Designing a Single-Arm Experiment with a Bernoulli Outcome

The SAS program RatePrePost.xls determines the minimum-cost sample size for a single-arm experiment with a Bernoulli outcome.

The null, alternative, and superiority hypotheses are diagrammed here.

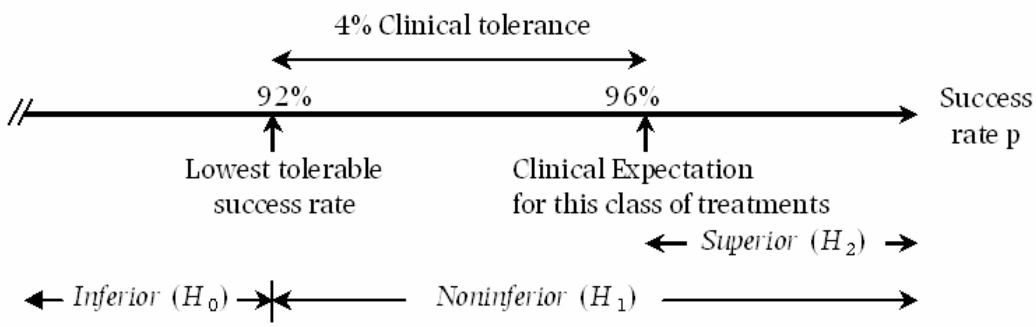


Figure 13.5 Hypotheses in a noninferiority study of a new treatment. The issue is whether the new treatment is inferior (intolerably lower than clinical expectation) or not.

In general, the upper bound of the null hypothesis is denoted p_0 and the lower bound of the superiority hypothesis is denoted p_1.

The cost structure is shown in Table 13.1 below. The unit of cost is the cost of committing a Type II error (declaring a truly superior treatment to be inferior), k is the cost ratio Type I Cost / Type II Cost, where a Type I error is declaring a truly inferior treatment to be non-inferior.

Table 13.1 Threshold loss structure.

	True status of the treatment		
		Noninferior (H_1)	
	Inferior (H_0)	Neither	Superior (H_2)
Decision	($p < p_0$)	($p_0 \leq p < p_1$)	($p_1 \leq p$)
Inferior	0	0	*1*
Noninferior	*k*	0	0

The cost of data is c units per subject (i.e. the cost per subject divided by the cost of a Type II error).

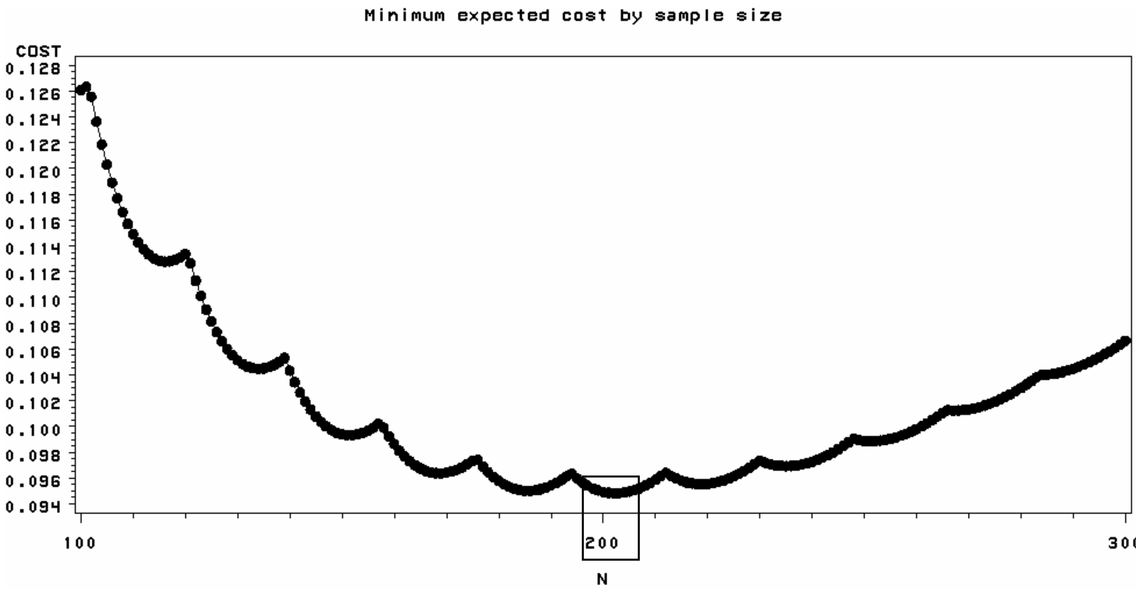
The prior distribution of the Bernoulli rate parameter, p, is assumed to be Beta(a,b).

The SAS macro RatePrePost.SAS computes the prior expected cost of basing a decision on n subjects and graphs that cost against a range of sample sizes (n) specified by the user. In addition the program graphs and prints a table of critical values (CV). The critical value is defined as the largest number of failures that would still result in rejecting the null hypothesis (inferiority) in favor of the alternative hypothesis (non-inferiority). The critical value is presented in raw form and also in a graph that shows the smallest observed success rate that would support the declaration of non-inferiority.

The ***macro call*** shown below produces Figure 13.9 and table 13.3 of Woodworth's, ***Biostatistics, A Bayesian Introduction***. The bold, underlined numbers can be replaced by values selected by the user. No other changes should be made to the program.

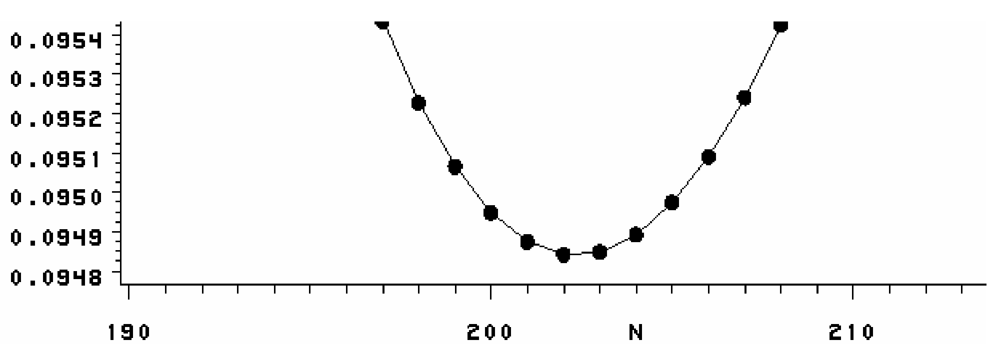
%RatePrePost(a=**<u>14</u>**, b=**1**, k=**<u>12</u>**, c=**<u>.0003</u>**, p0=**<u>.92</u>**, p1=**<u>.96</u>**, n=**<u>100</u>** TO **<u>300</u>** BY **<u>1</u>**);

The graph of minimum expected cost appears to have a minimum just near n=200.

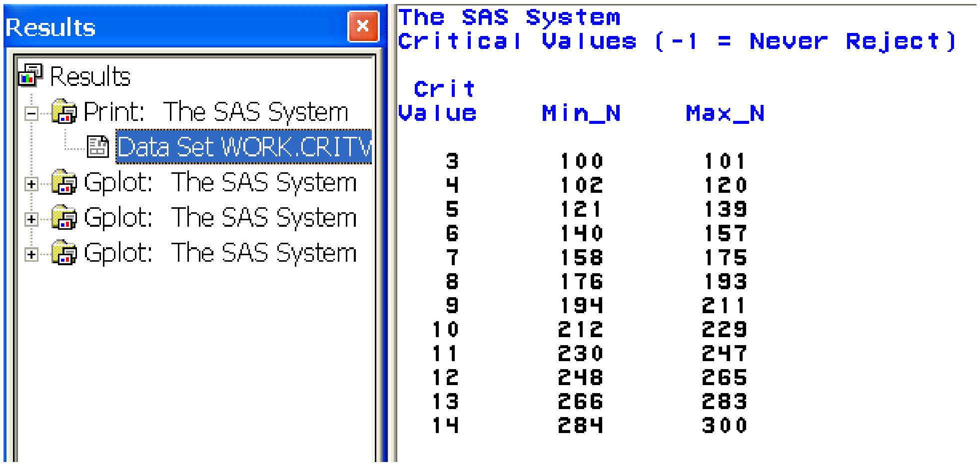


Re-running with a narrower range of n's it is clear that the minmum occurs at n = 202.

%RatePrePost(a=**<u>14</u>**, b=**1**, k=**<u>12</u>**, c=**<u>.0003</u>**, p0=**<u>.92</u>**, p1=**<u>.96</u>**, n=**<u>195</u>** TO **<u>225</u>** BY **<u>1</u>**);



The program also tabulates the critical values. For example, as the output shown on the next page, the critical value is X = 9 failures when n = 202, the optimal sample size. In other words, if there are 0 to 9 failures in 202 patients, the treatment is declared non-inferior, but if there are 10 or more failures it is declared inferior.

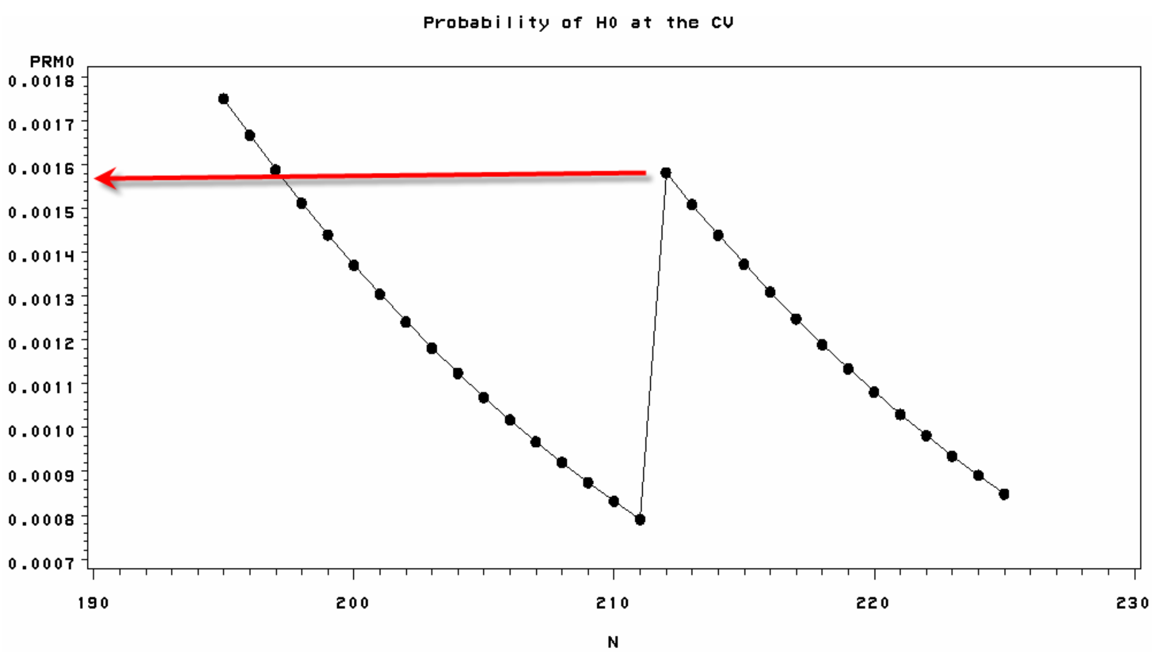


Results
Results
Print: The SAS System
Data Set WORK.CRITV
Gplot: The SAS System
Gplot: The SAS System
Gplot: The SAS System

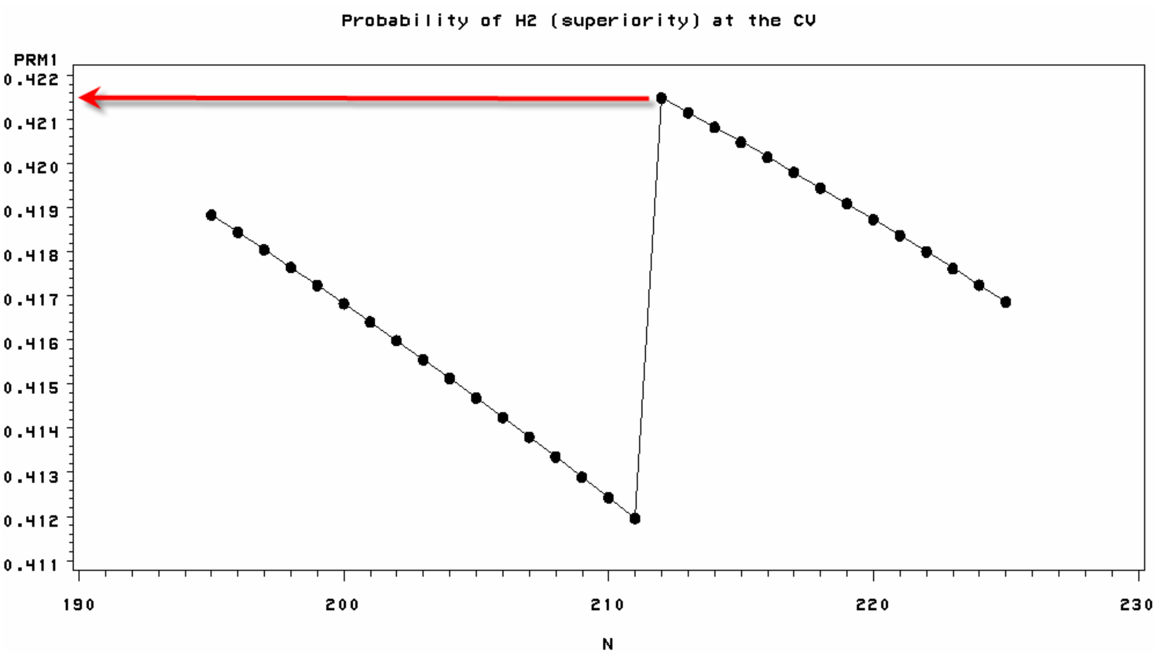
The SAS System
Critical Values (-1 = Never Reject)

Crit Value	Min_N	Max_N
3	100	101
4	102	120
5	121	139
6	140	157
7	158	175
8	176	193
9	194	211
10	212	229
11	230	247
12	248	265
13	266	283
14	284	300

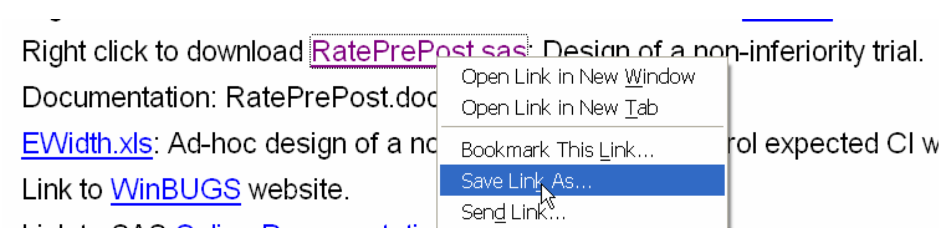
At the critical value the posterior probability of inferiority, $P(H_0 \mid Data)$ is about .0016 as shown by this graph of $P(H_0 \mid X=CV)$,



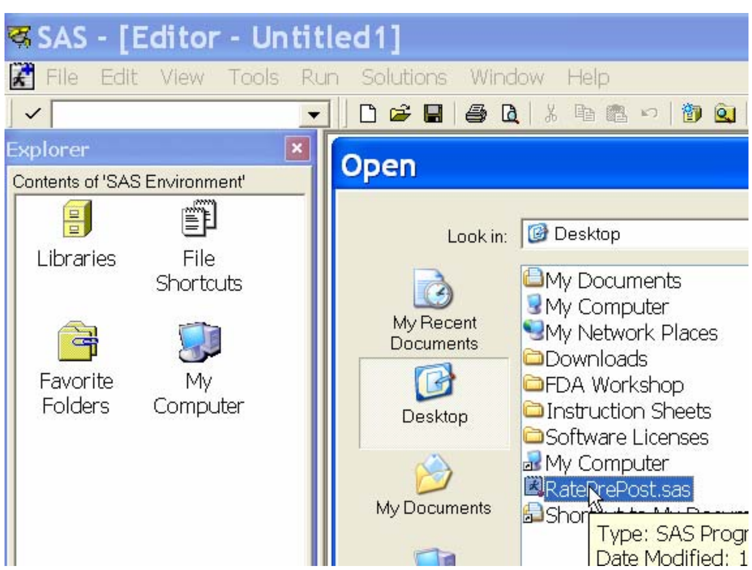
This graph of $P(H_2 \mid X = CV)$, the posterior probability of superiority at the critical valu8e, is about 0.42 or 42% for the optimal sample size.



To run RatePrePost.xls, first download it from the textbook website to a convenient directory,



Launch SAS and open the file you downloaded (in this case it was downloaded to the desktop),



Follow the instructions in the program:

Step 1:

```
/* Step 1. Highlight from %Macro to %MEND RatePrePost; and click the runner  *

%MACRO RatePrePost(a,b,k,c,p0,p1,n);
%LET ni=1;
PROC DATASETS LIBRARY=WORK;
     DELETE OUTMAT;
RUN;
QUIT;

. . .
PROC GPLOT DATA=OUTMAT;
     TITLE2 "Minimum Success Rate to Reject H0 by sample size";
     PLOT (CritRate)*N / OVERLAY;
RUN;
QUIT;
%MEND RatePrePost;
```

Step 2: Enter a,b,k,c,p_0, p_1, and the range of n's

```
/* Step 2.  Fill in your own values here                                      */
%RatePrePost(a=14,b=1,k=12,c=.0003,p0=.92,p1=.96,  n=100 TO 300 BY 1);
```

Step 3: Call the macro.

```
/* Step 3. Highlight the command you created in step 1 and click the runner  */
%RatePrePost(a=14,b=1,k=12,c=.0003,p0=.92,p1=.96,  n=100 TO 300 BY 1);
```

The output is three graphs and a table of critical values. To view them, expand the "results" directory and double click on the item(s) you want to look at.