the type I error (α) and required power ($1 - \beta$) you are willing to accept.

Power and sample size: Summary

1. Carefully consider and state the null hypothesis to be tested.
2. Select an appropriate statistical tests:
   - e.g., paired t-test
3. Choose a clinically significant effect size.
4. Provide an estimate of the variability.
   - according to previous studies or literature.
5. Select the type I error (α) and required power ($1 - \beta$) you are willing to accept.
6. Calcualte the sample size.

Power and sample size: Summary

1. Carefully consider and state the null hypothesis to be tested.
2. Select an appropriate statistical tests:
   - e.g., paired t-test
3. Choose a clinically significant effect size.
4. Provide an estimate of the variability.
   - according to previous studies or literature.
5. Select the type I error (α) and required power ($1 - \beta$) you are willing to accept.
6. Calcualte the sample size.
7. Adjust sample size estimate for dropout if necessary.