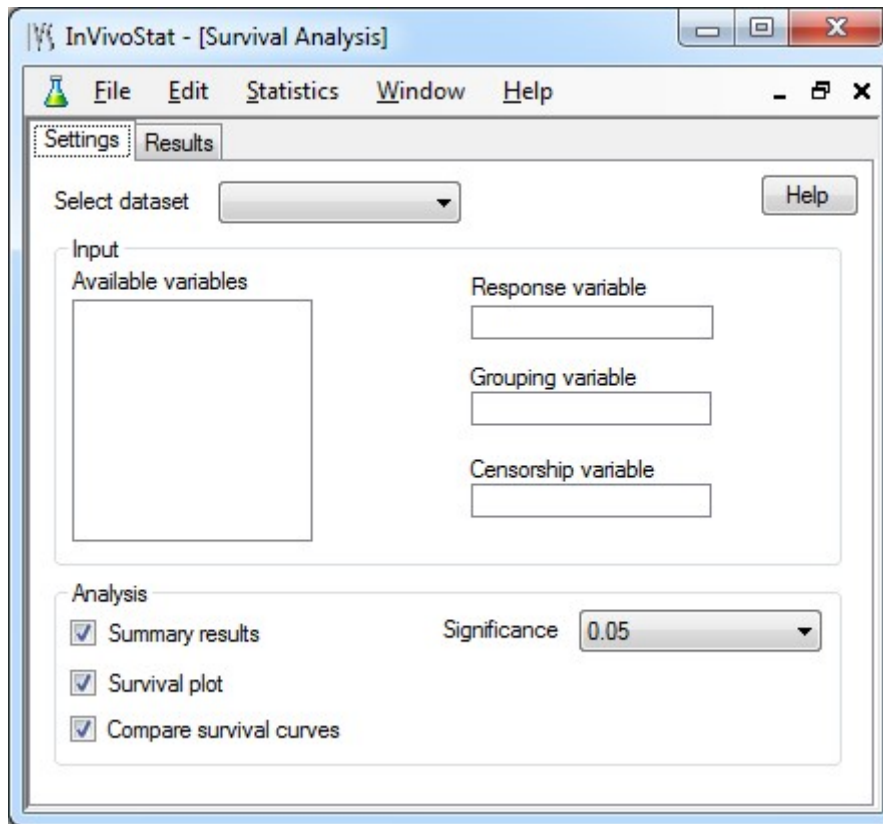


InVivoStat

Survival Analysis Module

Tipsheet

The Survival Analysis module in InVivoStat is available within the Additional Analyses sub-menu in the Statistics drop-down menu and is entitled ‘Survival Analysis’. The user interface is:



The Survival Analysis module allows the user to calculate the Kaplan-Meier non-parametric maximum likelihood estimates of the survival functions, produce a plot of the survival curves and also perform a log-rank (or Mantel-Haenszel) test to compare the survival times.

The module requires three input variables, the survival times (Response variable), the categorisation variable (Grouping variable) and a variable defining whether the observation is censored or not (Censorship variable). The values of the censorship variables are either 1 - denoting an uncensored observation, or 0 - denoting a censored observation.

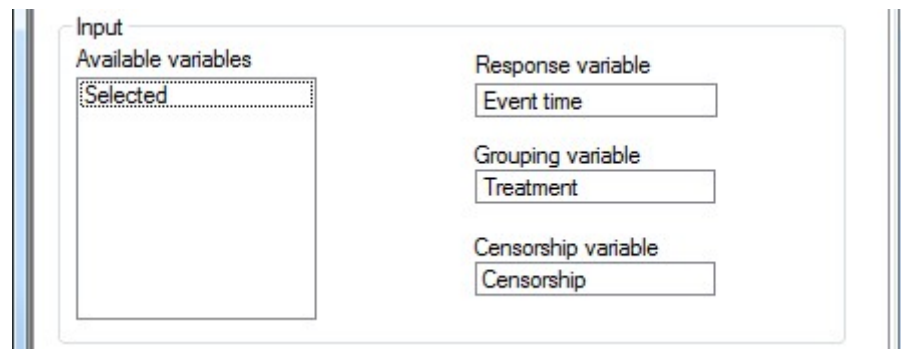
1 Analysis procedure

1.1 Select the dataset to be summarised

The analysis begins by selecting a dataset from the drop-down list of available datasets.

1.2 Select the Response, Group and Censorship variables to analyse


Input variables can be selected by drag and dropping from the list of available variables into the Response, Grouping and Censorship variable boxes.



1.3 Selecting the results

The user can now select the options they wish to display in the output window. Options include a table of the summary results, a plot of the Kaplan-Meier survival curves and a table summarising the log-rank test to compare the survival curves. The user also has the option to change the default significance level from 5% to another value of their choice.

The summary results table includes the median and its confidence interval, which are defined by drawing a horizontal line at 0.5 on the plot of the survival curve and its confidence bands (not included on InVivoStat plots for clarity). The intersection of the line with the lower CI band defines the lower limit for the median's interval, and similarly for the upper band. If any of the intersections is not a point, then we use the smallest point of intersection, e.g., if the survival curve were exactly equal to 0.5 over an interval.



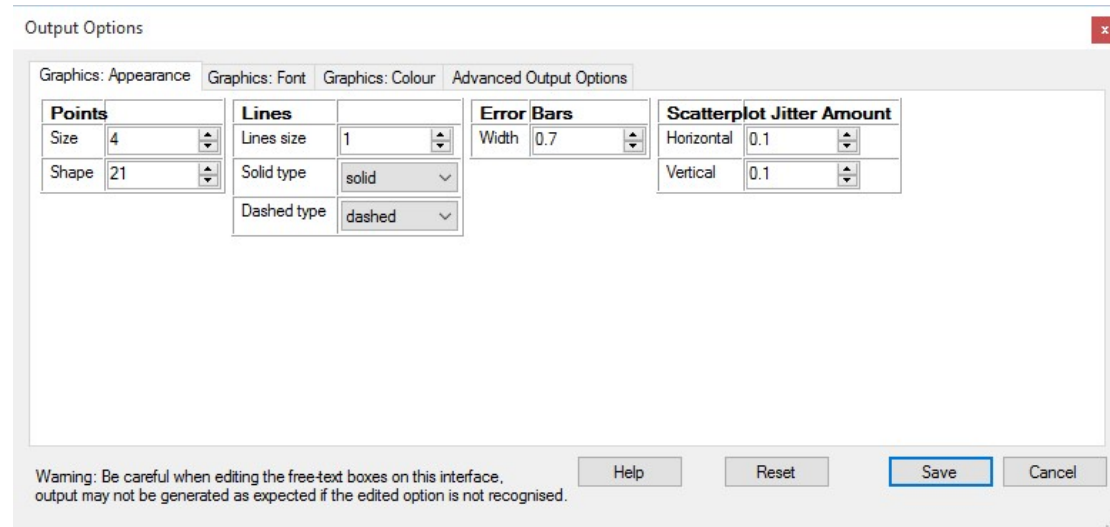
2 Controlling the output

The user has the ability to control various aspects of the output. These are available from the

Statistics → Options → Output Options

menu and should be selected before performing the analysis.

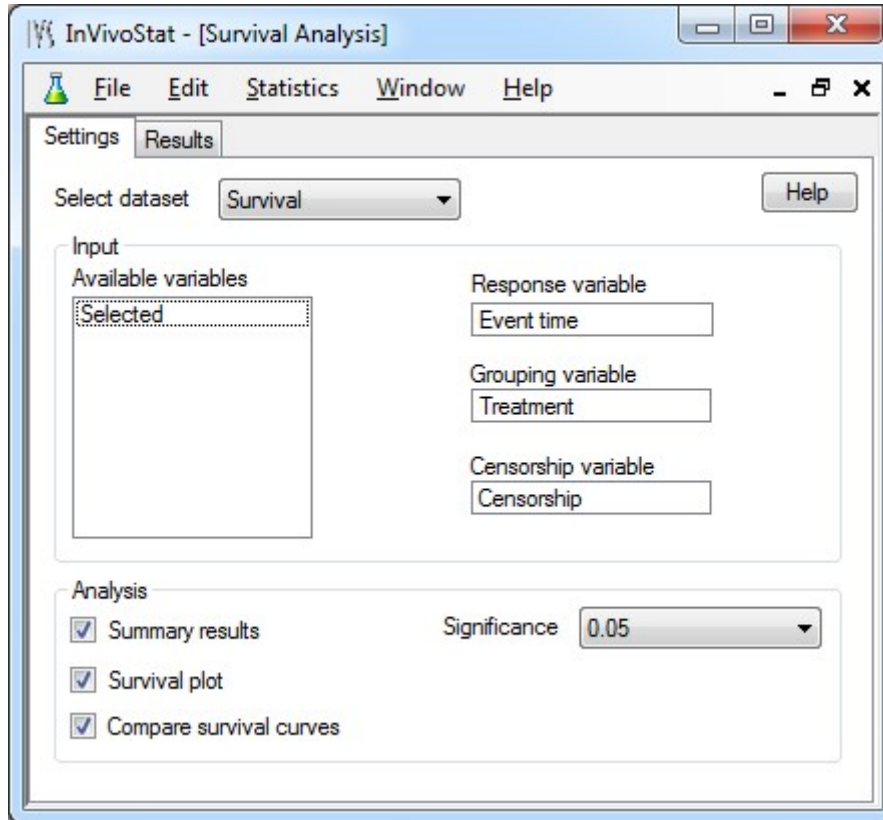
Users can manipulate various global characteristics of the plots produced. Plots can be generated in pdf format and also in black and white.



More information on the options can be found in the Getting Started tipsheet.

3 Sample output

Options:



InVivoStat Survival Analysis

Analysis information

The response Event time has been analysed in the Survival Analysis module, with grouping variable Treatment and censorship variable Censorship.

Note, in this analysis InVivoStat assumes that censored observations are given the value 0 in the censorship variable Censorship and 1 otherwise.

Summary results

	Records	n	Start size	Events	Median	Lower 95% CI	Upper 95% CI
Group							
Control	24	24	24	18	48	34	96
Low dose	18	18	18	14	30	23	156
Mid dose	26	26	26	20	141	28	245
Top dose	8	8	8	6	115	63	152

Comparing survival curves

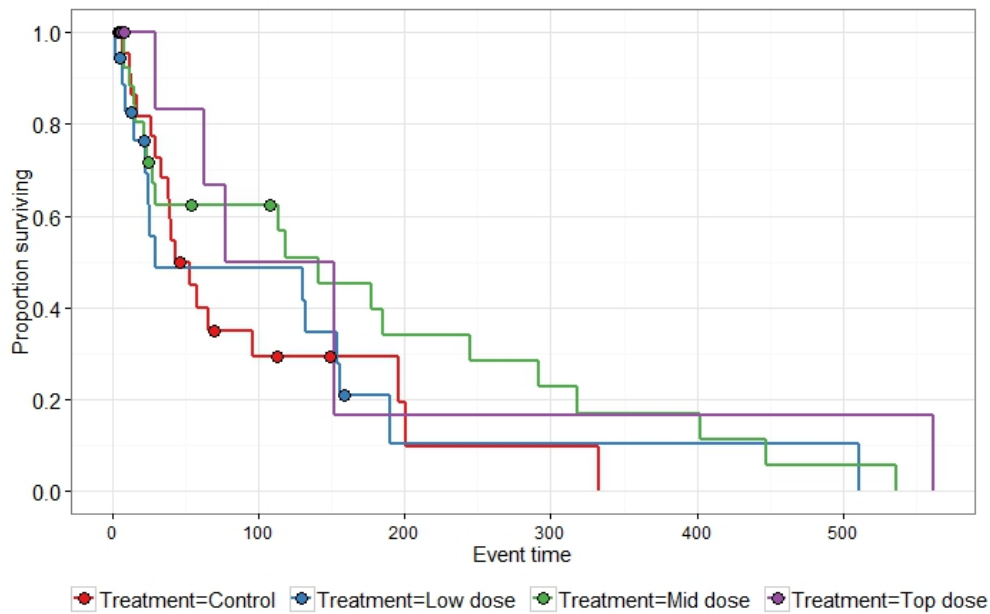
	N	Observed	Expected	$(O-E)^2/E$	$(O-E)^2/V$	Chi-sq	p-value
Group							
Control	24	18	14.70	0.74	1.07	2.67	0.4458
Low dose	18	14	11.62	0.49	0.63		
Mid dose	26	20	23.20	0.44	0.78		
Top dose	8	6	8.48	0.72	0.99		

Conclusion: The survival curves were not statistically significantly different.

This analysis implements the G-rho family of Harrington and Fleming (1982), with weights on each death of 1, where S is the Kaplan-Meier estimate of survival. This is the log-rank or Mantel-Haenszel test.

For more information on the theoretical approaches that are implemented within this module, see Bate and Clark (2014).

Kaplan-Meier survival plot



Censored observations are highlighted on the Kaplan-Meier survival plot with a filled circle.

Statistical references

Bate ST and Clark RA. (2014). *The Design and Statistical Analysis of Animal Experiments*. Cambridge University Press.

Harrington DP and Fleming TR. (1982). A class of rank test procedures for censored survival data. *Biometrika* 69, 553-566.

R references

R Development Core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <http://www.R-project.org>.

Baptiste Auguie (2012). gridExtra: functions in Grid graphics. R package version 0.9.1. <http://CRAN.R-project.org/package=gridExtra>

Barret Schloerke, Jason Crowley, Di Cook, Heike Hofmann, Hadley Wickham, Francois Briatte, Moritz Marbach and Edwin Thoen (2014). GGally: Extension to ggplot2. R package version 0.4.5. <http://CRAN.R-project.org/package=GGally>

Erich Neuwirth (2011). RColorBrewer: ColorBrewer palettes. R package version 1.0-5. <http://CRAN.R-project.org/package=RColorBrewer>

H. Wickham. ggplot2: elegant graphics for data analysis. Springer New York, 2009.

H. Wickham. Reshaping data with the reshape package. Journal of Statistical Software, 21(12), 2007.

Hadley Wickham (2011). The Split-Apply-Combine Strategy for Data Analysis. Journal of Statistical Software, 40(1), 1-29. URL <http://www.jstatsoft.org/v40/i01/>.

Hadley Wickham (2012). scales: Scale functions for graphics. R package version 0.2.3. <http://CRAN.R-project.org/package=scales>

Lecoutre, Eric (2003). The R2HTML Package. R News, Vol 3. N. 3, Vienna, Austria.

Louis Kates and Thomas Petzoldt (2012). proto: Prototype object-based programming. R package version 0.3-10. <http://CRAN.R-project.org/package=proto>

Therneau T (2014). `_A Package for Survival Analysis in S_`. R package version 2.37-7, URL: <http://CRAN.R-project.org/package=survival>.

Analysis dataset

	Event time	Censorship	Treatment
1	2	1	Low dose
2	4	0	Control
3	5	0	Control
4	5	0	Low dose
5	6	0	Top dose
6	7	1	Control
7	7	1	Low dose
8	8	1	Mid dose
9	8	0	Mid dose
10	8	1	Mid dose
11	8	0	Top dose
12	9	1	Low dose
13	12	1	Control
14	12	1	Mid dose
15	13	1	Control
16	13	0	Low dose
17	15	1	Low dose
18	15	1	Mid dose
19	16	1	Mid dose
20	16	0	Mid dose
21	17	1	Control
22	22	0	Low dose
23	22	1	Mid dose
24	23	1	Low dose
25	24	1	Mid dose
26	24	0	Mid dose
27	25	1	Low dose
28	25	0	Mid dose
29	26	1	Low dose
30	27	1	Control
31	28	1	Mid dose

32	30	1	Control
33	30	1	Low dose
34	30	1	Mid dose
35	30	1	Top dose
36	34	1	Control
37	38	1	Control
38	39	1	Control
39	40	1	Control
40	43	1	Control
41	46	0	Control
42	53	1	Control
43	54	0	Mid dose
44	58	1	Control
45	63	1	Top dose
46	66	1	Control
47	70	0	Control
48	78	1	Top dose
49	96	1	Control
50	108	0	Mid dose
51	113	0	Control
52	114	1	Mid dose
53	119	1	Mid dose
54	130	1	Low dose
55	132	1	Low dose
56	141	1	Mid dose
57	149	0	Control
58	152	1	Top dose
59	152	1	Top dose
60	154	1	Low dose
61	156	1	Low dose
62	159	0	Low dose
63	177	1	Mid dose
64	185	1	Mid dose

65	190	1	Low dose
66	196	1	Control
67	201	1	Control
68	245	1	Mid dose
69	292	1	Mid dose
70	318	1	Mid dose
71	333	1	Control
72	402	1	Mid dose
73	447	1	Mid dose
74	511	1	Low dose
75	536	1	Mid dose
76	562	1	Top dose