

"I enjoy using your software tremendously!"

— Marc Buyse, Executive Director,
IDDI (International Drug Development Institute),
Brussels, Belgium

Means | Proportions | Correlations | ANOVA | Regression | Logistic | **Survival** | General

A computer program for
statistical power analysis
and confidence intervals

POWER AND
PRECISION

Power Analysis for Survival Analysis

One of the new modules in **Version 2** of this acclaimed program.

**WORK
INCREDIBLY
FAST!!**

**GET THE BIG
PICTURE
IN SECONDS!!**

Major innovation in computational speed

- Compute power by **formula rather than simulation**, even when accrual rates, hazard rates, and attrition rates vary from one time interval to the next.
- Graph power as a function of study duration, accrual patterns, treatment effect, attrition, or any other parameter **in just seconds** — and get a clear picture of each factor's impact in your study.
- This speed is made possible by the new algorithm which bypasses the simulation, coupled with an extremely powerful interface. With any other program, the same task would require many hours of tedious computations.

WORK INTERACTIVELY

Group	Duration (Months)			Sample Size		Treatment Effect			Attrition
	Accrual Period	Follow Up	Total Duration	N Per Month	Total Patients	Hazard Rate	Median Survival	24 Month Survival	Drop Rate Per Month
Standard treatment	6	18	24	Varies	68	0.10	6.93	0.09	0.02
New treatment				Varies	68	0.05	13.86	0.30	
<input type="checkbox"/> Enter the hazard ratio				22.7	136	0.50			

Alpha= 0.05, Tails= 2 Power: **90%**

Summary - Power
For this study design (total duration of 24 months, including 6 months accrual, with variable accrual), hazard rates (.100 vs. .050), attrition rates (.0.02), sample size (68 and 68), and alpha (0.05, 2-tailed), power is 0.90.
This means that 90% of studies will have sufficient power to detect a treatment effect, rejecting the null hypothesis.

Accrual: Number of Patients Entered Per Month

Month Number	Total Number of Patients
Prior	0
1	14
2	14
3	27
4	27
5	27
6	27

Event rates: Cumulative survival

Months from Study Entry	Standard treatment	New treatment
0	1.0	1.0
2	0.8	0.9
4	0.6	0.8
6	0.4	0.7
8	0.3	0.6
10	0.25	0.55
12	0.2	0.5
14	0.18	0.45
16	0.16	0.4
18	0.15	0.35
20	0.14	0.3
22	0.13	0.25
24	0.12	0.2



← Modify the accrual, follow-up, sample size, hazard rates, attrition, or any parameter...

← And immediately see the impact on power.

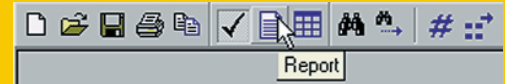
Or, click "Find N" and the program will find the sample size automatically.

← The graph of cumulative survival serves as a clear and compelling picture of the treatment effect.

WORK IN MINUTES RATHER THAN HOURS!



Create a Report with a single click!



CREATE

a report which explains the study design and assumptions.

VERIFY

that all elements of the study have been specified correctly.

USE

the report as a teaching tool, and as an example of how a power analysis should be described.

EDIT

the report and include it in your study plan or grant application.

The report is shown unedited. The group names (New treatment), time interval (months), and subject type (patients) are based on user-set preferences.

Power for a test of the null hypothesis

One goal of the proposed study is to test the null hypothesis that the hazard rate, which is assumed to be constant across all study intervals, is identical in the two groups (standard treatment and new treatment).

Study design. This hypothesis will be tested in a study in which patients are entered and then followed until either (a) the terminal event occurs, or (b) they drop out of the study, or (c) the study ends and the patient is censored while still being actively followed. The study design calls for an accrual period of 6 months and a follow-up period of 18 months. In other words, the first patient to enter the study will be followed for a maximum of 24 months while the last patient to enter the study will be followed for a maximum of 18 months.

Effect size. Computation of power is based on a hazard ratio of 0.50. Specifically, it assumes instantaneous hazard rates of 0.10 for the standard treatment group versus 0.05 for the new treatment group. Since the hazard rate is constant across intervals this is equivalent to median survival times of 6.93 months for the standard treatment group versus 13.86 months for the new treatment group. It is also equivalent to a cumulative survival at 24 months of 0.09 for the standard treatment group versus 0.30 for the new treatment group (see graph). This effect was selected as the smallest effect that would be important to detect, in the sense that any smaller effect would not be of clinical or substantive significance. It is also assumed that this effect size is reasonable, in the sense that an effect of this magnitude could be anticipated in this field of research.

Sample size. A total of 68 patients will be entered into the standard treatment group and a total of 68 patients will be entered into the standard treatment group. Patients will be entered into the study at a variable rate, as shown below.

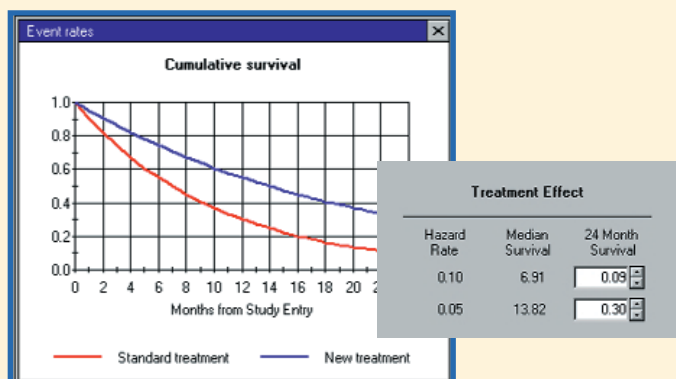
Attrition. The computation assumes an attrition rate of 0.02 per month. This means that 2% of the patients who enter (for example) the second month of the study will drop out of the study during that month. This attrition (or drop-out) rate is separate from the censoring of patients that takes place when the study ends.

Alpha and Tails. The criterion for significance (alpha) has been set at 0.05. The test is 2-tailed, which means that an effect in either direction will be interpreted.

Power. For this study design, sample size, attrition rate, alpha and tails, and the population effect size described above, the study will have power of 90.2% to yield a statistically significant result.

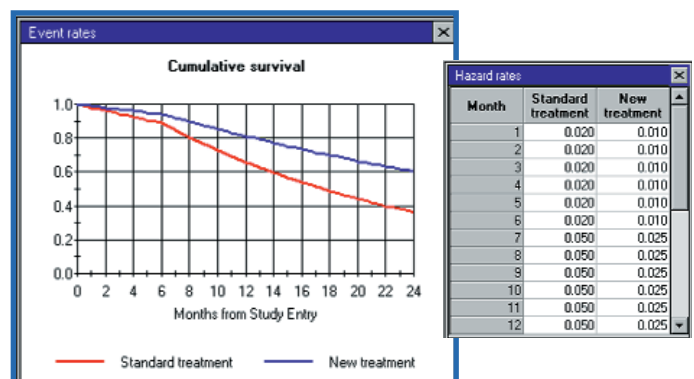
Enter the treatment effect using a seamless interface—the graph of cumulative survival is updated automatically.

If the hazard rates are constant—



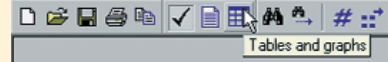
Enter the hazard rate OR the median survival OR the cumulative survival. The program computes the other two values and automatically updates the graph of cumulative survival.

If the hazard rates vary—



One click opens a grid where you can enter the hazard rate for each interval. Proportional hazards are permitted but not required. No simulations are required to computer power, so you can still find the required sample size with a single click!

Assess the impact of all parameters in just seconds!



1. Click "Tables and Graphs." The program picks up all parameters from the main screen and uses these to select a plausible range of values for the sample size. The initial table and graph are created immediately.
Total time: 1 second

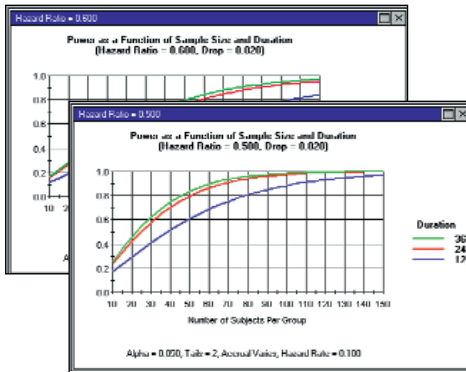
Power And Precision - [Survival analysis]

Power as a Function of Sample size, Study Duration, Drop Rate, Hazard Ratio

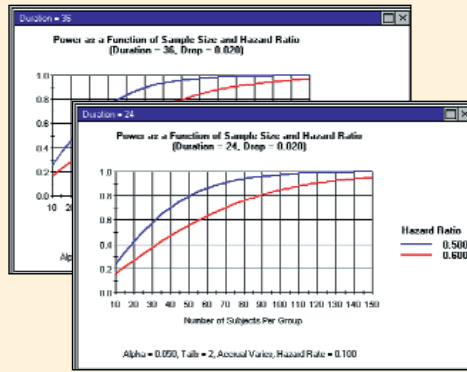
Duration	Hazard Ratio	Drop	N1= N2=	Sample Size																			
				10	15	20	25	30	35	40	45	50	55	60	65	70	75	80	85	90	95		
12	0.500	0.020		0.169	0.231	0.292	0.351	0.408	0.463	0.514	0.562	0.607	0.649	0.686	0.720	0.751	0.780	0.805	0.828	0.849	0.867		
		0.040		0.161	0.218	0.274	0.330	0.384	0.436	0.485	0.531	0.575	0.615	0.653	0.688	0.720	0.749	0.776	0.800	0.822	0.842		
	0.600	0.020		0.119	0.154	0.190	0.226	0.261	0.297	0.331	0.365	0.399	0.431	0.462	0.493	0.522	0.550	0.577	0.603	0.627	0.651		
		0.040		0.114	0.146	0.180	0.213	0.246	0.279	0.312	0.344	0.375	0.406	0.436	0.465	0.493	0.520	0.546	0.571	0.595	0.619		
24	0.500	0.020		0.239	0.333	0.422	0.505	0.579	0.646	0.703	0.754	0.796	0.833	0.863	0.889	0.910	0.927	0.941	0.953	0.963	0.970		
		0.040		0.214	0.297	0.377	0.452	0.522	0.586	0.643	0.695	0.740	0.779	0.813	0.843	0.868	0.890	0.908	0.924	0.937	0.948		
	0.600	0.020		0.195	0.211	0.268	0.319	0.372	0.422	0.470	0.515	0.558	0.599	0.638	0.671	0.703	0.732	0.760	0.784	0.807	0.827		
		0.040		0.143	0.190	0.238	0.286	0.332	0.378	0.421	0.464	0.504	0.542	0.578	0.612	0.644	0.674	0.702	0.728	0.752	0.775		
36	0.500	0.020		0.260	0.363	0.459	0.547	0.624	0.691	0.748	0.796	0.836	0.869	0.896	0.918	0.935	0.949	0.960	0.969	0.976	0.982		
		0.040		0.227	0.315	0.400	0.480	0.552	0.617	0.675	0.726	0.770	0.808	0.841	0.868	0.891	0.911	0.927	0.941	0.952	0.961		
	0.600	0.020		0.167	0.228	0.287	0.346	0.402	0.456	0.507	0.555	0.599	0.640	0.678	0.712	0.744	0.773	0.798	0.822	0.843	0.861		
		0.040		0.148	0.200	0.252	0.302	0.351	0.399	0.445	0.489	0.531	0.570	0.607	0.642	0.674	0.704	0.731	0.757	0.780	0.802		

2. Add any number of factors with a few clicks. Here, we will use three levels of duration (12, 24, 36 months), two levels of treatment effect (risk ratio of .50 and .60), and two rates for attrition (.02 and .04). The program automatically nests the factors, populates the table, and creates the graphs.
Total time: 20 seconds

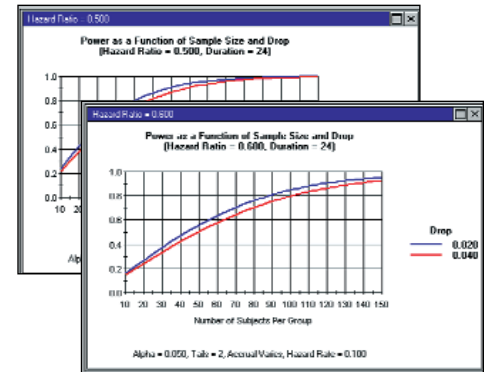
Simply drag and drop columns in the table to instantly highlight the impact of any parameter. For example...



Assess the impact of study duration. Power increases substantially as duration is increased from 12 to 24 months, but there is virtually no impact on power if the study duration is increased beyond that point. **Total time: 1 second.**



Assess the impact of treatment effect. If we elect to plan for the smaller treatment effect we will need to increase the sample size by 40 patients per group. This is true for a 24 month study (foreground) or 36 months (background). **Total time: 1 second.**



Assess the impact of attrition (drop-outs). In this example, an attrition rate of 4% per month as compared with 2% per month will have only a modest impact on power. This holds true across all levels of treatment effect and duration. **Total time: 1 second.**

• Use with these graphs at meetings to develop an appropriate study plan

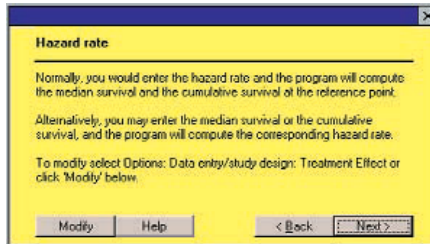
• Include the graphs in your reports and grant applications



Tools and Features

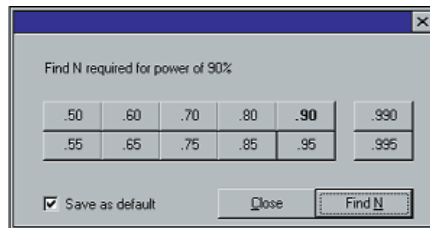
INTERACTIVE GUIDE

This guide alerts you to the program's features and offers suggestions for increasing power.



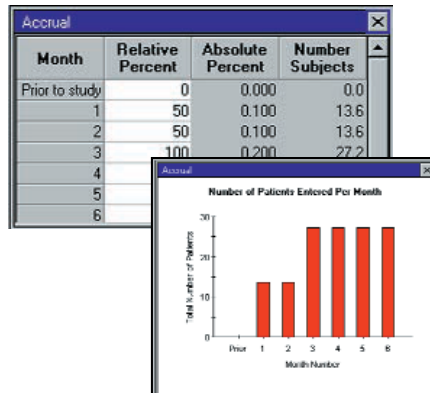
FIND THE SAMPLE SIZE AUTOMATICALLY

Click "Find N" and the program displays the sample size required for any level of power. You may specify an allocation ratio (e.g., 2:1) and you may specify that the accrual rate should vary from one time interval to the next.



ACCRUAL RATES

If the accrual rate varies simply specify the relative proportion of subjects to be entered during each interval (e.g. 1:1:2:2). When you click *Find N* the program computes and graphs the actual number to be entered during each interval.



Survival Analysis Options

Accrual

- Prior to study
- Constant rate for a given number of intervals
- Varies from one interval to the next

Hazard rates

- Constant for all study intervals
- Varies from one interval to the next, proportional
- Varies from one interval to the next, non-proportional

Attrition (non-compliance or drop-out)

- None
- Constant rate
- Varies by time and/or by group

Statistical tests

- Log Rank, Wilcoxin

Graphs

- Export as WMF, EMF, BMP, copy to clipboard

Reports

- Export as RTF, copy to clipboard

Tables

- Export as data or as picture, copy to clipboard

Includes the procedures you need

In addition to survival analysis, includes modules to compute power for means, proportions, analysis of variance and covariance, multiple linear regression, logistic regression, equivalence tests, and more.

Printed manual and Help system

The printed manual (300 pages) explains the logic and proper application of power analysis. It also includes worked examples for each statistical procedure and details for all algorithms. An extensive Help system provides step-by-step instructions for each procedure.

Developed by a team of experts

Michael Borenstein, David Schoenfeld, Jesse Berlin, Edward Lakatos, Hannah Rothstein, Jacob Cohen

Comments and Reviews

"This is stunning in its clarity and efficiency."

— **Dr. Sal Mannuzza,**
New York University School of Medicine

"This software is great and the ease of use is amazing. I normally use [another program] and was prepared to spend hours... With your program I had the graphs in minutes and the graphs got it exactly right. An incredible effort. Thanks!!"

— **Ricardo Pietrobon, Director of Outcomes Research,**
Division of Orthopedic Surgery and Ambulatory Anesthesia, Duke University

"In summary, this software was obviously developed by those who have conducted power analyses for numerous proposals. The authors are well aware of the "What ifs?" that we are asked, and that we ask of ourselves, as we conduct power analyses as a part of planning trials. With its great flexibility and speed, this nicely designed software would be well used by anyone involved in the design of clinical trials and other research projects."

— **Dr. Andrew Leon, Software Review,**
Controlled Clinical Trials,
20:202-204 (1999)

Biostat™

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