

样本量估算及PASS软件操作

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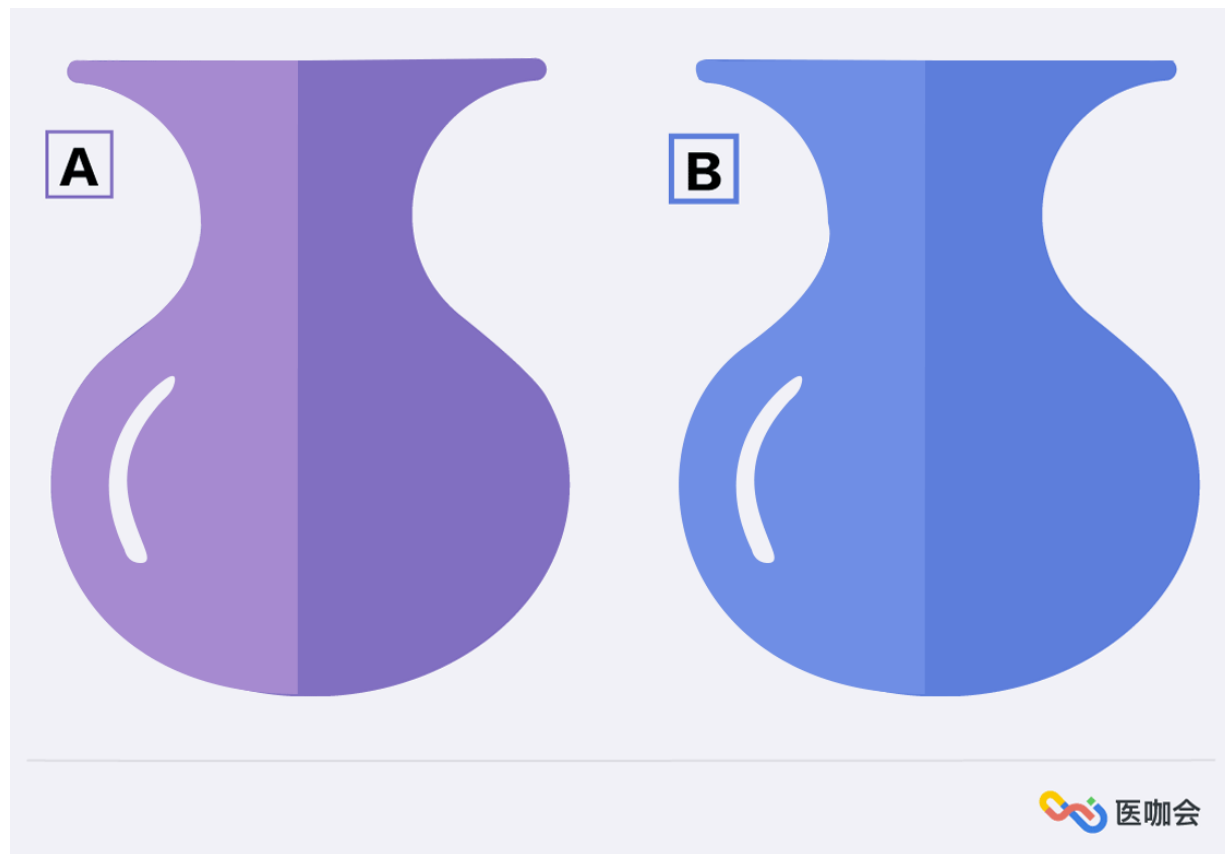
2017年7月

应该选取多少样本

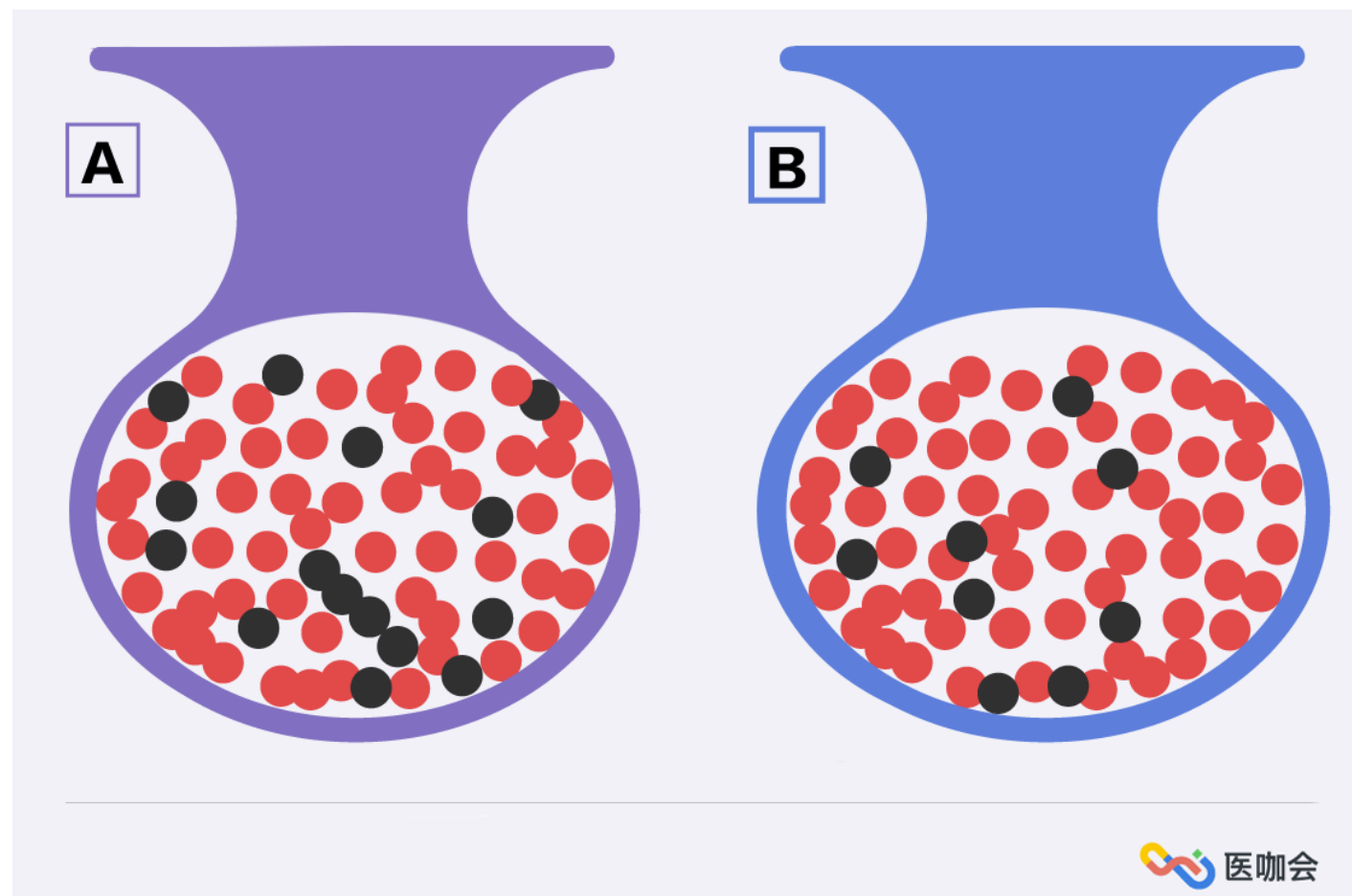
一位研究者在学术会议上报告了一项用于绵羊的药物研究，他说道：“用药之后，三分之一的绵羊状态有了显著改善，三分之一没有任何变化，另外三分之一跑掉了。”

其他研究者问他一共使用了几只绵羊，他回答道：三只……

应该选取多少样本



应该选取多少样本



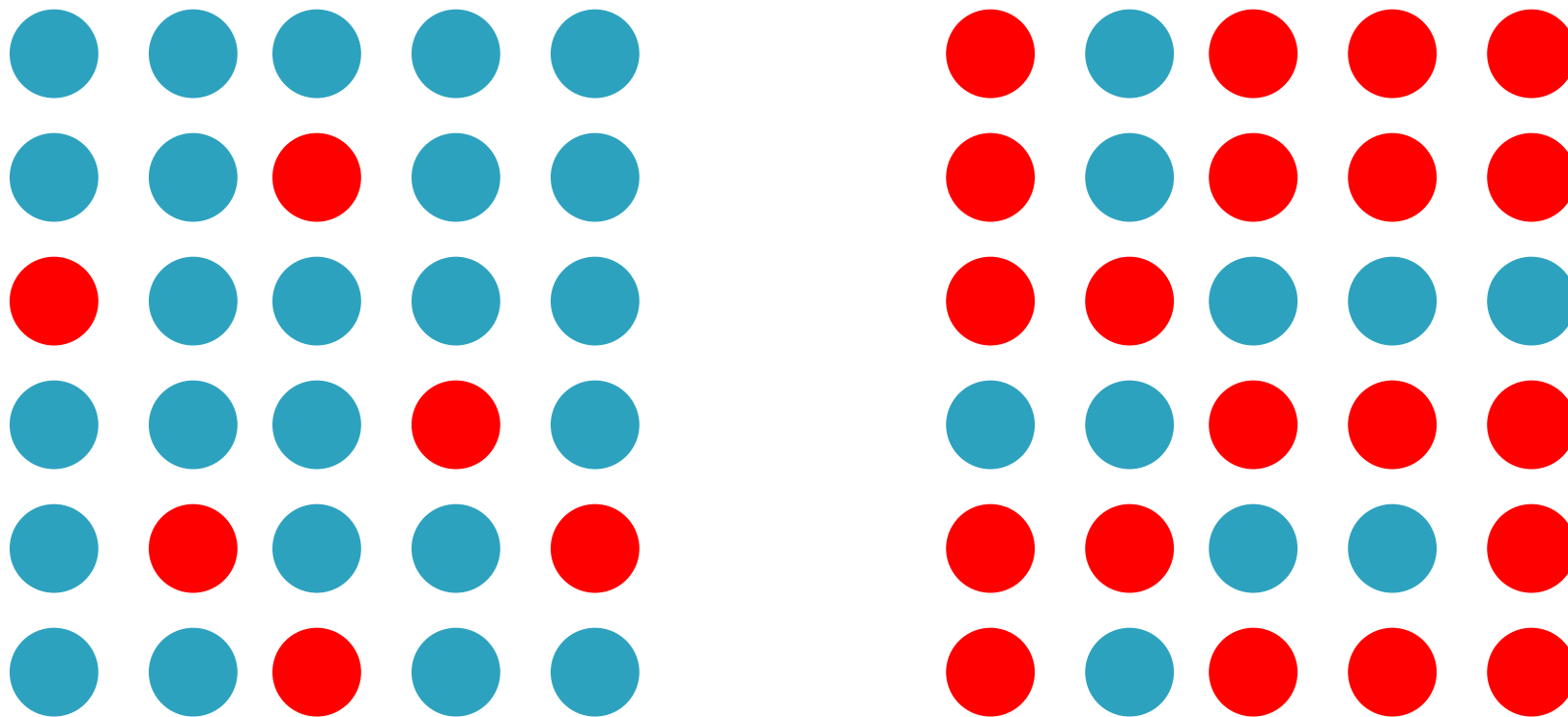
应该调查多少人

某学校有500名学生，要了解学生中能够说出父母亲生日的人的比例，可以采取简单的随机抽样的方法进行调查。

有的同学认为，应当调查250名学生，否则样本没有代表性。但另外一些学生同学认为，调查100名足矣。

到底需要调查对少人？

应该调查多少人



样本量越大，样本的估计越接近总体的实际状况。

为什么要估算样本量

▶ 不足的样本量

- ✓ 可重复性差，不能排除偶然因素的影响
- ✓ 检验效能低，阴性结果难以解释

▶ 过大的样本量

- ✓ 负担不起（财力、人力、时间）
- ✓ 增加临床研究的难度

▶ 合适的样本量

- ✓ 确保研究得到有价值、可靠的信息

估算样本量的目的

在保证某个**临床试验/临床研究**的结论具有一定科学性、真实性和可靠性前提下，**估算某研究所需的最小观察例数。**

估算样本量的步骤

一、确定研究设计类型

▶ 研究设计方案不同，样本量的估计方法不同

- ✓ 随机对照试验/队列研究

- ✓ 病例对照研究

- ✓ 横断面调查

- ✓ 诊断试验

- ✓

二、确定结局指标

▶ 结局指标不同，样本量的估计方法不同

- ✓ 连续变量：如年龄，身高；
- ✓ 二分类变量：如发病率，死亡率；
- ✓ 生存数据；
- ✓ 等级变量(有序多分类)：如痊愈、显效、好转、无效。

需要估计样本量的常见研究类型

研究设计类型

- ▶ RCT/队列研究
- ▶ 病例对照研究
- ▶ 横断面调查

结局指标类型

- ▶ 连续变量
- ▶ 二分类变量
- ▶ 生存数据

二、确定结局指标

✓ 多个结局指标 → 估算每个结局指标所需的样本量 → 取样本数量最大者

✓ 主要指标和次要指标

估算每个结局指标所需的样本量，取样本数量最大者

仅估计主要指标所需样本量（比较常见）

研究结果的可能结论

		真实情况	
		无差异	有差异
试验结论	无差异	结论正确	II 型错误 (可能性= β)
	有差异	I 型错误 (可能性= α)	结论正确 (可能性= $1-\beta$, 把握度)



三、确定检验水平和检验效能

1. 检验水准 α

- ✓ α 错误又称第一类错误。 α 越小，所需样本量越大。
- ✓ 通常取 $\alpha = 0.05$ 。

2. 把握度 $1 - \beta$

- ✓ β 错误又称第二类错误。 β 越小， $1 - \beta$ 越大，把握度越大，所需样本量越大。
- ✓ 通常取 β 为 0.20 或 0.10。

三、确定检验水平和检验效能

1、假设检验的过程

原假设：无差异 备择假设：有差异

2、 α 和 P

α : 提前确定的检验水准

P : 如果原假设为真，观察到与现有数据相同（或更极端）的概率。

四、确定差值

- ✓ 不同组之间的差值越大，所需样本量越小，差值越小，所需样本量越大。
- ✓ 差值的估计：查阅文献、预实验或专业上认为有意义的差值。

五、确定总体标准差或总体率

- ✓ 结局指标为数值变量时，总体标准差 σ 为估计样本量所必须的条件。
- ✓ 结局指标为分类变量时，有时总体率 π 为估计样本量条件。
- ✓ 总体标准差 σ 和总体率 π 的估计：查阅文献、预实验或对研究作出合理的假设来获得。

六、确定单双侧检验

- ▶ 单侧检验需要的样本量比双侧检验小。
- ▶ 如果我们肯定试验组的效果要高于对照组，那么我们可以用单侧检验。但是经验告诉我们，有时我们的判断是错的，很多研究结果最后发现试验组效果更差，如果存在这种可能，那么应该用双侧检验。
- ▶ 单双侧检验到底该如何选择，目前有一定争议。

七、计算样本量

▶ 查表

▶ 公式

两样本率的检验

$$N = \left[\frac{(z_{\alpha} \sqrt{\pi_c(1-\pi_c)}(Q_1^{-1} - Q_2^{-1}) + z_{\beta} \sqrt{\pi_1(1-\pi_1)/Q_1 + \pi_2(1-\pi_2)/Q_2})}{\pi_1 - \pi_2} \right]^2$$

▶ 软件：**PASS**、SAS、SamplePower等

八、校正样本量

- ▶ PASS软件计算的样本量是最少需要量。
- ▶ 受试者可能有不合作者、中途失访、意外死亡等（失访、无应答等）。因此需对样本量进行校正。

Example

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Trial of Bilateral versus Single Internal-Thoracic-Artery Grafts

On the basis of a previous systematic review, we estimated that the use of *bilateral internal–thoracic–artery grafting* (術式A) would result in mortality at 10 years that was 5 percentage points lower than mortality with *single internal–thoracic–artery grafting* (術式B) (20% vs. 25%). We calculated that 2928 patients would need to be enrolled in order for the trial to detect this expected difference with 90% power at the 5% significance level.

METHODS

TRIAL DESIGN

This two-group, multicenter, randomized trial was conducted in 28 cardiac surgical centers in seven

STATISTICAL ANALYSIS

On the basis of a previous systematic review,¹⁷ we estimated that the use of bilateral internal-thoracic-artery grafting would result in mortality at 10 years that was 5 percentage points lower than mortality with single internal-thoracic-artery grafting (20% vs. 25%). We calculated that 2928 patients would need to be enrolled in order for the trial to detect this expected difference with 90% power at the 5% significance level. The aim was to

RESULTS

PATIENTS

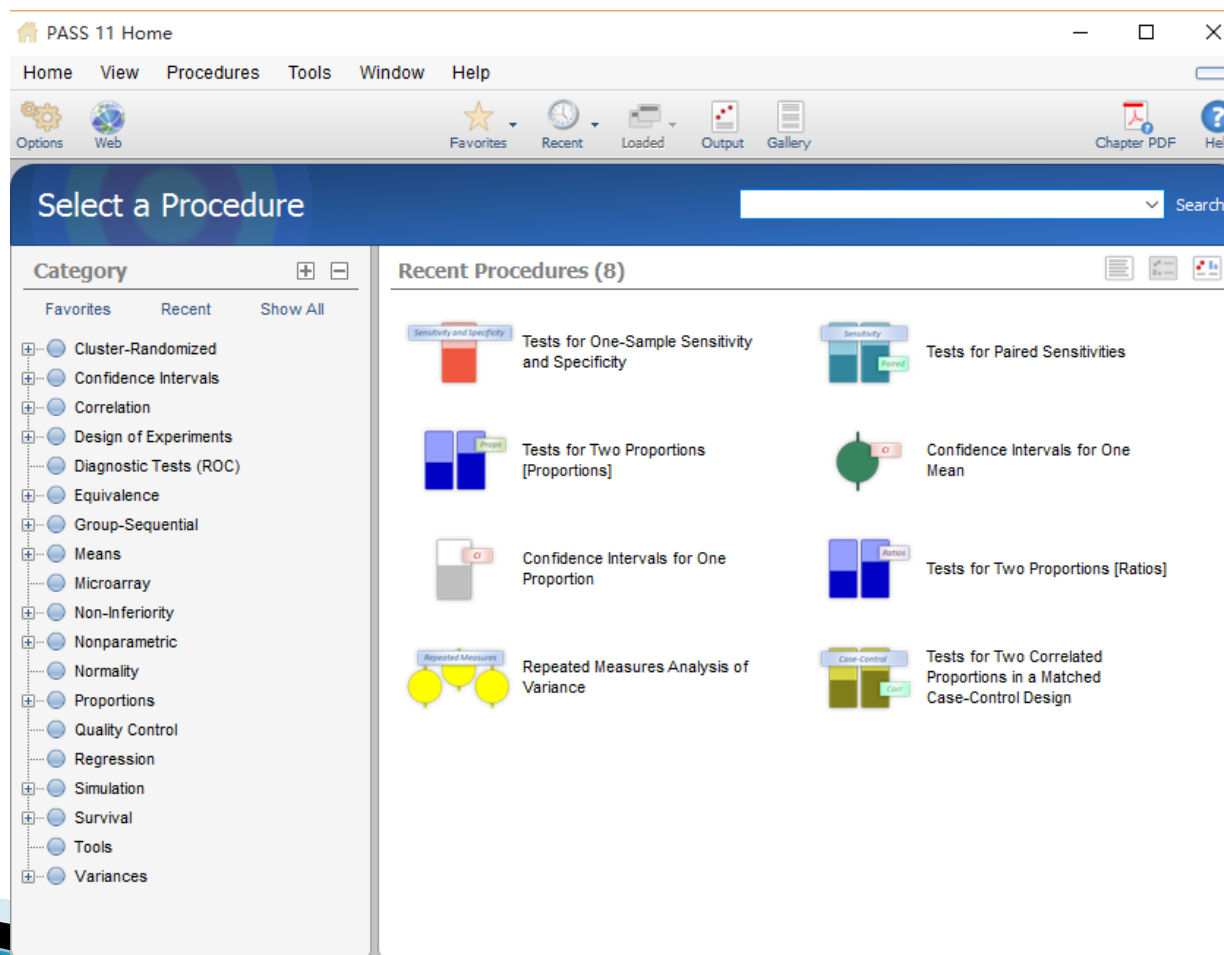
From June 2004 through December 2007, we enrolled 3102 patients at 28 cardiac surgery centers in seven countries. A total of 1554 patients were randomly assigned to the single-graft group and 1548 to the bilateral-graft group. Figure 1 shows

- 1、RCT
- 2、结局：分类变量
- 3、两组差值：20% VS 25%
- 4、检验水准 α ：0.05
- 5、把握度 $1-\beta$ (power) :0.9
- 6、双侧
- 7、校正样本含量

PASS软件计算样本量

PASS软件

► 下载地址<http://www.ncss.com/software/pass/>



需要估计样本量的常见研究类型

研究设计类型

- ▶ RCT/队列研究
- ▶ 病例对照研究
- ▶ 横断面调查

结局指标类型

- ▶ 连续变量
- ▶ 二分类变量
- ▶ 生存数据

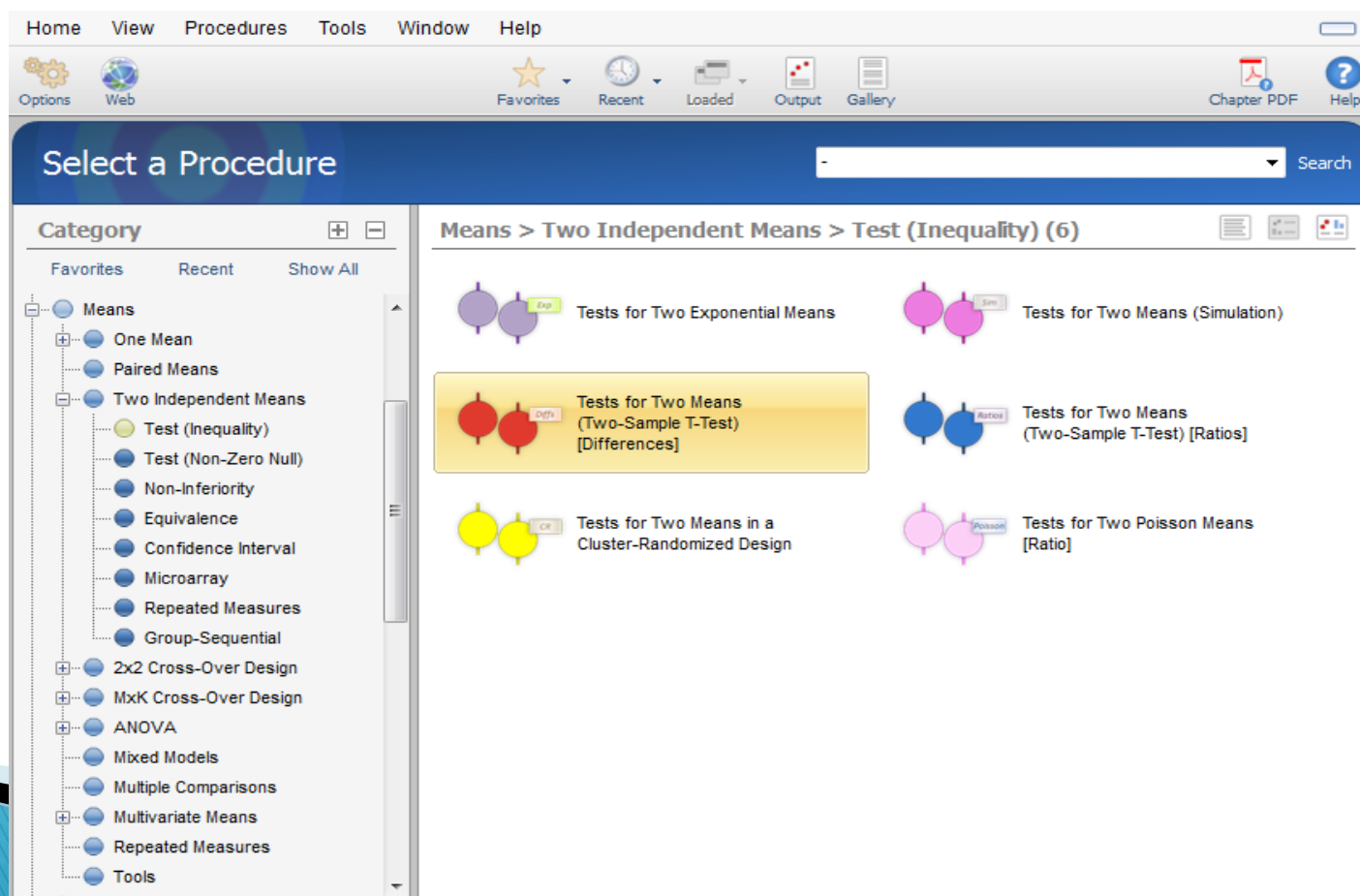
RCT/队列研究 + 连续变量

1、研究问题

某研究者拟开展一项**随机对照试验**，探讨合理膳食是否能降低**血清胆固醇**。估计对照组血清胆固醇水平的平均值为 (215 ± 30) mg/dl，合理膳食估计可以使干预组较对照组降低 15mg/dl。设 $\alpha = 0.05$ （双侧），把握度 $1 - \beta = 0.90$ ，请估算干预组和对照组所需样本量。

2、PASS软件计算

选择Means→Two Independent Means→Test (Inequality)→Test for Two Means(Two-Sample T-Test)[Differences]



Run

Data

Iterations

Reports

Plot Setup

Data

Solve For

Find (Solve For): N1

Error Rates

Power (1-Beta): 0.9

Alpha (Significance Level): .05

Sample Size

N1 (Sample Size Group 1): 5 to 45 by 10

N2 (Sample Size Group 2): Use R

R (Sample Allocation Ratio): 1.0

Effect Size

Means

Mean1 (Mean of Group 1): 215

Mean2 (Mean of Group 2): 200

Standard Deviations

S1 (Standard Deviation Group 1): 30

S2 (Standard Deviation Group 2): S1

☒ Known Standard Deviations

Test

Alternative Hypothesis: Ha: Mean1 $\neq$ Mean2

Nonparam. Adj. (M-W Test): Ignore

Known Standard Deviation

If the standard deviation is known, the normal distribution is used.

If the std. deviation is not known, the t distribution is used.

Since calculations involving the normal distribution are quicker than those involving the t distribution, you might want to use KNOWN for preliminary work and then assume NOT KNOWN for the final results.

N1: 样本量

α 和把握度 ($1-\beta$)

N2: Use R=1.0 表示两组样本量相等

两组的均值

S1: N1的标准差
S2=S1: 两组标准差相等

- ▶ **PASS**软件给出了样本量计算的结果、参考文献、报告中的名词定义和总结性描述。
- ▶ **N1**: 干预组样本量: 85例。
- ▶ **N1**: 对照组样本量: 85例。

Two-Sample T-Test Power Analysis

Numeric Results for Two-Sample T-Test

Null Hypothesis: Mean1=Mean2. Alternative Hypothesis: Mean1≠Mean2

The standard deviations were assumed to be known and equal.

Power	Allocation			Alpha	Beta	Mean1	Mean2	S1	S2
	N1	N2	Ratio						
0.90314	85	85	1.000	0.05000	0.09686	215.0	200.0	30.0	30.0

3、撰写结论

本研究为平行随机对照研究。干预组为合理膳食组，对照组为空白对照，血清胆固醇水平为主要观察的结局指标。根据既往文献报道，估计对照组血清胆固醇水平的平均值为 (215 ± 30) mg/dl，合理膳食可以使干预组较对照组降低15mg/dl。设 $\alpha=0.05$ （双侧）， $\beta=0.10$ 。利用PASS 11软件计算得到干预组和对照组的样本量 $N1=N2=85$ 例。假定研究对象的脱落率为10%，则需样本量 $N1=N2=85 \div 0.9=95$ 例。

4、样本量影响因素

- ✓ 不同组之间的差值越大，所需样本量越小，差值越小，所需样本量越大。
- ✓ 结局指标为数值变量时，总体标准差 σ 为估计样本含量所必须的条件。

差值越小，样本量越大

Mean1 (Means of Group 1): 215
Mean2 (Means of Group 2): 195 200 205

Two-Sample T-Test Power Analysis

Numeric Results for Two-Sample T-Test

Null Hypothesis: Mean1=Mean2. Alternative Hypothesis: Mean1≠Mean2
The standard deviations were assumed to be known and equal.

	Allocation									
Power	N1	N2	Ratio	Alpha	Beta	Mean1	Mean2	S1	S2	
0.90423	48	48	1.000	0.05000	0.09577	215.0	195.0	30.0	30.0	
0.90314	85	85	1.000	0.05000	0.09686	215.0	200.0	30.0	30.0	
0.90130	190	190	1.000	0.05000	0.09870	215.0	205.0	30.0	30.0	

Run

Data

Iterations

Reports

Plot Setup

Solve For

Find (Solve For): N1

Error Rates

Power (1-Beta): 0.9

Alpha (Significance Level): .05

Sample Size

N1 (Sample Size Group 1): 5 to 45 by 10

N2 (Sample Size Group 2): Use R

R (Sample Allocation Ratio): 1.0

Effect Size

Means

Mean1 (Mean of Group 1): 215

Mean2 (Mean of Group 2): 195 200 205

Standard Deviations

S1 (Standard Deviation Group 1): 30

S2 (Standard Deviation Group 2): S1

☒ Known Standard Deviations

Test

Alternative Hypothesis: Ha: Mean1 ≠ Mean2

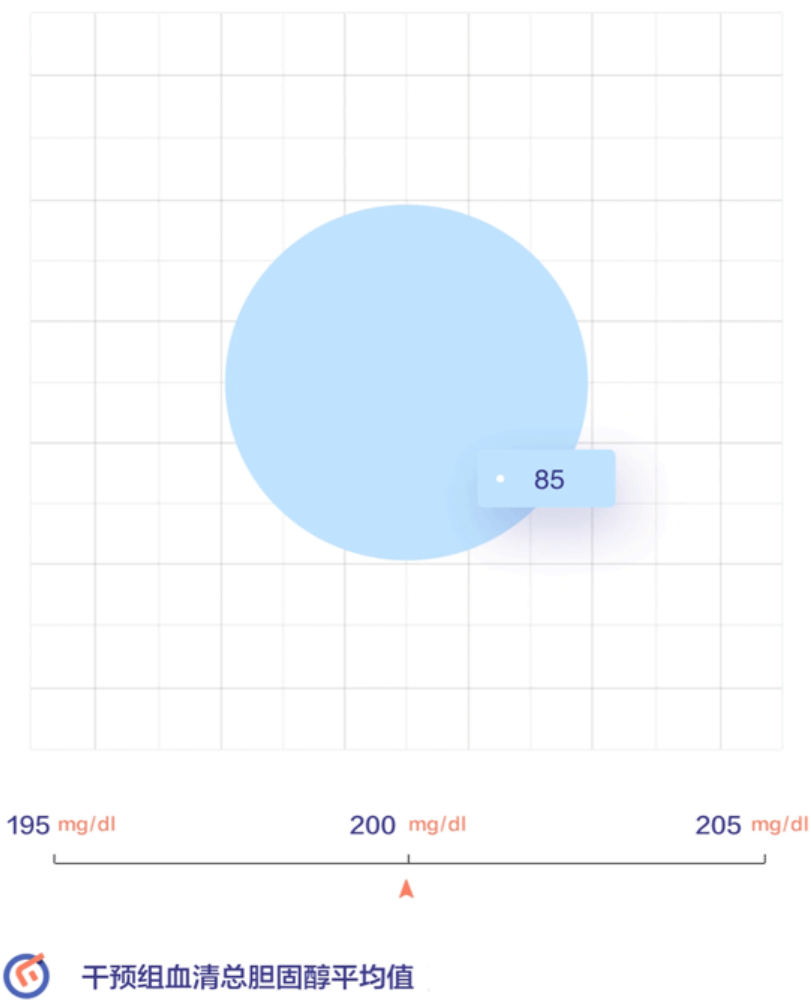
Nonparam. Adj. (M-W Test): Ignore

Add This Procedure to Favorites List

差值越小，样本量越大

对照组保持215mg/dl不变，干预组变化

干预组均值	对照组均值	均值之差	每组样本量
195	215	20	48
200	215	15	85
205	215	10	190



差值越小，样本量越大

Mean1 (Means of Group 1): 220 215 210
Mean2 (Means of Group 2): 200

Two-Sample T-Test Power Analysis

Numeric Results for Two-Sample T-Test

Null Hypothesis: Mean1=Mean2. Alternative Hypothesis: Mean1≠Mean2

The standard deviations were assumed to be known and equal.

Power	Allocation			Alpha	Beta	Mean1	Mean2	S1	S2
	N1	N2	Ratio						
0.90130	190	190	1.000	0.05000	0.09870	210.0	200.0	30.0	30.0
0.90314	85	85	1.000	0.05000	0.09686	215.0	200.0	30.0	30.0
0.90423	48	48	1.000	0.05000	0.09577	220.0	200.0	30.0	30.0

Run

Data

Iterations

Reports

Plot Setup

Solve For

Find (Solve For): N1

Error Rates

Power (1-Beta): 0.9

Alpha (Significance Level): .05

Sample Size

N1 (Sample Size Group 1): 5 to 45 by 10

N2 (Sample Size Group 2): Use R

R (Sample Allocation Ratio): 1.0

Effect Size

Means

Mean1 (Mean of Group 1): 220 215 210

Mean2 (Mean of Group 2): 200

Standard Deviations

S1 (Standard Deviation Group 1): 30

S2 (Standard Deviation Group 2): S1

☒ Known Standard Deviations

Test

Alternative Hypothesis: Ha: Mean1 ≠ Mean2

Nonparam. Adj. (M-W Test): Ignore

Add This Procedure to Favorites List

差值越小，样本量越大

Mean1 (Means of Group 1): 220 to 210 by 5
Mean2 (Means of Group 2): 200

Two-Sample T-Test Power Analysis

Numeric Results for Two-Sample T-Test

Null Hypothesis: Mean1=Mean2. Alternative Hypothesis: Mean1≠Mean2

The standard deviations were assumed to be known and equal.

Power	Allocation			Alpha	Beta	Mean1	Mean2	S1	S2
	N1	N2	Ratio						
0.90130	190	190	1.000	0.05000	0.09870	210.0	200.0	30.0	30.0
0.90314	85	85	1.000	0.05000	0.09686	215.0	200.0	30.0	30.0
0.90423	48	48	1.000	0.05000	0.09577	220.0	200.0	30.0	30.0

Run

Data

Iterations

Reports

Plot Setup

Solve For

Find (Solve For): N1

Error Rates

Power (1-Beta): 0.9

Alpha (Significance Level): .05

Sample Size

N1 (Sample Size Group 1): 5 to 45 by 10

N2 (Sample Size Group 2): Use R

R (Sample Allocation Ratio): 1.0

Effect Size

Means

Mean1 (Mean of Group 1): 220 to 210 by 5

Mean2 (Mean of Group 2): 200

Standard Deviations

S1 (Standard Deviation Group 1): 30

S2 (Standard Deviation Group 2): S1

☒ Known Standard Deviations

Test

Alternative Hypothesis: Ha: Mean1 ≠ Mean2

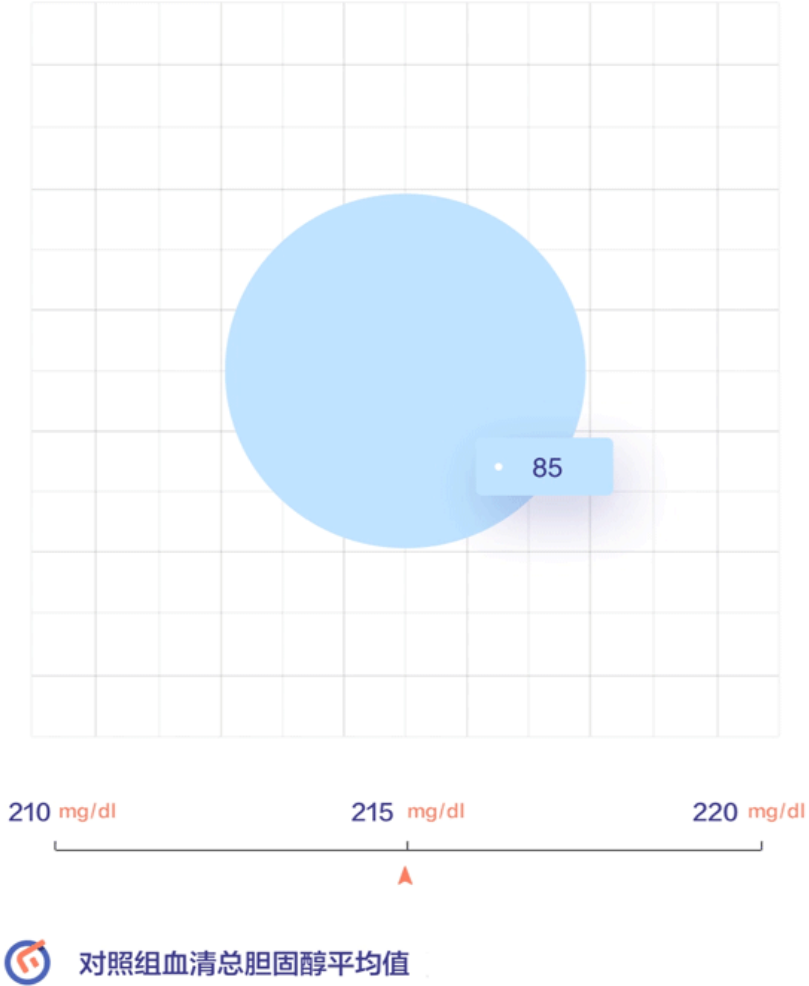
Nonparam. Adj. (M-W Test): Ignore

Add This Procedure to Favorites List

差值越小，样本量越大

干预组保持200mg/dl不变，对照组变化

干预组均值	对照组均值	均值之差	每组样本量
200	220	20	48
200	215	15	85
200	210	10	190



差值越小，样本量越大

干预组均值	对照组均值	均值之差	每组样本量
195	215	20	48
200	215	15	85
205	215	10	190

干预组均值	对照组均值	均值之差	每组样本量
200	220	20	48
200	215	15	85
200	210	10	190

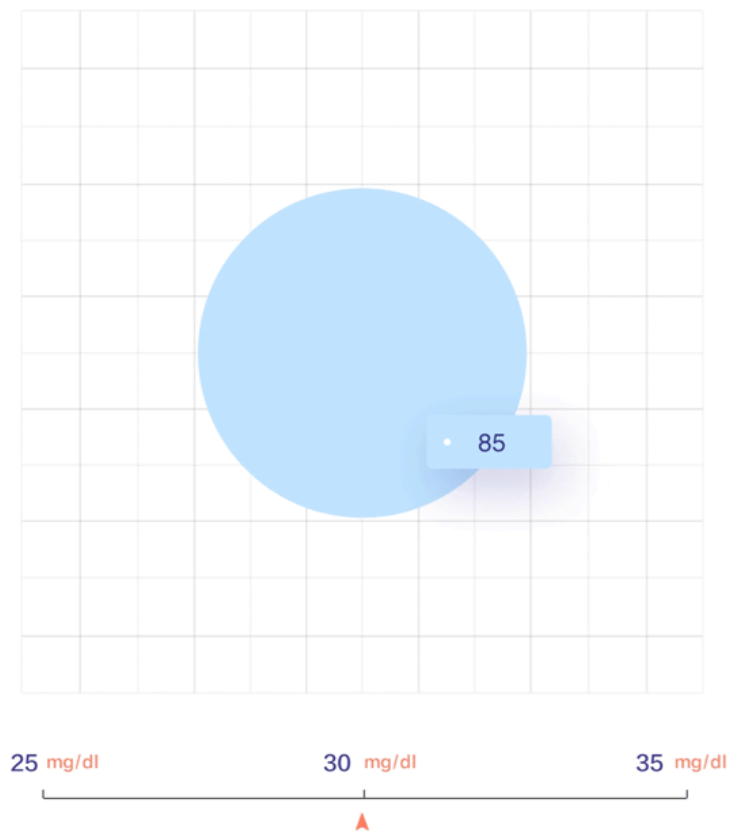
血清总胆固醇估计值（mg/dl）与样本量的关系

干预组均值	对照组均值	均值之差	每组样本量
195	215	20	48
200	220	20	48
200	215	15	85
205	215	10	190
200	210	10	190

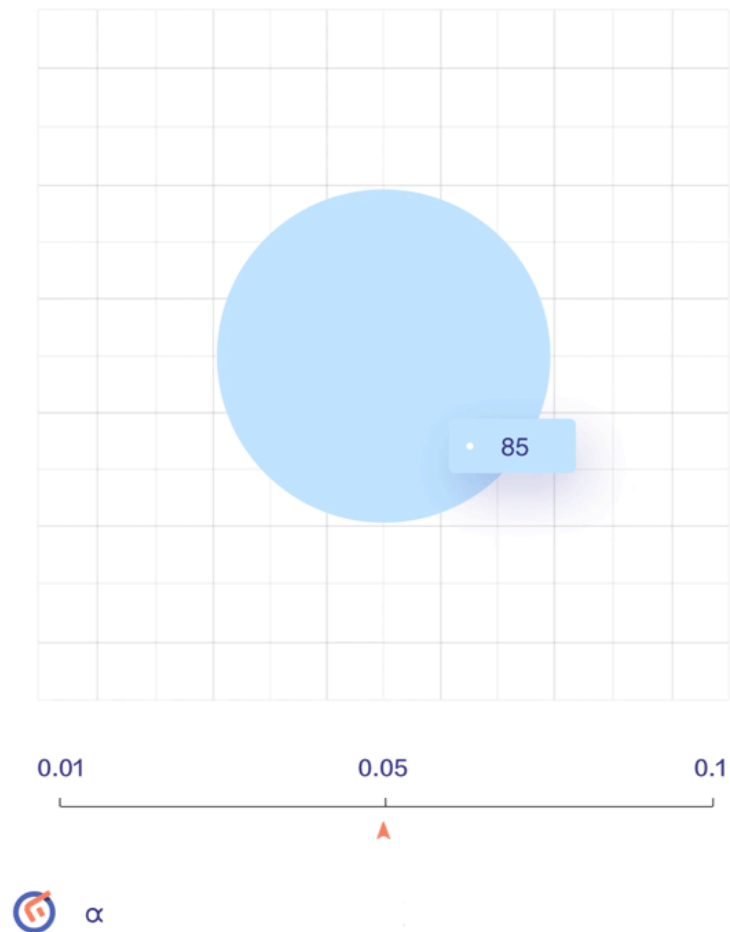
4、样本量影响因素

- ✓ 不同组之间的差值越大，所需样本量越小，差值越小，所需样本含越大。
- ✓ 结局指标为数值变量时，总体标准差 σ 为估计样本量所必须的条件。

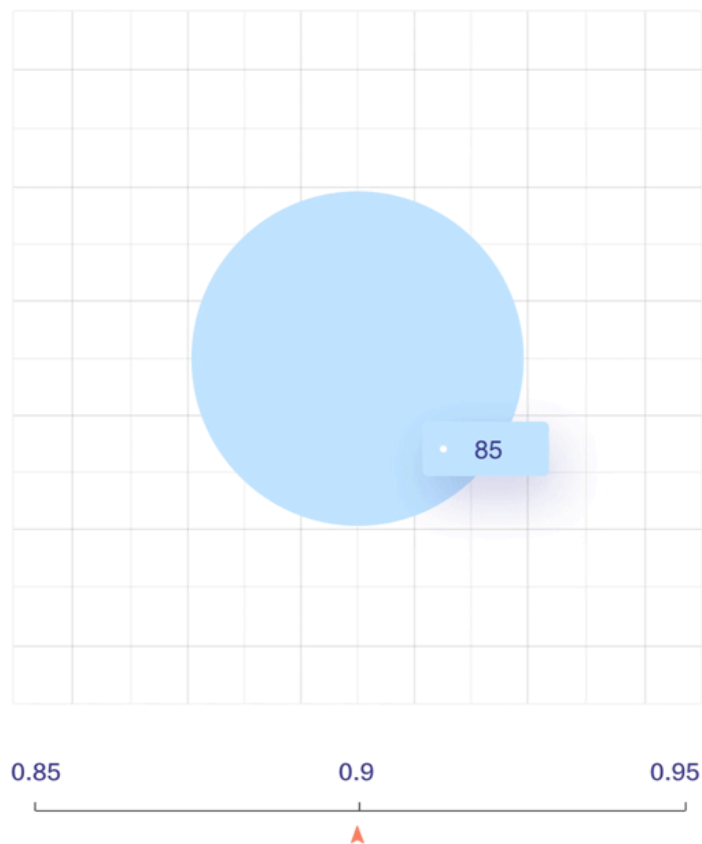
标准差越大，样本量越大



α 越小，样本量越大



把握度越小（ β 越大），样本量越小



 把握度 $1 - \beta$

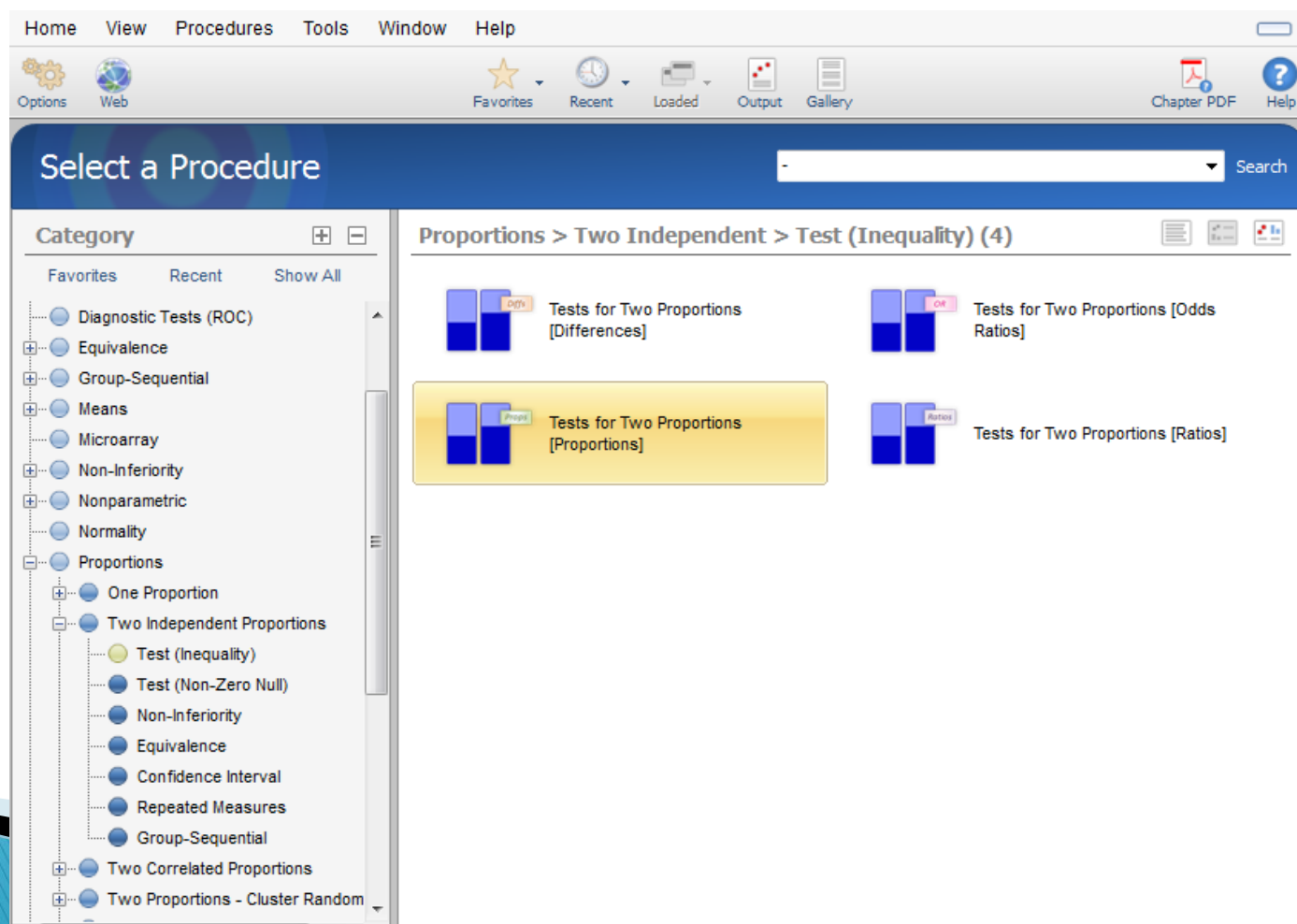
RCT/队列研究 + 分类变量

1、研究问题

某研究者拟开展一项**随机对照试验**，探讨使用某药物是否能降低**高血压病的发病率**。估计安慰剂对照组的发病率为**40%**。实施干预措施1年后，估计干预组的发病率为**20%**。规定 $\alpha=0.01$ （双侧）， $\beta=0.10$ ，请计算干预组和对照组所需样本量。

2、PASS软件计算

- ▶ 选择Proportions→Two Independent Proportions→Test (Inequality)→Test for Two Proportions[Proportions]



File View Run Procedures Tools Window Help

Reset Open Save As Home Favorites Recent Loaded Output Gallery Chapter PDF Help

Run

Data

Options
Reports
Plot Setup

Data

Solve For

Find (Solve For): N1

Error Rates

Power (1-Beta): 0.9

Alpha (Significance Level): .01

Sample Size

N1 (Sample Size Group 1): 200

N2 (Sample Size Group 2): Use R

R (Sample Allocation Ratio): 1.0

Effect Size

P1 (Treatment Group Proportion | H1): 0.2

P2 (Control Group Proportion): 0.4

Test

Alternative Hypothesis (H1): Two-Sided

Test Type: Z Test (Pooled)

Procedure Progress

Display Chart

Guide Me: Start

N1: 样本量

α 和把握度 ($1-\beta$)

N2: Use R=1.0 表示两组样本量相等

两组的率

- ▶ **Sample Size Grp 1 (N1): 干预组样本量: 154例。**
- ▶ **Sample Size Grp 2 (N2): 对照组样本量: 154例。**

Two Independent Proportions (Null Case) Power Analysis
 Numeric Results of Tests Based on the Difference: P1 - P2
 H0: P1-P2=0. H1: P1-P2=D1<>0. Test Statistic: Z test with pooled variance

	Sample Size Grp 1 N1	Sample Size Grp 2 N2	Prop H1 Grp 1 or Trtmnt P1	Prop Grp 2 or Control P2	Diff if H0 D0	Diff if H1 D1	Target Alpha	Actual Alpha	Beta
Power	154	154	0.2000	0.4000	0.0000	-0.2000	0.0100		0.0994

3、撰写结论

本研究为平行随机对照研究。干预组为使用药物组，对照组为使用安慰剂组，高血压病发病率为主要观察的结局指标。根据既往文献报道，估计安慰剂对照组的发病率为40%。实施干预措施1年后，估计干预组的发病率为20%。设 $\alpha=0.01$ （双侧）， $\beta=0.10$ 。利用PASS 11软件计算得到干预组和对照组的样本量 $N1=N2=154$ 例。假定研究对象的脱落率为10%，则需样本量 $N1=N2=154 \div 0.9=171$ 例。

Example

METHODS

TRIAL DESIGN

This two-group, multicenter, randomized trial was conducted in 28 cardiac surgical centers in seven

STATISTICAL ANALYSIS

On the basis of a previous systematic review,¹⁷ we estimated that the use of bilateral internal-thoracic-artery grafting would result in mortality at 10 years that was 5 percentage points lower than mortality with single internal-thoracic-artery grafting (20% vs. 25%). We calculated that 2928 patients would need to be enrolled in order for the trial to detect this expected difference with 90% power at the 5% significance level. The aim was to

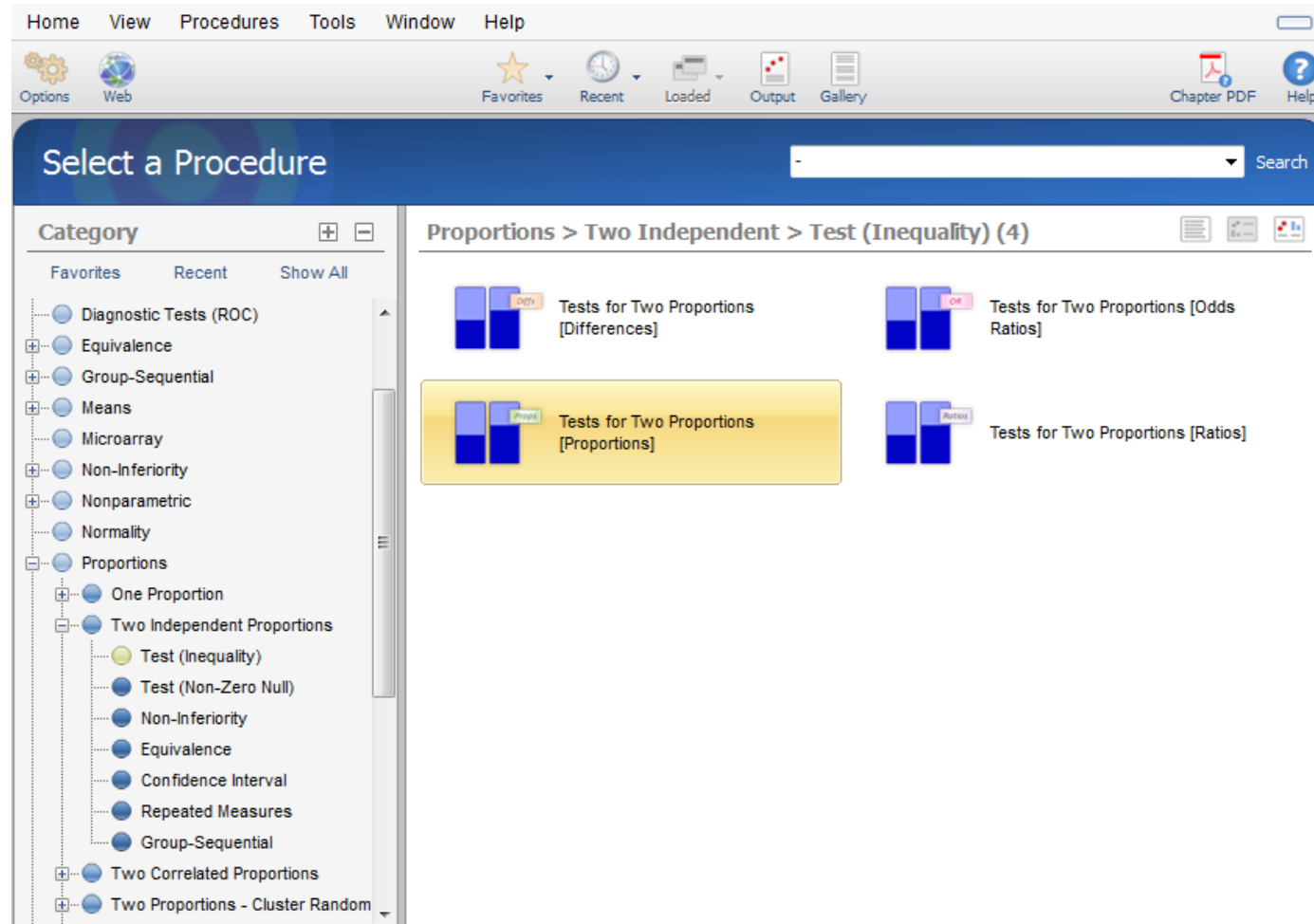
RESULTS

PATIENTS

From June 2004 through December 2007, we enrolled 3102 patients at 28 cardiac surgery centers in seven countries. A total of 1554 patients were randomly assigned to the single-graft group and 1548 to the bilateral-graft group. Figure 1 shows

- 1、RCT
- 2、结局：分类变量
- 3、两组差值：20% VS 25%
- 4、检验水准 α ：0.05
- 5、把握度 $1-\beta$ （power）：0.9
- 6、双侧
- 7、校正样本含量

选择Proportions→Two Independent Proportions→Test (Inequality)→Test for Two Proportions[Proportions]



Tests for Two Proportions [Proportions]

File View Run Procedures Tools Window Help

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Run

Data

Options

Reports

Plot Setup

Data

Solve For

Find (Solve For): N1

Error Rates

Power (1-Beta): 0.90

Alpha (Significance Level): 0.05

Sample Size

N1 (Sample Size Group 1): 50 to 400 by 50

N2 (Sample Size Group 2): Use R

R (Sample Allocation Ratio): 1.0

Effect Size

P1 (Treatment Group Proportion | H1): 0.2

P2 (Control Group Proportion): 0.25

Test

Alternative Hypothesis (H1): Two-Sided

Test Type: Z Test (Pooled)

R (Sample Allocation Ratio)

Enter a value (or range of values) for R, the allocation ratio between samples.

$R = N2/N1$

This value is only used when N2 is set to "Use R".

When used, N2 is calculated from N1 using the formula:

$N2 = [R \times N1]$

where [Y] is the next integer $\geq Y$.

Note that setting $R = 1.0$ forces $N2 = N1$.

Guide Me: Start

N1: 样本量

α 和把握度 ($1-\beta$)

N2: Use R=1.0 表示两组样本量相等

两组的率

Two Independent Proportions (Null Case) Power Analysis

Numeric Results of Tests Based on the Difference: $P1 - P2$

$H0: P1-P2=0$. $H1: P1-P2=D1 \neq 0$. Test Statistic: Z test with pooled variance

	Sample Size Grp 1 N1	Sample Size Grp 2 N2	Prop H1 Grp 1 or Trtmnt P1	Prop Grp 2 or Control P2	Diff if H0 D0	Diff if H1 D1	Target Alpha	Actual Alpha	Beta
Power	1464	1464	0.2000	0.2500	0.0000	-0.0500	0.0500		0.0999

Note: exact results based on the binomial were only calculated when both N1 and N2 were less than 100.

STATISTICAL ANALYSIS

On the basis of a previous systematic review,¹⁷ we estimated that the use of bilateral internal-thoracic-artery grafting would result in mortality at 10 years that was 5 percentage points lower than mortality with single internal-thoracic-artery grafting (20% vs. 25%). We calculated that 2928 patients would need to be enrolled in order for the trial to detect this expected difference with 90% power at the 5% significance level. The aim was to

$$1464 * 2 = 2928$$

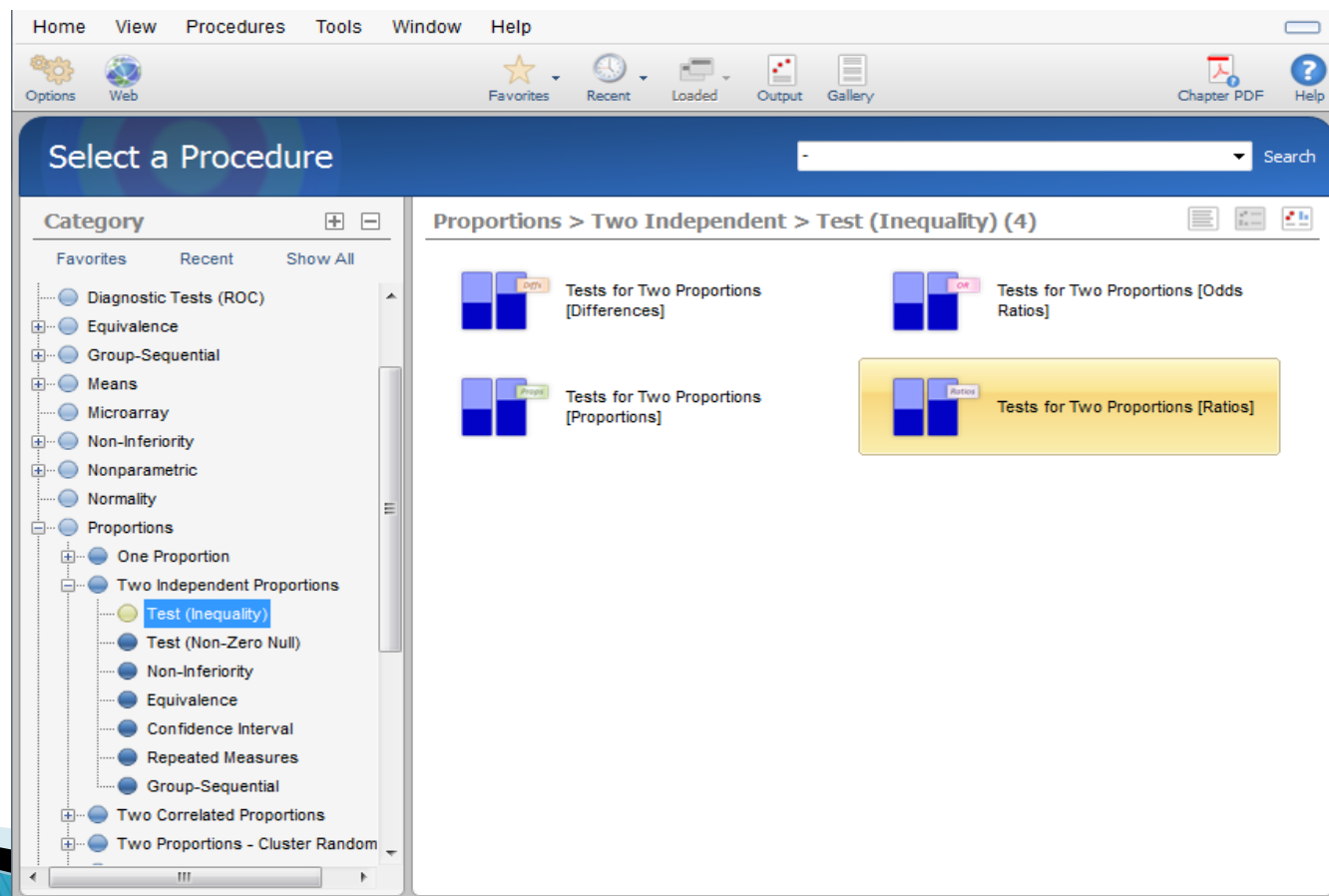
RCT/队列研究 + RR

1、研究问题

某研究者拟开展一项随机对照试验，探讨使用某药物是否能降低高血压病的发病率。估计安慰剂对照组的发病率为40%。实施干预措施1年后，估计干预组相对于对照组发病风险的RR为0.5。规定 $\alpha=0.01$ （双侧）， $\beta=0.10$ ，请计算干预组和对照组所需样本量。

2、PASS软件计算

- ▶ 选择Proportions→Two Independent Proportions→Test (Inequality)→Test for Two Proportions[Ratios]



File View Run Procedures Tools Window Help

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Run

Data

Options

Reports

Plot Setup

Data

Solve For

Find (Solve For): N1

Error Rates

Power (1-Beta): 0.90

Alpha (Significance Level): 0.01

Sample Size

N1 (Sample Size Group 1): 50 to 400 by 50

N2 (Sample Size Group 2): Use R

R (Sample Allocation Ratio): 1.0

Effect Size

R1 (Ratio $H_1 = P_1 / P_2$): 0.5

P2 (Control Group Proportion): 0.4

P1 = the proportion in the treatment group = $R_1 \times P_2$

Test

Alternative Hypothesis (H1): Two-Sided

Test Type: Z Test (Pooled)

Test Type

Specify which type of test will be used in all searching and reporting.

Note that "C.C." is short for "Continuity Correction." This refers to the adding or subtracting $1/(2n)$ to (or from) the numerator of the z-value to bring the normal approximation closer to the binomial distribution.

Guide Me: Start

N1: 样本量

 α 和把握度 ($1-\beta$)

N2: Use R=1.0 表示两组样本量相等

RR和对照组的率

- ▶ **Sample Size Grp 1 (N1): 干预组样本量: 154例。**
- ▶ **Sample Size Grp 2 (N2): 对照组样本量: 154例。**

Two Independent Proportions (Null Case) Power Analysis
Numeric Results of Tests Based on the Ratio: P1 / P2
H0: P1/P2=1. H1: P1/P2=R1<>1. Test Statistic: Z test with pooled variance

	Sample Size Grp 1	Sample Size Grp 2	Prop H1 Grp 1 or Trtmnt P1	Prop Grp 2 or Control P2	Ratio if H0 R0	Ratio if H1 R1	Target Alpha	Actual Alpha	Beta
Power	N1	N2							
0.9006	154	154	0.2000	0.4000	1.000	0.500	0.0100		0.0994

3、撰写结论

本研究为平行随机对照研究。干预组为使用药物组，对照组为使用安慰剂组，高血压病发病率为主要观察的结局指标。根据既往文献报道，估计安慰剂对照组的发病率为40%。实施干预措施1年后，估计干预组相对于对照组发病风险的RR为0.5。设 $\alpha=0.01$ （双侧）， $\beta=0.10$ 。利用PASS 11软件计算得到干预组和对照组的样本量 $N_1=N_2=154$ 例。假定研究对象的脱落率为10%，则需样本量 $N_1=N_2=154 \div 0.9=171$ 例。

4、率和RR的关系

A. 干预组发病率20%，对照组发病率40%。

B. $RR = \text{干预组发病率} / \text{对照组发病率} = 0.5$

利用PASS 11软件计算得到病例组和对照组的样本量 $N1=N2=154$ 例。

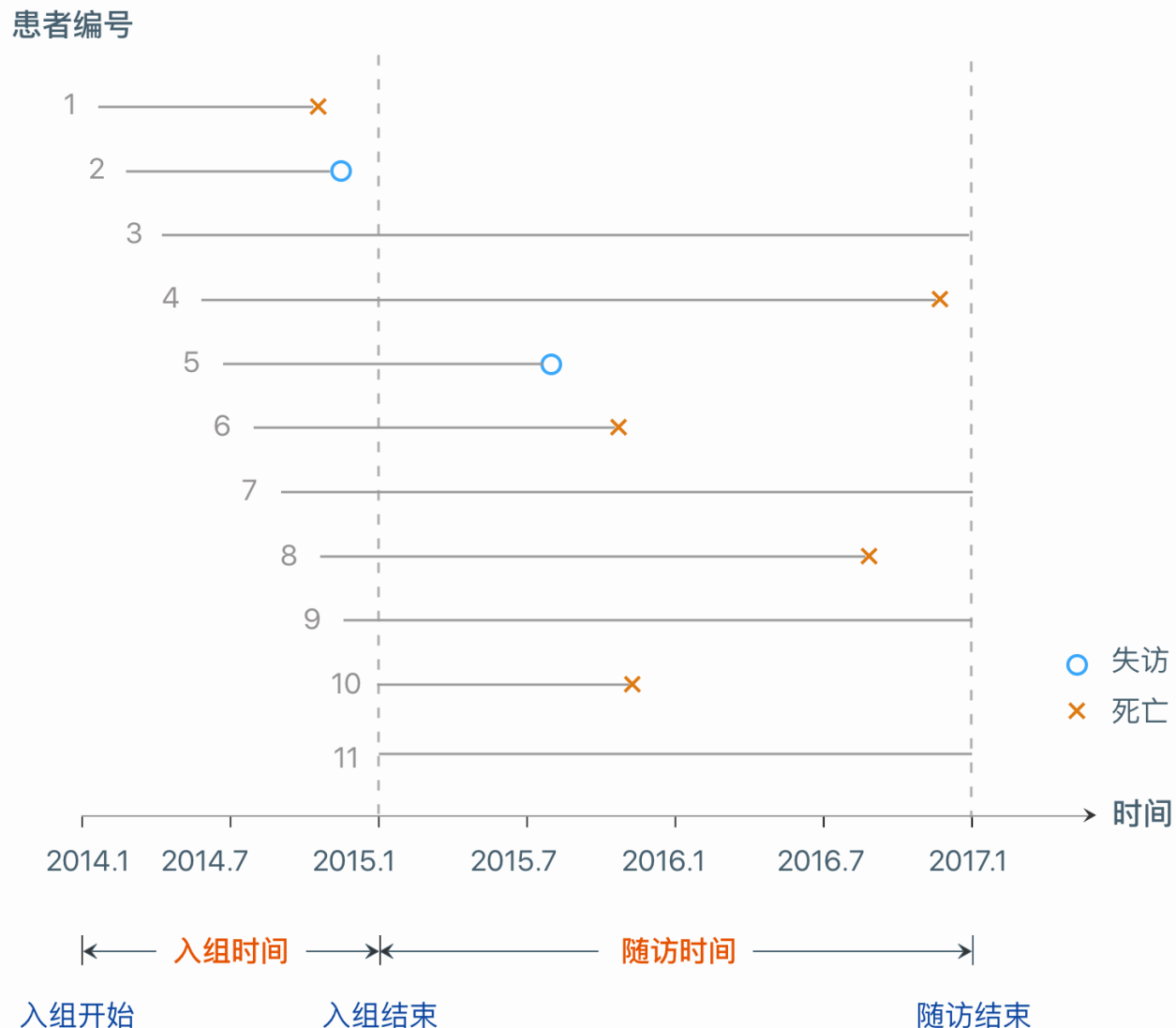
RCT/队列研究 + 生存数据（Logrank检验）

1、研究问题

某研究者拟开展一项**随机对照试验**，探讨某免疫抑制剂相对于安慰剂，是否能改善肺癌患者的**中位生存期**。根据预试验结果，估计对照组的中位生存期为**6个月**，干预组的中位生存期为**8个月**。研究的入组时间预计为**10个月**，随访时间计划**12个月**。取 $\alpha=0.05$ （双侧）， $\beta=0.1$ 。如果研究对象入组速度基本保持不变，试验组对照组的**比例为1:1**，请估算研究所需要的样本量。

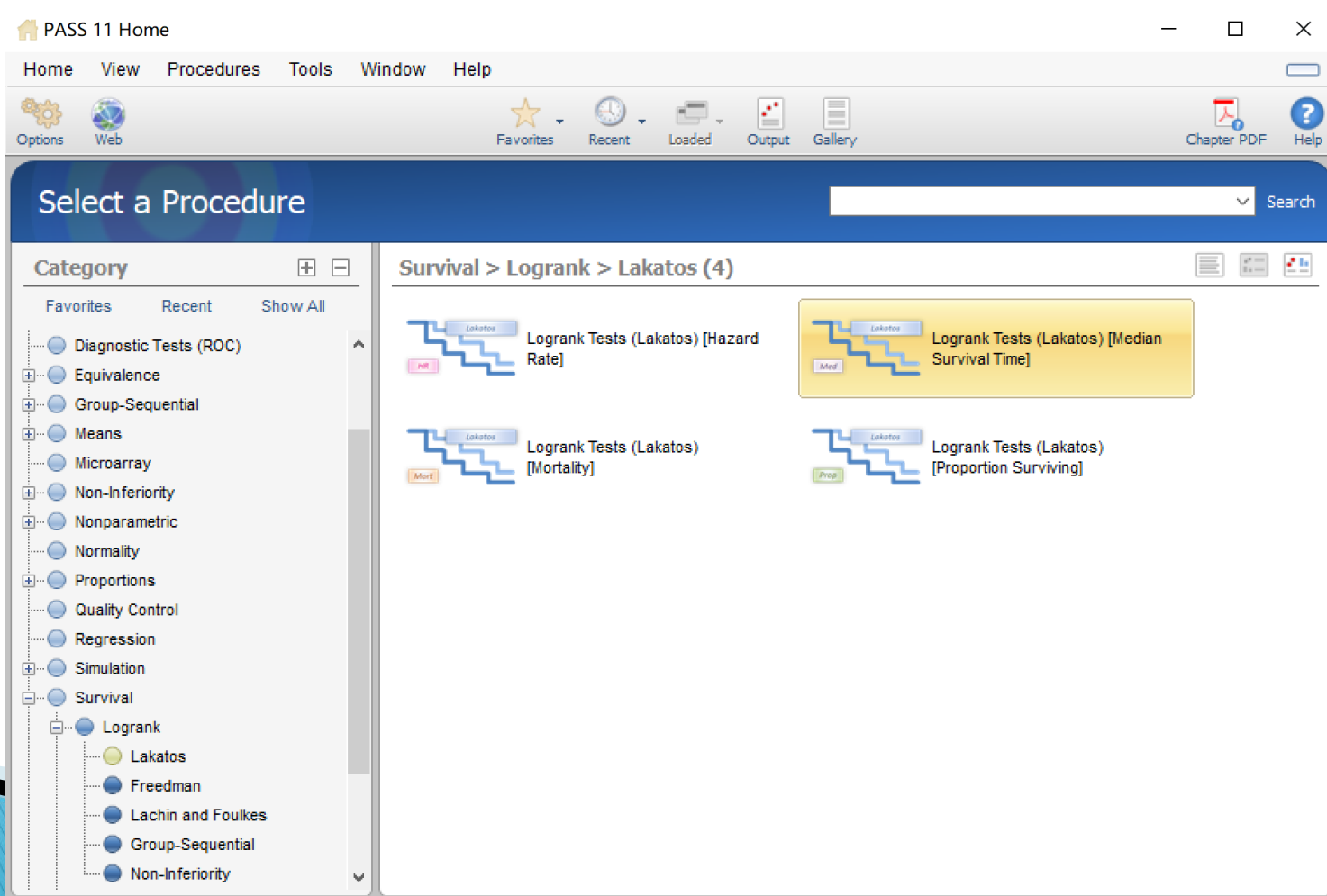
参数概念

- ▶ 中位生存时间 (mOS)：即50%的患者死亡时所对应的时间。
- ▶ 入组时间：第1例患者入组到最后一例患者入组的时间。
- ▶ 随访时间：最后1例患者入组完成，到试验截止日期的时间。
随访时间 $\neq$ 观察时间
- ▶ HR：风险比，是两组患者瞬时死亡概率之比。



2、PASS软件计算

- ▶ 选择Survival → Logrank → Lakatos → Logrank Tests(Lakatos)[Median Survival Time]



Logrank Tests (Lakatos) [Median Survival Time]

File View Run Procedures Tools Window Help

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Run

Data

Options Reports Plot Setup Abbreviations

Solve For

Find (Solve For): N (Total Sample Size)

Error Rates

Power (1-Beta): 0.90

Alpha (Significance Level): .05

Sample Size

N (Total Sample Size): 50 100

Proportion in Control Group: 0.5

Effect Size

T1 (Median Survival Time - Control): 6

Treatment Group Parameter: T2 (Med. Survival Time - Treatment)

T2 (Median Survival Time - Treatment): 8

HR (Hazard Ratio = T1/T2): 0.50

Duration

Accrual Time (Integers Only): 10

Accrual Pattern: Equal

Total Time (Integers Only): 22

Proportion Lost or Switching Groups during a Single Time Period

Controls Lost: 0.0 Treatments Lost: 0.0

Controls Switch to Treatments: 0.0 Treatments Switch to Controls: 0.0

Test

Alternative Hypothesis: Two-Sided

Find (Solve For)

Select the parameter to be solved for in terms of the other parameters.

Note

This parameter will be displayed on the vertical axis of the plot(s).

Guide Me: Start

N1: 样本量

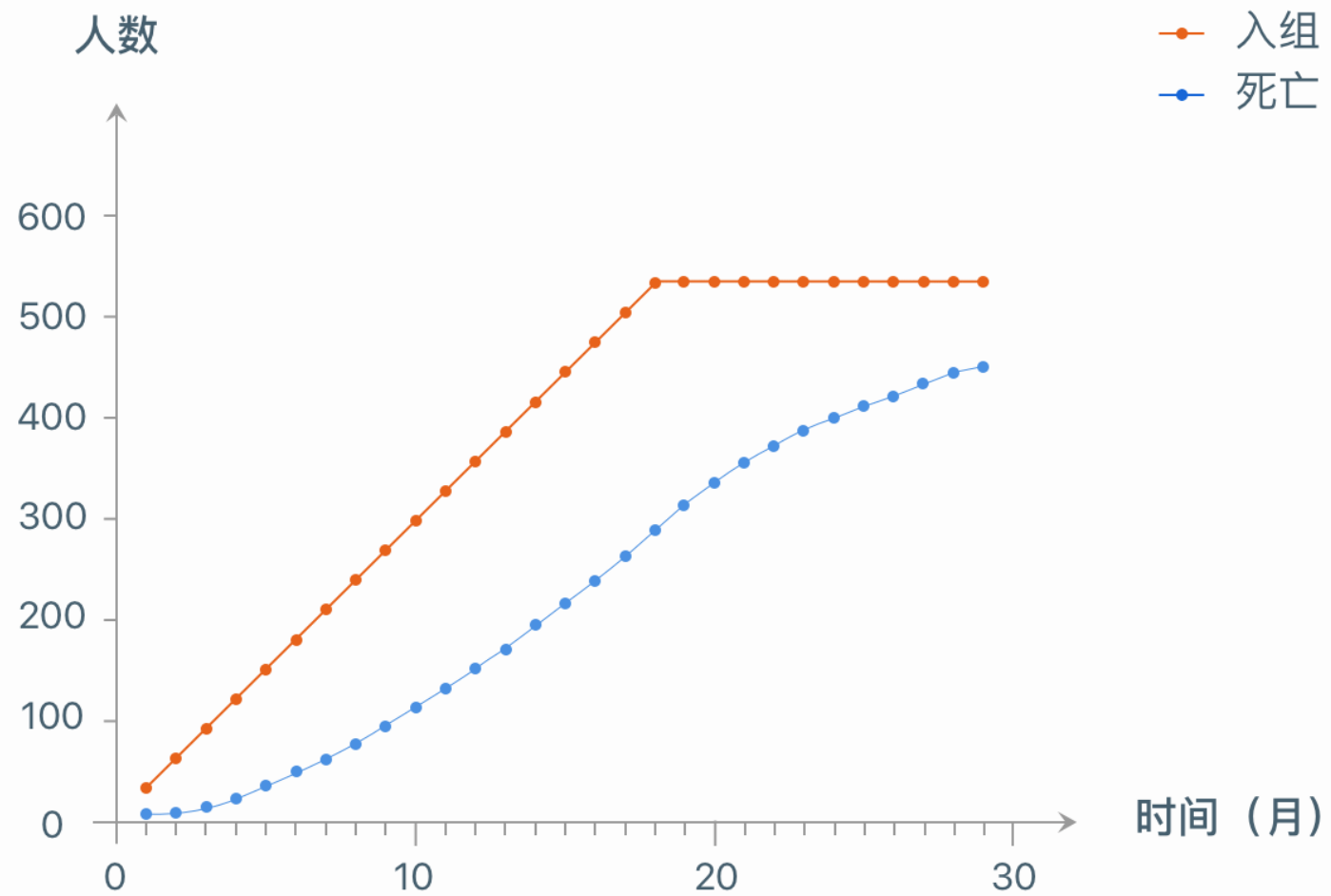
α 和把握度 ($1-\beta$)

0.5表示试验组与对照组的
比值为1:1

对照组中位生存期

试验组参数&中位生存期

入组时间和总时间
Accrual pattern-Equal:表示
等比例入组



Logrank Tests (Lakatos) [Median Survival Time]

File View Run Procedures Tools Window Help

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Run

Data

Options Reports Plot Setup Abbreviations

Solve For

Find (Solve For): N (Total Sample Size)

Error Rates

Power (1-Beta): 0.90

Alpha (Significance Level): .05

Sample Size

N (Total Sample Size): 50 100

Proportion in Control Group: 0.5

Effect Size

T1 (Median Survival Time - Control): 6

Treatment Group Parameter: T2 (Med. Survival Time - Treatment)

T2 (Median Survival Time - Treatment): 8

HR (Hazard Ratio = T1/T2): 0.50

Duration

Accrual Time (Integers Only): 10

Accrual Pattern: Equal

Total Time (Integers Only): 22

Proportion Lost or Switching Groups during a Single Time Period

Controls Lost: 0.0 Treatments Lost: 0.0

Controls Switch to Treatments: 0.0 Treatments Switch to Controls: 0.0

Test

Alternative Hypothesis: Two-Sided

Find (Solve For)

Select the parameter to be solved for in terms of the other parameters.

Note

This parameter will be displayed on the vertical axis of the plot(s).

Guide Me: Start

N1：样本量

α 和把握度（ $1-\beta$ ）

0.5表示试验组与对照组的
比值为1:1

对照组中位生存期

参数及试验组中位生存期

入组时间和总时间
Accrual pattern-Equal:表示
等比例入组

时间单位保持一致！！

- ▶ **N1: 试验组样本量: 315例。**
- ▶ **N2: 对照组样本量: 316例。**

Logrank Test Power Analysis														
Numeric Results in Terms of Sample Size when the Test is Two-Sided														
Power	N1	N2	N	Haz Ratio (HR)	Ctrl Med Surv Time (M1)	Trt Med Surv Time (M2)	Acc- rual Time/ Total Time Pat'n	Acc- rual Time/ Total Time	Ctrl Loss	Trt Loss	Ctrl to Trt	Trt to Ctrl	Alpha	Beta
0.9002	315	316	631	0.7500	6.00	8.00	Equal	10 / 22	0.0000	0.0000	0.0000	0.0000	0.0500	0.0998

Numeric Results in Terms of Events when the Test is Two-Sided

	Ctrl	Trt	Total	Haz	Ctrl	Trt	Acc-	Time/				Ctrl	Trt		
	Evts	Evts	Evts	Ratio	Med	Med	rual	Total				to	to	Alpha	Beta
Power	(E1)	(E2)	(E)	(HR)	Surv	Surv	Pat'n	Time	Loss	Loss		Trt	Ctrl		
0.9002	268.7	240.9	509.6	0.7500	Time	Time	Equal	10 / 22	0.0000	0.0000	0.0000	0.0000	0.0000	0.0500	0.0998

- ▶ 决定样本量的实际上是事件数（死亡数）。事件数由 α 、 β 和HR三者决定。
- ▶ 事件数是通过两组的事件发生概率和试验持续时间推算出来的。试验持续时间越长，获得同样的事件数量所需的样本量就会越小。
- ▶ 入组速度是受现实情况影响较大的因素，本例中入组速度需要63.1例/月，研究者需要估计试验能否达到这样的水平。如果高于此水平，可以缩短入组时间。如果低于此水平则必须延长入组时间，然后重新计算样本量。

3、撰写结论

本研究为随机对照试验。干预组为使用免疫抑制剂组，对照组为使用安慰剂组，肺癌患者的中位生存期为主要观察的结局指标。根据预试验结果，估计对照组的中位生存期为6个月，干预组的中位生存期为8个月。研究的入组时间预计为10个月，随访时间计划12个月。取 $\alpha=0.05$ （双侧）， $\beta=0.1$ 。如果研究对象入组速度基本保持不变，试验组对照组比例1:1，利用PASS 11软件计算得到干预组样本量 $N1=315$ 例，对照组样本量 $N2=316$ 例。实际研究时，两组各选择320例。

Lost & Switch

Logrank Tests (Lakatos) [Median Survival Time]

File View Run Procedures Tools Window Help

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Run

Data

Options

Reports

Plot Setup

Abbreviations

Solve For

Find (Solve For): N (Total Sample Size)

Error Rates

Power (1-Beta): 0.90

Alpha (Significance Level): .05

Sample Size

N (Total Sample Size): 50 100

Proportion in Control Group: 0.5

Effect Size

T1 (Median Survival Time - Control): 6

Treatment Group Parameter: T2 (Med. Survival Time - Treatment)

T2 (Median Survival Time - Treatment): 8

HR (Hazard Ratio = T1/T2): 0.50

Duration

Accrual Time (Integers Only): 10

Accrual Pattern: Equal

Total Time (Integers Only): 22

Proportion Lost or Switching Groups during a Single Time Period

Controls Lost: 0.0

Treatments Lost: 0.0

Controls Switch to Treatments: 0.0

Treatments Switch to Controls: 0.0

Test

Alternative Hypothesis: Two-Sided

Find (Solve For)

Select the parameter to be solved for in terms of the other parameters.

Note

This parameter will be displayed on the vertical axis of the plot(s).

Guide Me: Start

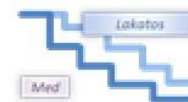
不同参数计算样本量

▶ $HR = \frac{\text{试验组Hazard rate}}{\text{对照组Hazard rate}}$

Survival > Logrank > Lakatos (4)



Logrank Tests (Lakatos) [Hazard Rate]



Logrank Tests (Lakatos) [Median Survival Time]



Logrank Tests (Lakatos) [Mortality]



Logrank Tests (Lakatos) [Proportion Surviving]

- ▶ 中位生存时间、死亡率（如5年死亡率），生存率，这些参数都可以进行相互换算。
- ▶ 如果生存数据满足指数分布，则：

- 死亡风险(Hazard rate) = $\frac{\ln 2}{mOS}$

- $HR = \frac{\text{对照组mOS}}{\text{实验组mOS}}$

- t年死亡率 = $e^{-\text{Hazard rate} * t}$

- t年生存率 = 1 - t年死亡率

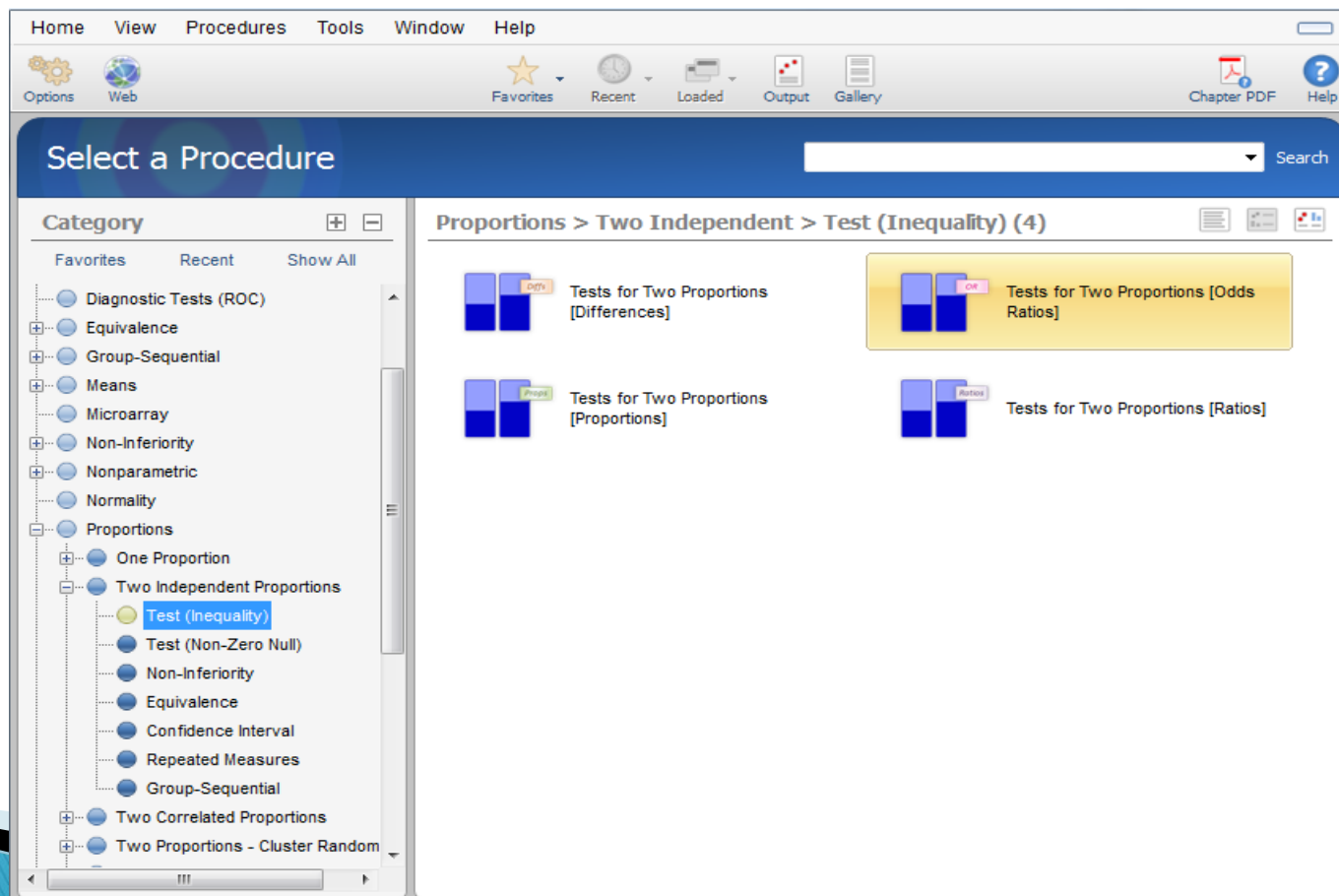
成组设计的病例对照研究 + OR

1、研究问题

某研究者拟进行一项**病例对照研究**，探讨吸烟与肺癌的关系。选择肺癌患者为病例组，选择非肺癌患者为对照组。预期吸烟者发生肺癌的**比值比（OR值）为2.0**，对照组人群中的吸烟率约为**20%**，**设**
 $\alpha=0.05$ ， **$\beta=0.10$** 。拟定病例组和对照组采用相等样本量，请问如何估计病例组和对照组的样本量？

2、PASS软件计算

- ▶ 选择Proportions→Two Independent Proportions→Test (Inequality)→Test for Two Proportions[Odds Ratios]



File View Run Procedures Tools Window Help

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Run

Data

Options

Reports

Plot Setup

Data

Solve For

Find (Solve For): N1

Error Rates

Power (1-Beta): 0.90

Alpha (Significance Level): 0.05

Sample Size

N1 (Sample Size Group 1): 50 to 400 by 50

N2 (Sample Size Group 2): Use R

R (Sample Allocation Ratio): 1.0

Effect Size

OR1 (Odds Ratio) $H_1 = O_1 / O_2$: 2

P2 (Control Group Proportion): 0.2

P1 = the proportion in the treatment group

$OR_1 = [P_1 / (1 - P_1)] / [P_2 / (1 - P_2)]$

Test

Alternative Hypothesis (H_1): Two-Sided

Test Type: Z Test (Pooled)

Alpha

Alpha is the probability of obtaining a FALSE POSITIVE on the statistical test. That is, it is the probability of rejecting a true null hypothesis.

The null hypothesis is usually that the parameters of interest (means, proportions, etc.) are all equal.

Range

Since Alpha is a probability, it is bounded by 0 and 1. Commonly, it is between 0.001 and 0.250

Recommended

Alpha is often set to 0.05 for two-sided tests and to 0.025 for one-sided tests (such as non-inferiority tests).

Notes

You can enter a list of values such as .05 .10 .15

or .05 to .15 by .01

Guide Me: Start

N1: 样本量

α 和把握度 ($1 - \beta$)

N2: Use R=1.0 表示两组样本量相等

OR和对照组的率

- ▶ **Sample Size Grp 1 (N1): 病例组样本量: 230例。**
- ▶ **Sample Size Grp 2 (N2): 对照组样本量: 230例。**

Two Independent Proportions (Null Case) Power Analysis

Numeric Results of Tests Based on the Odds Ratio: O1 / O2

H0: O1/O2=1. H1: O1/O2=OR1<>1. Test Statistic: Z test with pooled variance

	Sample Size Grp 1	Sample Size Grp 2	Prop H1 Grp 1 or Trtmnt P1	Prop Grp 2 or Control P2	O.R. if H0 OR0	O.R. if H1 OR1	Target Alpha	Actual Alpha	Beta
Power	N1	N2							
0.9011	230	230	0.3333	0.2000	1.000	2.000	0.0500		0.0989

3、撰写结论

本研究为成组设计的病例对照研究。病例组为肺癌患者，对照组为非肺癌患者，吸烟为主要观察的暴露因素。根据既往文献报道，对照组（非肺癌患者）人群中的吸烟率约为20%。预期吸烟者发生肺癌的比值比为2.0，设 $\alpha=0.05$ ， $\beta=0.10$ 。利用PASS 11软件计算得到病例组和对照组的样本量 $N1=N2=230$ 例。假定研究对象的无应答率为10%，则需样本量 $N1=N2=230 \div 0.9=256$ 例。假定问卷合格率为90%，则共需样本量为 $N1=N2=256 \div 0.9=284$ 例。

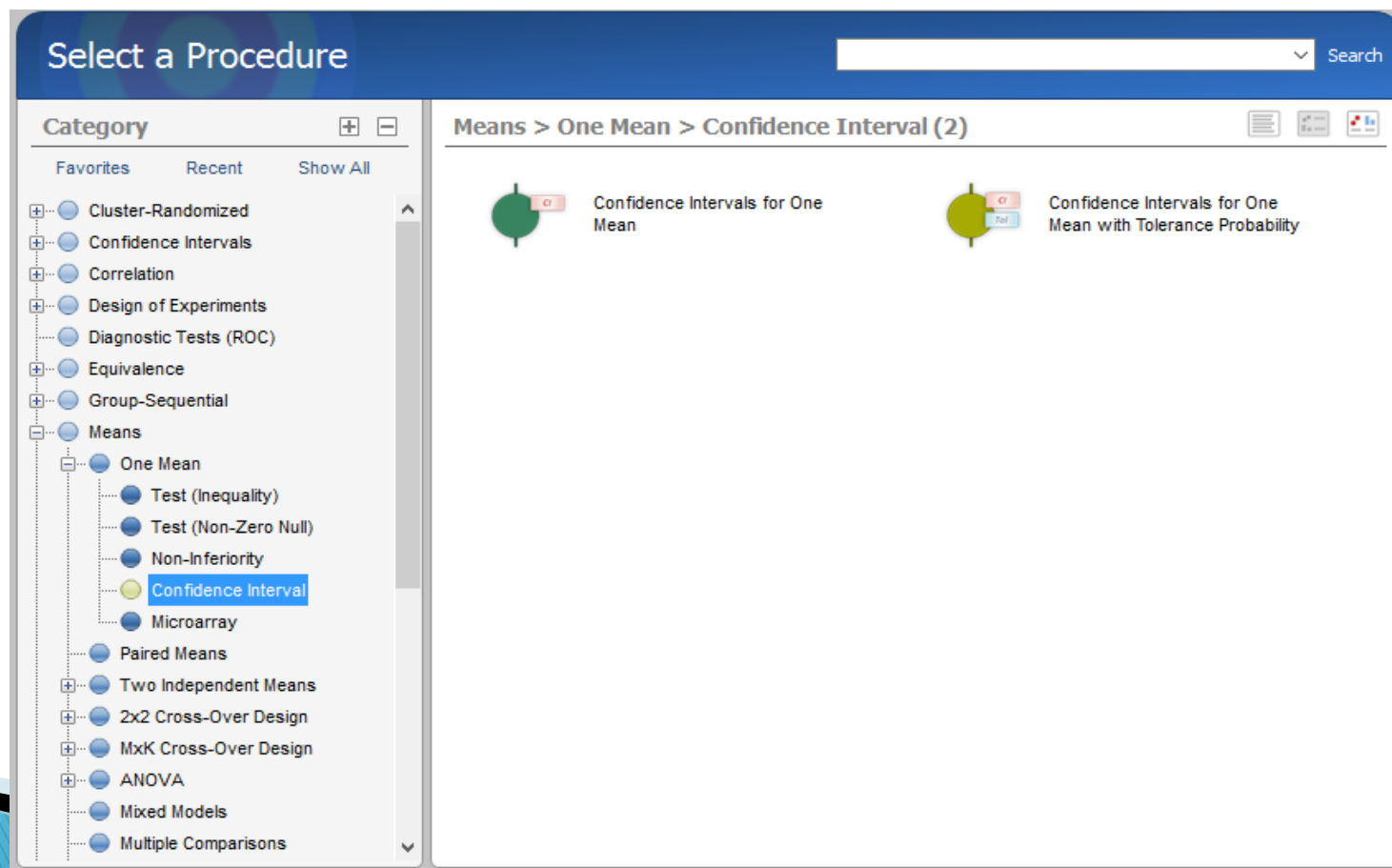
横断面调查 + 连续变量

1、研究问题

某研究者拟开展一项横断面调查，调查某县高三年级男生的身高。据文献报道，邻县高三年级男生的身高均值大约为173cm，标准差约为10cm。规定容许误差为1cm，置信度 $1-\alpha=0.95$ ，已知该县高三年级男生共有3800人，则样本含量至少应有多少人？

2、PASS软件计算

- ▶ 选择Means→One Mean→Confidence Interval→Confidence Interval for One Mean



Confidence Intervals for One Mean

File View Run Procedures Tools Window Help

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Run

Data

Iterations Reports Plot Setup

Solve For

Find (Solve For): N (Sample Size)

Confidence

Confidence Level (1 - Alpha): 0.95

Sample Size

N (Sample Size): 5 to 40 by 5

Precision

Distance from Mean to Limit(s): 1

Standard Deviation

S (Standard Deviation): 10

☐ Known Standard Deviation

One-Sided or Two-Sided Interval

Interval Type: Two-Sided

Population

Population Size: 3800

Population Size

This is the number of subjects in the population.

Usually, you assume that samples are drawn from a very large (infinite) population. Occasionally, however, situations arise in which the population of interest is of limited size. In these cases, appropriate adjustments must be made.

Finite Population Correction Factor:

When a finite population size is specified, the standard deviation is reduced according to the formula:

$$S1^2 = (1 - n/N)S^2$$

where n is the sample size, N is the population size, S is the original standard deviation, S1 is the new standard deviation, and X^2 means X times X.

The quantity n/N is often called the sampling fraction.

Guide Me: Start

N：样本量

置信度

容许误差

标准差

3800的有限总体

- ▶ Distance from Mean to Limit(s)是指均值到置信区间上限（或下限）的宽度，即容许误差。本例中，容许误差为1cm。
- ▶ Know Standard Deviation选项：勾选→表示研究者认为结局指标符合正态分布；不勾选→表示研究者认为结局事件符合t分布。
（不勾选时样本量略大，一般情况下可以不勾选）
- ▶ Population Size选项：当调查对象总体数量可以认为是无限大时，填写Infinite；当知道调查对象大约总体数量时，填入相应的数值或近似值。
（不同总体数量，样本量差别较大，请务必填入）

▶ Sample Size (N): 样本量: 352例。

Confidence Intervals for One Mean Numeric Results for Two-Sided Confidence Intervals with Unknown Standard Deviation

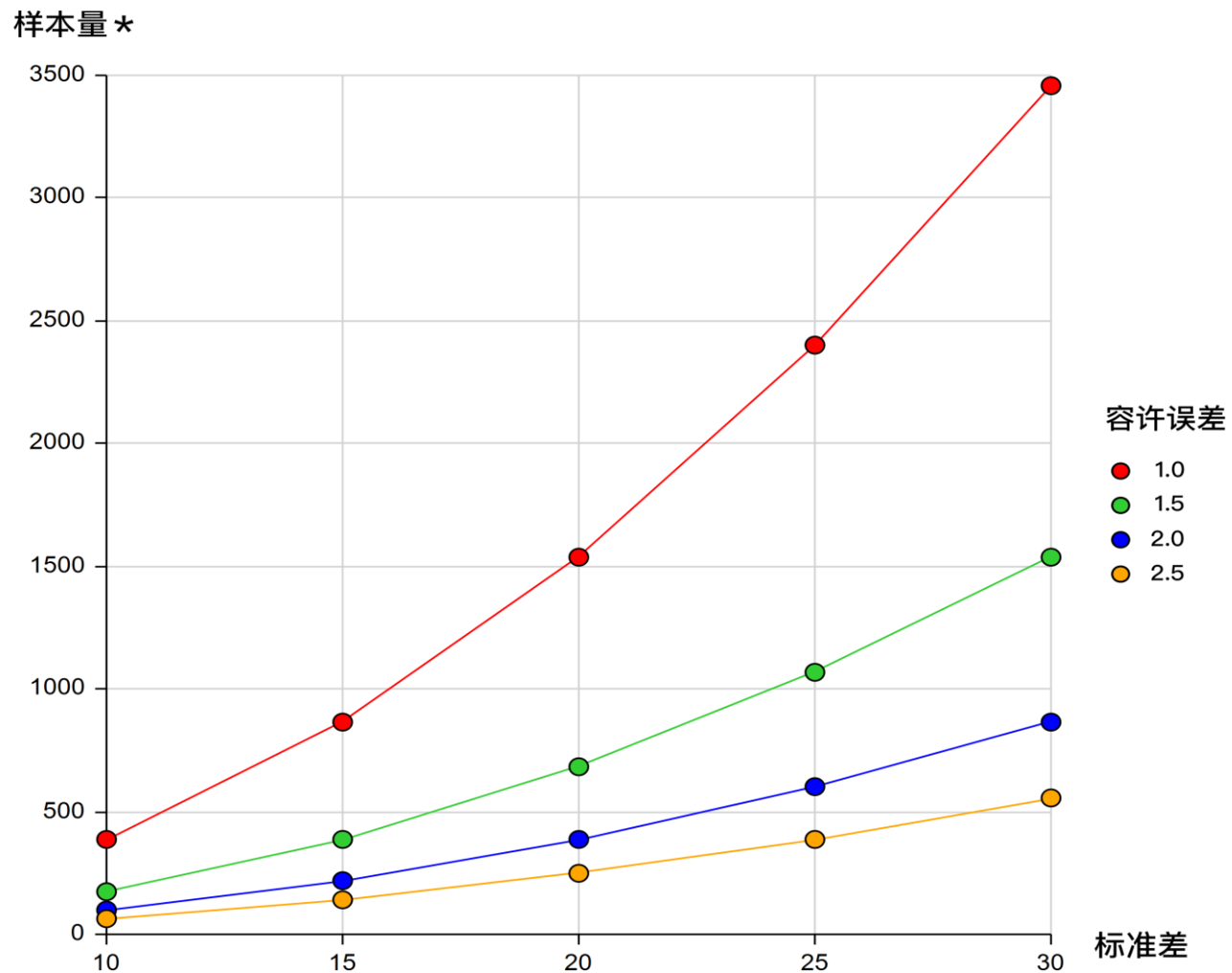
Confidence Level	Sample Size (N)	Target Distance from Mean to Limits	Actual Distance from Mean to Limits	Standard Deviation (S)
0.950	352	1.000	0.999	10.000

Population size = 3800

3、撰写结论

本研究为横断面调查，目的是调查某县高三年级男生的身高。据文献报道，邻县高三年级男生的身高均值大约为173cm，标准差约为10cm。规定容许误差为1cm，置信度 $1-\alpha=0.95$ ，已知该县高三年级男生共有3800人，利用PASS 11软件计算得到需要调查的样本量 $N=352$ 例。假定应答率为90%，则共需样本量为 $N=352\div 0.9=391$ 例。

4、标准差、容许误差和样本量的关系



标准差、容许误差与样本量的关系（置信度=0.95）

* 假定总体为无限总体

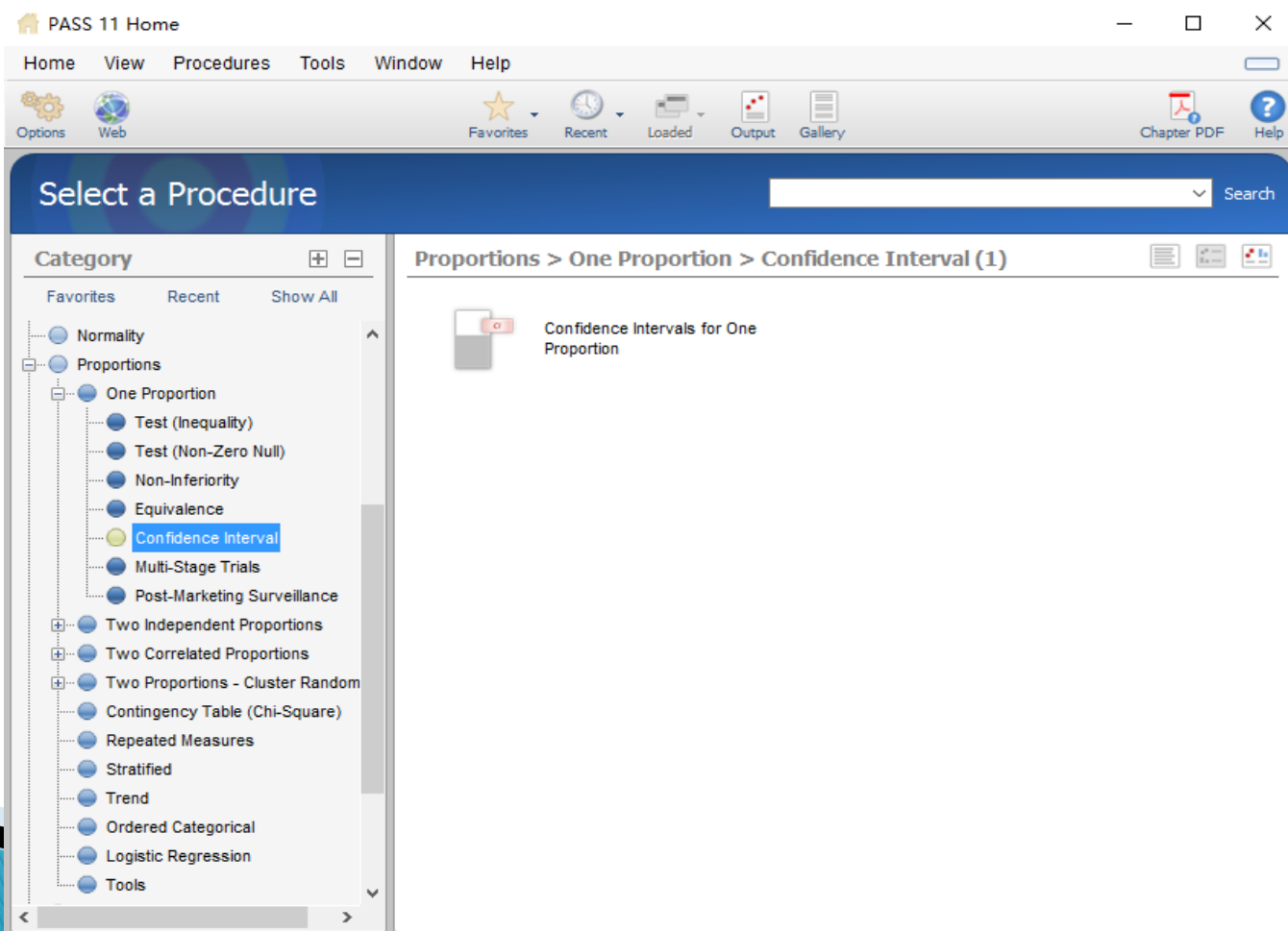
横断面调查 + 分类变量

1、研究问题

某研究者拟开展一项横断面调查，调查北京市40岁及以上人群的高血压患病率。根据其它地区同类调查的结果，估计该年龄段人群中的高血压患病率为30%。规定允许误差为3%，置信度 $1-\alpha=0.95$ ，则至少应该调查多少人？

2、PASS软件计算

- ▶ 选择选择Proportions→One Proportion→Confidence Interval→Confidence Interval for One Proportion



Confidence Intervals for One Proportion

File View Run Procedures Tools Window Help

Reset Open Save As Home Favorites Recent Loaded Output Gallery Chapter PDF Help

Run

Data

Iterations
Reports
Plot Setup

Solve For

Find (Solve For): N (Sample Size)

Confidence

Confidence Level (1 - Alpha): 0.95

Sample Size

N (Sample Size):

Precision

Confidence Interval Width (Two-Sided): 0.06

Distance from P to Limit (One-Sided): 0.05

Proportion

P (Proportion): 0.3

Confidence Interval Method

Confidence Interval Formula: Exact (Clopper-Pearson)

One-Sided or Two-Sided Interval

Interval Type: Two-Sided

Interval Type

Specify whether the interval to be used will be a two-sided confidence interval, an interval that has only an upper limit, or an interval that has only a lower limit.

Guide Me: Start

N: 样本量

置信度

可信区间宽度

总体率估计值

与连续变量的重要区别：

- ▶ Distance from Mean to Limit(s) → Confidence Interval Width (Two-Sided)
- ▶ 均值到上或下95%可信区间的距离 → 可信区间上下限的距离（**两倍于前者**）
- ▶ 无Population Size选项

连续变量

Run

Data

Solve For

Find (Solve For): N (Sample Size)

Confidence

Confidence Level (1 - Alpha): 0.95

Sample Size

N (Sample Size): 5 to 40 by 5

Precision

Distance from Mean to Limit(s): 1

Standard Deviation

S (Standard Deviation): 10

☐ Known Standard Deviation

One-Sided or Two-Sided Interval

Interval Type: Two-Sided

Population

Population Size: Infinite

Add This Procedure to Favorites List

分类变量

Run

Data

Solve For

Find (Solve For): N (Sample Size)

Confidence

Confidence Level (1 - Alpha): 0.95

Sample Size

N (Sample Size): 5 to 40 by 5

Precision

Confidence Interval Width (Two-Sided): 0.06

Distance from P to Limit (One-Sided): 0.05

Proportion

P (Proportion): 0.3

Confidence Interval Method

Confidence Interval Formula: Exact (Clopper-Pearson)

One-Sided or Two-Sided Interval

Interval Type: Two-Sided

Add This Procedure to Favorites List

► Sample Size (N): 样本量: 928例。

Confidence Intervals for One Proportion - New
Numeric Results for Two-Sided Confidence Intervals for One Proportion
Confidence Interval Formula: Exact (Clopper-Pearson)

Confidence Level	Sample Size (N)	Target Width	Actual Width	Proportion (P)	Lower Limit	Upper Limit	Width if P = 0.5
0.950	928	0.060	0.060	0.300	0.271	0.331	0.065

Population Size选项解决方法

遇到的总体是有限总体，怎么办？例如，计算样本量需要1000人，但是总人群只有900人，怎么办？

$$n = \frac{n_0}{1 + \frac{n_0}{N}}$$

↵

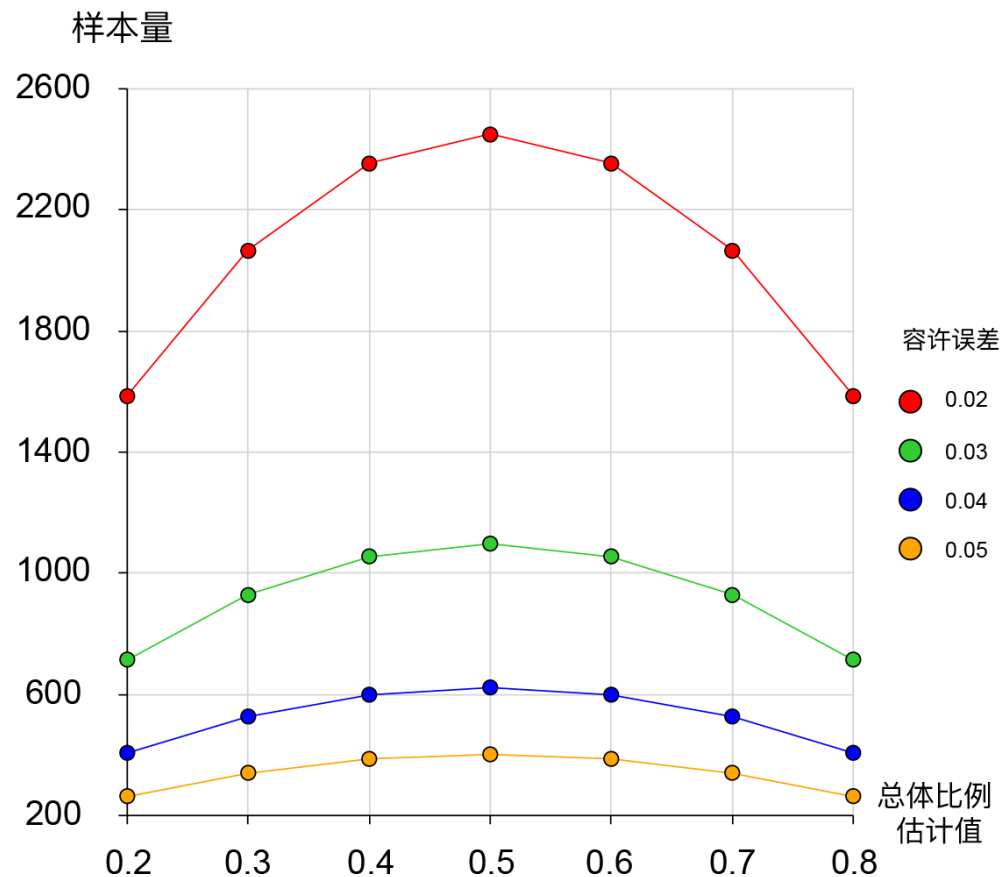
n: 最终样本量 n_0 : PASS 计算的样本量 N: 总人群数量↵

$$\text{例子中最终的样本量 } n = \frac{1000}{1 + \frac{1000}{900}} = 474 \text{ 例}$$

3、撰写结论

本研究为横断面调查，目的是调查北京市40岁及以上人群的高血压患病率。根据其它地区同类调查的结果，该年龄段人群中高血压患病率大约为30%。规定容许误差为3%，置信度 $1-\alpha=0.95$ ，利用PASS 11软件计算得到需要调查的样本量 $N=928$ 例。假定研究对象的无应答率为10%，则需样本量 $N=928\div0.9=1031$ 例。假定问卷合格率为90%，则共需样本量为 $N=1031\div0.9=1146$ 例。

4、总体比例估计值、容许误差和样本量的关系



总体比例估计值、容许误差与样本量的关系 (置信度=0.95)

北京医助科技有限公司



医咖会

样本量估算合集: <http://mp.weixin.qq.com/s/gl-hNRuPvukWfSckDYKrMw>

谢谢！

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