

STK4080/9080 SURVIVAL AND EVENT HISTORY ANALYSIS

Slides 10: Nonparametric tests

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3.3.1 in ABG: Two-sample tests

For these slides, see also Chapter 4 of ASAUR

Consider two counting processes $N_1(t)$ and $N_2(t)$ with intensity processes of the multiplicative form

$$\lambda_h(t) = Y_h(t)\alpha_h(t); \quad h = 1, 2$$

We want to test the null hypothesis

$$H_0 : \alpha_1(t) = \alpha_2(t) \text{ for } 0 \leq t \leq t_0$$

Usually we will choose $t_0 = \tau$, the upper time limit of study.

The common (but unknown) value of the $\alpha_h(t)$ under H_0 will be called $\alpha(t)$.

Comparison of Nelson-Aalen or Kaplan-Meier curves

- ▶ Let $\hat{A}_h(t)$, be the Nelson-Aalen estimators of $A_h(t) = \int_0^t \alpha_h(s) ds$
- ▶ or let $\hat{S}_h(t)$ be the Kaplan-Meier estimators of $S_h(t) = \exp\{-\int_0^t \alpha_h(s) ds\}$, $h = 1, 2$.

Then under the null hypothesis we would expect $\hat{A}_1(t) \approx \hat{A}_2(t)$ and $\hat{S}_1(t) \approx \hat{S}_2(t)$ (for all t) and may do a graphical check.

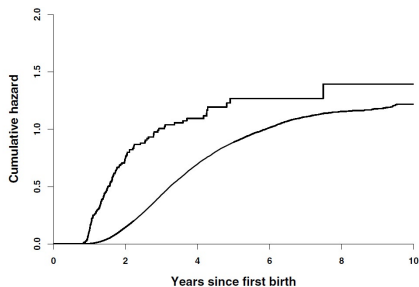


Fig. 3.1 Nelson-Aalen estimates for the time between first and second births. Lower curve: first child survived one year; upper curve: first child died within one year.

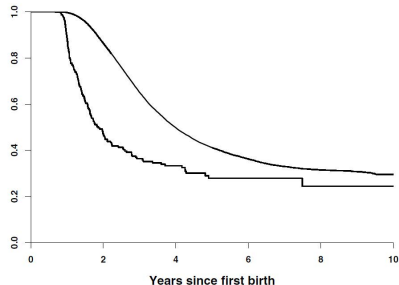


Fig. 3.11 Kaplan-Meier estimates for the time between first and second birth. Upper curve: first child survived one year; lower curve: first child died within one year.

A general two-sample test based on the $\hat{A}_h(t)$

Recall the Nelson-Aalen estimators

$$\hat{A}_h(t) = \int_0^t \frac{1}{Y_h(u)} dN_h(u) = \sum_{T_j \leq t} \frac{1}{Y_h(T_j)}$$

and consider the test statistic

$$Z_1(t_0) = \int_0^{t_0} L(t) \{d\hat{A}_1(t) - d\hat{A}_2(t)\}$$

Here $L(t)$ is a non-negative predictable weight process that is zero whenever at least one of the $Y_h(t)$ are zero.

The choice

$$L(t) = Y_1(t)Y_2(t)/Y_{\bullet}(t)$$

with $Y_{\bullet}(t) = Y_1(t) + Y_2(t)$ gives the **log-rank test**, to be considered later.

Two-sample tests

If the null hypothesis is true, we have $\alpha_1(t) = \alpha_2(t) = \alpha(t)$, so

$$dN_h(t) = Y_h(t)\alpha(t)dt + dM_h(t); \quad h = 1, 2 \quad (*)$$

$$\begin{aligned} \text{Then } Z_1(t_0) &= \int_0^{t_0} L(t)\{d\hat{A}_1(t) - d\hat{A}_2(t)\} \\ &= \int_0^{t_0} \frac{L(t)}{Y_1(t)} dN_1(t) - \int_0^{t_0} \frac{L(t)}{Y_2(t)} dN_2(t) \\ &= \int_0^{t_0} \frac{L(t)}{Y_1(t)} dM_1(t) - \int_0^{t_0} \frac{L(t)}{Y_2(t)} dM_2(t) \end{aligned}$$

(at the last = we use (*) and cancel the term with $\alpha(t)$).

Thus $Z_1(t_0)$ is a mean zero martingale (in t_0) when the null hypothesis is true

In particular $E\{Z_1(t_0)\} = 0$ under H_0 .

Two-sample tests (cont.)

$$\text{Recall: } Z_1(t_0) = \int_0^{t_0} \frac{L(t)}{Y_1(t)} dM_1(t) - \int_0^{t_0} \frac{L(t)}{Y_2(t)} dM_2(t)$$

so the predictable variation process under H_0 is

$$\begin{aligned}\langle Z_1 \rangle(t_0) &= \int_0^{t_0} \left(\frac{L(t)}{Y_1(t)} \right)^2 \lambda_1(t) dt + \int_0^{t_0} \left(\frac{L(t)}{Y_2(t)} \right)^2 \lambda_2(t) dt \\ &= \int_0^{t_0} \frac{L^2(t)}{Y_1(t)} \alpha(t) dt + \int_0^{t_0} \frac{L^2(t)}{Y_2(t)} \alpha(t) dt \\ &= \int_0^{t_0} \frac{L^2(t) Y_{\bullet}(t)}{Y_1(t) Y_2(t)} \alpha(t) dt \quad (\bullet \text{ means sum over 1 and 2})\end{aligned}$$

Under H_0 we may estimate $\alpha(t)dt$ by $dN_{\bullet}(t)/Y_{\bullet}(t)$ (Nelson-Aalen). Thus we can estimate $\langle Z_1 \rangle(t_0)$ under H_0 by:

$$V_{11}(t_0) = \int_0^{t_0} \frac{L^2(t)}{Y_1(t) Y_2(t)} dN_{\bullet}(t)$$

Note: $\langle M_1 + M_2 \rangle(t) = \langle M_1 \rangle(t) + \langle M_2 \rangle(t)$ when M_1, M_2 are orthogonal (see equations (2.28) and (2.44) in ABG)

Two-sample tests (cont.)

The standardized test statistic

$$U(t_0) = \frac{Z_1(t_0)}{\sqrt{V_{11}(t_0)}}$$

is approximately standard normal under H_0 (can be shown by martingale central limit theorem).

Alternatively we may use the test statistic

$$X^2(t_0) = \frac{Z_1(t_0)^2}{V_{11}(t_0)}$$

which is approximately chi-square distributed with 1 df under H_0

Weight functions $L(t)$

Table 3.2 Choice of weight process $L(t)$ for a number of two-sample tests

Test	Weight process ^a	Key references
Log-rank	$Y_1(t)Y_2(t)/Y_*(t)$	Mantel (1966), Peto and Peto (1972)
Gehan-Breslow	$Y_1(t)Y_2(t)$	Gehan (1965), Breslow (1970)
Efron ^b	$\widehat{S}_1(t-)\widehat{S}_2(t-)J_1(t)J_2(t)$	Efron (1967)
Tarone-Ware	$Y_1(t)Y_2(t)/\sqrt{Y_*(t)}$	Tarone and Ware (1977)
Peto-Prentice	$\widetilde{S}(t-)Y_1(t)Y_2(t)/(Y_*(t)+1)$	Peto and Peto (1972), Prentice (1978)
Harrington-Fleming	$\widehat{S}(t-)^p Y_1(t)Y_2(t)/Y_*(t)$	Harrington and Fleming (1982)

^a $\widehat{S}_1(t)$ and $\widehat{S}_2(t)$ are the Kaplan-Meier estimators computed separately for each of the two samples, $\widehat{S}(t)$ is the Kaplan-Meier estimator based on the combined sample, and $\widetilde{S}(t) = \prod_{s \leq t} (1 - \frac{\Delta N_*(s)}{Y_*(s)+1})$ is a slightly modified version of the Kaplan-Meier estimator based on the combined sample.

^b Modified as described by Andersen et al. (1993, page 352).

Towards the log-rank test

The test statistic $Z_1(t_0)$ and its variance estimator may be given an alternative formulation. This may be useful to obtain a better understanding of the test, and it opens for a generalization to more than two samples.

Now let $L(t)$ be of the form

$$L(t) = \frac{Y_1(t)Y_2(t)}{Y_{\bullet}(t)}K(t)$$

for a weight process $K(t)$ such that $K(t) = 0$ whenever $Y_{\bullet}(t) = 0$.

Then for the log-rank test we have $K(t) = I\{Y_{\bullet}(t) > 0\}$.

Putting this into the definition of $Z_1(t_0)$ we get after some algebra,

$$\begin{aligned}Z_1(t_0) &= \int_0^{t_0} K(t)dN_1(t) - \int_0^{t_0} K(t)\frac{Y_1(t)}{Y_{\bullet}(t)}dN_{\bullet}(t) \\V_{11}(t_0) &= \int_0^{t_0} K^2(t)\frac{Y_1(t)Y_2(t)}{Y_{\bullet}(t)^2}dN_{\bullet}(t)\end{aligned}$$

The log-rank test

For $K(t) = I\{Y_{\bullet}(t) > 0\}$ we get

$$\begin{aligned}Z_1(t_0) &\equiv \int_0^{t_0} K(t) dN_1(t) - \int_0^{t_0} K(t) \frac{Y_1(t)}{Y_{\bullet}(t)} dN_{\bullet}(t) \\&= N_1(t_0) - \int_0^{t_0} \frac{Y_1(t)}{Y_{\bullet}(t)} dN_{\bullet}(t) \\&= N_1(t_0) - E_1(t_0) \equiv O_1 - E_1 \\&= \text{observed} - \text{expected} \quad \text{in sample 1}\end{aligned}$$

Thus the standardized log-rank test statistic can be written

$$\frac{Z_1}{\sqrt{V_{11}}} = \frac{O_1 - E_1}{\sqrt{V_{11}}} \sim_{H_0} N(0, 1) \quad \text{or} \quad \left(\frac{Z_1}{\sqrt{V_{11}}} \right)^2 = \frac{(O_1 - E_1)^2}{V_{11}} \sim_{H_0} \chi_1^2$$

The log-rank test (cont.)

Note that if we define $Z_2(t_0)$ by changing the roles of sample 1 and sample 2 in $Z_1(t_0)$, we will have $Z_2(t_0) = -Z_1(t_0)$.

Hence, since V_{11} is symmetric in sample 1 and 2, we may well use the statistics

$$\frac{O_2 - E_2}{\sqrt{V_{11}}} \sim N(0, 1) \quad \text{and} \quad \frac{(O_2 - E_2)^2}{V_{11}} \sim \chi_1^2$$

Approximation of the log-rank test

Often good approximation

$$\frac{(O_1 - E_1)^2}{V_{11}} \gtrsim \frac{(O_1 - E_1)^2}{E_1} + \frac{(O_2 - E_2)^2}{E_2}$$

In general the left hand side is larger or equal to the right hand side and the approximation is close when

- ▶ Same censoring pattern in both groups
- ▶ Small (moderate) difference in mortality

To see this, note that when the above assumptions hold we have, for some q ,

$$\frac{Y_1(t)}{Y_{\bullet}(t)} \approx q \text{ and } \frac{Y_2(t)}{Y_{\bullet}(t)} \approx 1 - q$$

for all t .

Approximation of the log-rank test (cont.)

This gives

$$V_{11} = \int_0^{t_0} \frac{Y_1(t)Y_2(t)}{Y_{\bullet}(t)^2} dN_{\bullet}(t) \approx q(1-q)N_{\bullet}(t_0)$$

and

$$\frac{1}{V_{11}} \approx \frac{1}{q(1-q)N_{\bullet}(t_0)} = \frac{1}{qN_{\bullet}(t_0)} + \frac{1}{(1-q)N_{\bullet}(t_0)} \approx \frac{1}{E_1} + \frac{1}{E_2}$$

since $E_1 = \int_0^{t_0} \frac{Y_1(t)}{Y_{\bullet}(t)} dN_{\bullet}(t) \approx qN_{\bullet}(t_0)$ and similarly for E_2 . Thus

$$\begin{aligned} \frac{(O_1 - E_1)^2}{V_{11}} &\approx \frac{(O_1 - E_1)^2}{E_1} + \frac{(O_1 - E_1)^2}{E_2} \\ &= \frac{(O_1 - E_1)^2}{E_1} + \frac{(O_2 - E_2)^2}{E_2} \end{aligned}$$

since $O_1 - E_1 = E_2 - O_2$.

Hand-calculation of log-rank test

$$O_1 - E_1 = N_1(t_0) - \int_0^{t_0} \frac{Y_1(t)}{Y_{\bullet}(t)} dN_{\bullet}(t), \quad V_{11} = \int_0^{t_0} \frac{Y_1(t)Y_2(t)}{Y_{\bullet}(t)^2} dN_{\bullet}(t)$$

Go through all failure times T_1, \dots, T_r :

	Group 1	Group 2	Total at T_j
# at risk at T_j	Y_{1j}	Y_{2j}	Y_j
Observed # fail at T_j	O_{1j}	O_{2j}	O_j
Est prob of fail under H_0			$\frac{O_j}{Y_j}$
Estim expect # failures	$E_{1j} = Y_{1j} \cdot \frac{O_j}{Y_j}$	$E_{2j} = Y_{2j} \cdot \frac{O_j}{Y_j}$	
Estimated variance			$V_j = \frac{Y_{1j}Y_{2j}O_j}{Y_j^2}$

Then sum over all failure times T_1, \dots, T_r :

$$O_h = \sum_{j=1}^r O_{hj}, \quad E_h = \sum_{j=1}^r E_{hj} \quad \text{for } h = 1, 2, \quad \text{and } V_{11} = \sum_{j=1}^r V_j$$

Test statistics are then

$$\frac{(O_1 - E_1)^2}{V_{11}} \quad \text{or the conservative} \quad \frac{(O_1 - E_1)^2}{E_1} + \frac{(O_2 - E_2)^2}{E_2}$$

Example for hand-calculation from ASAUR Chapter 4.1

There are two groups, C=Control, T=Treatment, with data below:

Table 4.1 Survival data

Patient	Survtime	Censor	Group
1	6	1	C
2	7	0	C
3	10	1	T
4	15	1	C
5	19	0	T
6	25	1	T

The calculations below are the same as in the setup of the previous slide, but with other notation (groups are below numbered 0 and 1, for example)

t_i	n_i	d_i	n_{0i}	d_{0i}	n_{1i}	d_{1i}	e_{0i}	e_{1i}	$v_{0i} = v_{1i}$
6	6	1	3	1	3	0	0.500	0.500	0.2500
10	4	1	1	0	3	1	0.250	0.750	0.1875
15	3	1	1	1	2	0	0.333	0.667	0.2222
25	1	1	0	0	1	1	0.000	1.000	0.0000
				2		2	1.083	2.917	0.6597

Example for hand-calculation (cont.)

t_i	n_i	d_i	n_{0i}	d_{0i}	n_{1i}	d_{1i}	e_{0i}	e_{1i}	$v_{0i} = v_{1i}$
6	6	1	3	1	3	0	0.500	0.500	0.2500
10	4	1	1	0	3	1	0.250	0.750	0.1875
15	3	1	1	1	2	0	0.333	0.667	0.2222
25	1	1	0	0	1	1	0.000	1.000	0.0000
				2		2	1.083	2.917	0.6597

The logrank test statistic is from this:

$$\frac{(O_0 - E_0)^2}{V} = \frac{(2 - 1.083)^2}{0.6597} = 1.2747$$

while the conservative one is

$$\begin{aligned} \frac{(O_0 - E_0)^2}{E_0} + \frac{(O_1 - E_1)^2}{E_1} &= \frac{(2 - 1.083)^2}{1.083} + \frac{(2 - 2.917)^2}{2.917} \\ &= 0.7764 + 0.2883 = 1.0647 \end{aligned}$$

These numbers should be compared to quantiles of χ_1^2 , e.g., 5% corresponds to 3.84.

Example for hand-calculation using R

```
> tt <- c(6, 7, 10, 15, 19, 25)
> delta <- c(1, 0, 1, 1, 0, 1)
> trt <- c(0, 0, 1, 0, 1, 1)
> survdiff(Surv(tt, delta) ~ trt)
```

	N	Observed	Expected	(O-E) ² /E	(O-E) ² /V
trt=0	3	2	1.08	0.776	1.27
trt=1	3	2	2.92	0.288	1.27

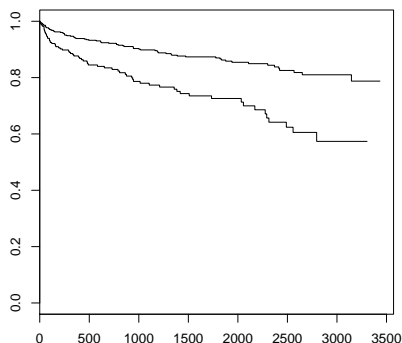
Chisq= 1.3 on 1 degrees of freedom, p= 0.259

Check with the hand-calculations on the previous slide!

Example Log-rank: Kidney transplantation

The data can be found in the R-library KMSurv

```
library(KMSurv); data(kidtran); attach(kidtran)
eldre <- (age>49)
# KM-plot:
fitK = survfit(Surv(time,delta)~eldre)
plot(fitK)
```



Example Log-rank: Kidney transplantation

```
eldre<-(age>49)
survdif(Surv(time,delta)~eldre)
```

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
eldre=FALSE	574	73	100.3	7.44	26.5
eldre=TRUE	289	67	39.7	18.81	26.5

Chisq= 26.5 on 1 degrees of freedom, p= 2.64e-07

Calculate also

$$\frac{(O_1 - E_1)^2}{E_1} + \frac{(O_2 - E_2)^2}{E_2} = 7.44 + 18.81 = 26.25 (< 26.5)$$

Harrington-Fleming weight: Kidney transplantation

```
> survdiff(Surv(time,delta)~eldre,rho=1)
```

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
eldre=FALSE	574	65.6	90.3	6.74	26
eldre=TRUE	289	60.9	36.2	16.80	26

Chisq= 26 on 1 degrees of freedom, p= 3.45e-07

```
> survdiff(Surv(time,delta)~eldre,rho=0.5)
```

	N	Observed	Expected	(O-E)^2/E	(O-E)^2/V
eldre=FALSE	574	69.2	95.1	7.08	26.3
eldre=TRUE	289	63.8	37.9	17.77	26.3

Chisq= 26.3 on 1 degrees of freedom, p= 2.98e-07

k-sample tests

Consider now k counting processes $N_1(t), N_2(t), \dots, N_k(t)$ with intensity processes of the multiplicative form

$$\lambda_h(t) = Y_h(t)\alpha_h(t); \quad h = 1, 2, \dots, k$$

We want to test the null hypothesis

$$H_0 : \alpha_1(t) = \dots = \alpha_k(t) \text{ for } 0 \leq t \leq t_0$$

We introduce (where δ_{hj} is a Kronecker delta)

$$Z_h(t_0) = \int_0^{t_0} K(t) dN_h(t) - \int_0^{t_0} K(t) \frac{Y_h(t)}{Y_{\bullet}(t)} dN_{\bullet}(t)$$
$$V_{hj}(t_0) = \int_0^{t_0} K^2(t) \frac{Y_h(t)}{Y_{\bullet}(t)} \left(\delta_{hj} - \frac{Y_j(t)}{Y_{\bullet}(t)} \right) dN_{\bullet}(t)$$

k-sample tests (cont.)

Note that $\sum_{h=1}^k Z_h(t_0) = 0$. (This was earlier seen for $k = 2$)

Therefore we only consider the first $k - 1$ of the $Z_h(t_0)$ when forming our test statistic.

We introduce the $k - 1$ dimensional vector

$$\mathbf{Z}(t_0) = (Z_1(t_0), \dots, Z_{k-1}(t_0))^T$$

and the $(k - 1) \times (k - 1)$ matrix

$$\mathbf{V}(t_0) = \begin{pmatrix} V_{11}(t_0) & V_{12}(t_0) & \cdots & V_{1,k-1}(t_0) \\ V_{21}(t_0) & V_{22}(t_0) & \cdots & V_{2,k-1}(t_0) \\ \cdots & \cdots & \cdots & \cdots \\ V_{k-1,1}(t_0) & V_{k-1,2}(t_0) & \cdots & V_{k-1,k-1}(t_0) \end{pmatrix}$$

k-sample tests (cont.)

Then the test statistic takes the form

$$X^2(t_0) = \mathbf{Z}(t_0)^T \mathbf{V}(t_0)^{-1} \mathbf{Z}(t_0)$$

The statistic is chi-square distributed with $k - 1$ d.f. when the null hypothesis is true.

For the log-rank test one may show that

$$\sum_{h=1}^k \frac{(N_h(t_0) - E_h(t_0))^2}{E_h(t_0)} \leq X^2(t_0) \quad (*)$$

where $E_h(t_0) = \int_0^{t_0} \{Y_h(t)/Y_{\bullet}(t)\} dN_{\bullet}(t)$

Thus the left-hand side of (*) provides a *conservative* version of the log-rank test (see also the case $k = 2$).

Example Log-rank: Kidney transplantation

Ex: Kidney transpl.

```
> agegr<-trunc(age/20)
```

```
> table(agegr)
```

```
 0   1   2   3
29 304 429 101
```

```
> survdiff(Surv(time,delta)~agegr)
```

Call:

```
survdiff(formula = Surv(time, death) ~ agegr)
```

	N	Observed	Expected	(O-E) ² /E	(O-E) ² /V
agegr=0	29	1	5.65	3.82	3.99
agegr=1	304	21	56.76	22.53	38.17
agegr=2	429	88	65.45	7.77	14.63
agegr=3	101	30	12.15	26.24	28.97

Chisq= 61.2 on 3 degrees of freedom, p= 3.26e-13

Stratified tests

Consider as an example the kidney transplant data:

Let $\alpha_{BM}(t)$ be the hazard for black men and $\alpha_{BF}(t)$, $\alpha_{WM}(t)$ and $\alpha_{WF}(t)$ the hazards for black females, white males and white females, respectively.

One may be interested in testing difference between races *irrespective* of differences between sexes, i.e.

$$H_0 : \alpha_{BM}(t) = \alpha_{WM}(t) \text{ and } \alpha_{BF}(t) = \alpha_{WF}(t)$$

We can immediately apply tests separately for men and women, but a combined (or stratified) test will instead be used.

Stratified tests (cont.)

We now consider the situation where we have k counting process in each of m strata:

$$N_{hs}(t) \text{ for } h = 1, \dots, k \text{ and } s = 1, \dots, m$$

with intensity processes of the multiplicative form

$$\lambda_{hs}(t) = Y_{hs}(t)\alpha_{hs}(t); \quad h = 1, \dots, k; \quad s = 1, \dots, m$$

We want to test the null hypothesis

$$H_0 : \alpha_{1s}(t) = \dots = \alpha_{ks}(t) \text{ for } 0 \leq t \leq t_0 \text{ for all } s = 1, \dots, m$$

Stratified tests (cont.)

For each stratum s we define similar quantities as above:

$$Z_{hs}(t_0) = \int_0^{t_0} K_s(t) dN_{hs}(t) - \int_0^{t_0} K_s(t) \frac{Y_{hs}(t)}{Y_{\bullet}(t)} dN_{\bullet s}(t)$$
$$V_{hjs}(t_0) = \int_0^{t_0} K_s^2(t) \frac{Y_{hs}(t)}{Y_{\bullet}(t)} \left(\delta_{hj} - \frac{Y_{js}(t)}{Y_{\bullet}(t)} \right) dN_{\bullet s}(t)$$

Further we define the $k - 1$ dimensional vectors

$$\mathbf{Z}_s(t_0) = (Z_{1s}(t_0), \dots, Z_{k-1,s}(t_0))^T$$

and the $(k - 1) \times (k - 1)$ dimensional matrices

$$\mathbf{V}_s(t_0) = \{V_{hjs}(t_0)\}_{h,j=1,\dots,k-1}$$

Stratified tests (cont.)

We now obtain the test statistic by aggregating information over the m strata:

$$X^2(t_0) = \left(\sum_{j=1}^m \mathbf{z}_s(t_0) \right)^T \left(\sum_{j=1}^m \mathbf{v}_s(t_0) \right)^{-1} \left(\sum_{j=1}^m \mathbf{z}_s(t_0) \right)$$

The statistic is chi-square distributed with the $k - 1$ d.f. when the null hypothesis is true.

Example: Kidney transplantation with strata

```
> survdiff(Surv(time,delta)~race,subset=(gender==1))
      N Observed Expected (O-E)^2/E (O-E)^2/V
race=1 432      73    71.9   0.0168   0.097
race=2  92     14    15.1   0.0801   0.097
```

Chisq= 0.1 on 1 degrees of freedom, p= 0.755

```
> survdiff(Surv(time,delta)~race,subset=(gender==2))
      N Observed Expected (O-E)^2/E (O-E)^2/V
race=1 280      39    44.79   0.748   4.85
race=2  59     14     8.21   4.076   4.85
```

Chisq= 4.8 on 1 degrees of freedom, p= 0.0277

```
> survdiff(Surv(time,delta)~race+strata(gender))
      N Observed Expected (O-E)^2/E (O-E)^2/V
race=1 712     112    116.7   0.188   1.13
race=2 151      28     23.3   0.942   1.13
```

Chisq= 1.1 on 1 degrees of freedom, p= 0.287

Other examples: Melanoma data, $k = 2$

```
# Read data:
path="http://www.uio.no/studier/emner/matnat/math/STK4080/
h14/melanoma.txt"
melanoma=read.table(path,header=T)
# Compute and plot Kaplan-Meier estimates for males and females:
fit.sex=survfit(Surv(lifetime,status==1)~sex,data=melanoma,
conf.type="plain")
plot(fit.sex, mark.time=F, xlab="Years after operation", lty=1:2,
xlim=c(0,10))
legend("bottomleft",c("females","males"),lty=1:2)
# Compute logrank test for the nullhypothesis that males and
# females have the same mortality due to malignant melanoma:
survdif(Surv(lifetime,status==1)~sex, data=melanoma)
```

Other examples: Melanoma data, $k = 3$

```
# Read data:
path="http://www.uio.no/studier/emner/matnat/math/STK4080/
h14/melanoma.txt"
melanoma=read.table(path,header=T)
# Compute and plot Kaplan-Meier estimates for the three thickness
# groups:
fit.sex=survfit(Surv(lifetime,status==1)~grthick,data=melanoma,
conf.type="plain")
plot(fit.sex, mark.time=F, xlab="Years after operation", lty=1:2,
xlim=c(0,10))
legend("topright",c("0-1 mm","2-5 mm","5+ mm"),lty=1:3)
# Compute logrank test for the nullhypothesis that the three
# thickness groups have the same mortality due to malignant
# melanoma:
survdif(Surv(lifetime,status==1)~grthick, data=melanoma)
```

Other examples: Melanoma data, stratified

```
# Read data:
path="http://www.uio.no/studier/emner/matnat/math/STK4080/
h14/melanoma.txt"
melanoma=read.table(path,header=T)
# Compute stratified logrank test for the null hypothesis that
# females and males have the same the mortality within each
# stratum defined by thickness group:
survdif(Surv(lifetime,status==1)~sex+strata(grthick),
data=melanoma)
```