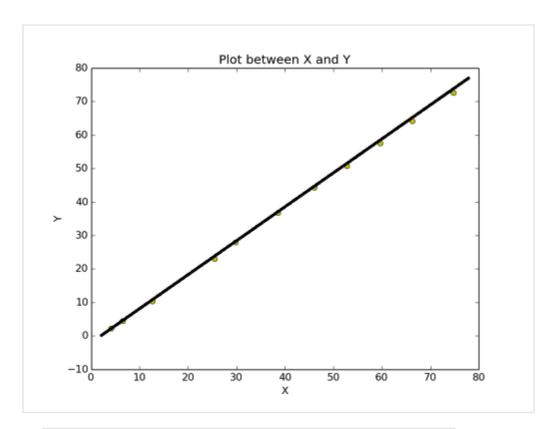
Introductory Statistics with R (Chap. 13~14)

Seungyeon Seo

Chap.13 Logistic Regression

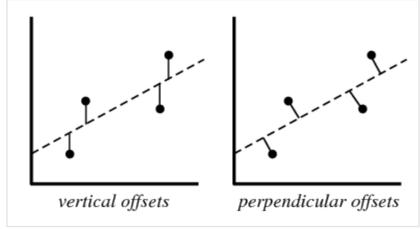
Linear Regression Analysis



모든 data들에 대해서 y = a + bx라는 식

Residual (error)
= real y data - expected y data
= real y data - (a + bx)
(because, expected y data = a + bx)

 $R^2 = (real y data - expected y data)^2$



Introduction

Data

Binary outcomes (only two possible values); Diseased / Nondiseased or 0 / 1

Purpose

Dose-response relationships

The effect of multiple variables simultaneously

Limitations

A limited range

Regression models – predicting off-scale values below zero or above

Solutions

The probabilities on a transformed scale



Logistic regression analysis

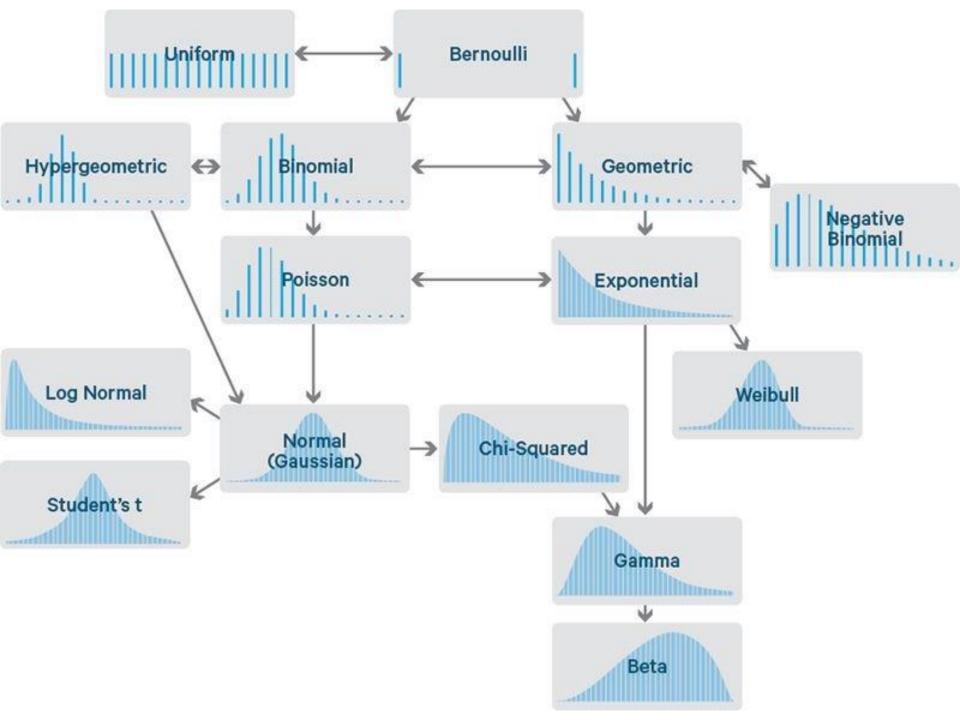
Alternatives

Due to mathematically convenient properties

Probit function

Log(-log p) – survival analysis models

- Logistic regression analysis
- 1. Response distribution (the binomial distribution)
- 2. Link function (logit $p = \log [p/(1-p)]$)
- Multiplicative Poission model
- 1. Link function (logit λ , λ is the mean of the Poisson-distributed observation)



Logistic Regression on Tabular Data

- 1. Response distribution (the binomial distribution)
- 2. Link function (logit $p = \log [p/(1-p)]$)

logit
$$p = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_k x_k$$

$$logit p = log [p/(1-p)] \rightarrow log \ odds$$

- 1. No error term as in linear models
- 2. No variance parameter as in the normal distribution

The method of maximum likelihood

The least-squares method

Conclusion; The likelihood function $L(\beta)$

2.The difference between the maximized value of -2 log *L* and the similar quantity under a "maximal model"

glm function

lm function (Linear normal Models)

- 1. The same model formulas
- 2. Extractor function (summary)
- 3. Family argument (family=binomial("logit"))

Logistic Regression on Tabular Data

data.frame function

```
> data.frame(smoking, obesity, snoring, n.tot, n.hyp)
  smoking obesity snoring n.tot n.hyp
       No
                No
                         No
                                60
                No
                                17
      Yes
                         No
3
       No
               Yes
                         No
                                        0
      Yes
               Yes
                         No
                              187
                                      35
                        Yes
       No
                No
                                85
                                      13
6
      Yes
                No
                        Yes
       No
               Yes
                        Yes
                                51
                                      15
                                23
                                        8
      Yes
               Yes
                        Yes
```

```
> expand.grid(smoking=no.yes, obesity=no.yes, snoring=no.yes)
  smoking obesity snoring
       No
               No
                       No
      Yes
               No
                       No
       No
              Yes
                       No
      Yes
              Yes
                       No
       No
               No
                      Yes
      Yes
            No
                      Yes
       No
              Yes
                      Yes
      Yes
              Yes
                      Yes
```

expand.grid function

```
> hyp.tbl <- cbind(n.hyp,n.tot-n.hyp)</pre>
> data.frame(smoking, obesity, snoring, n.tot, n.hyp)
                                                          > hyp.tbl
  smoking obesity snoring n.tot n.hyp
                                                               n.hyp
1
       No
                No
                         No
                                                           [1,]
                                                                       55
      Yes
                No
                         No
                                17
                                                           [2,]
                                                                       15
3
               Yes
       No
                         No
                                                           [3,]
              Yes
                         No
                                       0
4
      Yes
                                                           [4,]
5
                No
                              187
                                      35
       No
                        Yes
                                                           [5,]
                                                                 35
                                                                      152
6
      Yes
                No
                        Yes
                                85
                                      13
                                                           [6,]
                                                                  13
                                                                       72
               Yes
                                51
                                      15
       No
                        Yes
                                                           [7,]
                                                                  15
                                                                       36
                                23
      Yes
               Yes
                        Yes
                                        8
                                                           [8,]
                                                                       15
> glm(hyp.tbl~smoking+obesity+snoring,family=binomial("logit"))
                                                                              glm function
```

summary ()

```
> prop.hyp <- n.hyp/n.tot
> glm.hyp <- glm(prop.hyp~smoking+obesity+snoring,
+ binomial,weights=n.tot)

> glm.hyp <- glm(hyp.tbl~smoking+obesity+snoring,binomial)
> summary(glm.hyp)
```

> glm(hyp.tbl~smoking+obesity+snoring,binomial)

```
Call: glm(formula = hyp.tbl ~ smoking + obesity + snoring, ...

Coefficients:
(Intercept) smokingYes obesityYes snoringYes
-2.37766 -0.06777 0.69531 0.87194

Degrees of Freedom: 7 Total (i.e. Null); 4 Residual

Null Deviance: 14.13

Residual Deviance: 1.618 AIC: 34.54
```

```
Call:
glm(formula = hyp.tbl ~ smoking + obesity + snoring, family ...
Deviance Residuals:
-0.04344 0.54145 -0.25476 -0.80051 0.19759 -0.46602
-0.21262 0.56231
Coefficients:
          Estimate Std. Error z value Pr(>|z|)
smokingYes -0.06777 0.27812 -0.244 0.8075
obesityYes 0.69531 0.28509 2.439 0.0147 *
snoringYes 0.87194 0.39757 2.193 0.0283 *
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 '' 1
(Dispersion parameter for binomial family taken to be 1)
   Null deviance: 14.1259 on 7 degrees of freedom
Residual deviance: 1.6184 on 4 degrees of freedom
AIC: 34.537
Number of Fisher Scoring iterations: 4
```

Repeat of the model specification

```
Call:
glm(formula = hyp.tbl ~ smoking + obesity + snoring, family ...
Deviance Residuals:
        0.54145 -0.25476 -0.80051 0.19759 -0.46602
-0.04344
-0.21262
        0.56231
Coefficients:
          Estimate Std. Error z value Pr(>|z|)
smokingYes -0.06777 0.27812 -0.244 0.8075
obesityYes 0.69531 0.28509 2.439 0.0147 *
snoringYes 0.87194 0.39757 2.193 0.0283 *
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 '' 1
(Dispersion parameter for binomial family taken to be 1)
   Null deviance: 14.1259 on 7 degrees of freedom
Residual deviance: 1.6184 on 4 degrees of freedom
AIC: 34.537
Number of Fisher Scoring iterations: 4
```

- ❖ Contribution of each cell of the table to the deviance of the model (1부터 8까지 각각의 수치가 전체 deviance 에 기여하는 정도를 나타냄)
- Corresponding the sum of squares in linear normal models

```
Call:
glm(formula = hyp.tbl ~ smoking + obesity + snoring, family ...
Deviance Residuals:
        0.54145 -0.25476 -0.80051 0.19759 -0.46602
-0.04344
-0.21262
         0.56231
Coefficients:
           Estimate Std. Error z value Pr(>|z|)
(Intercept) -2.37766 0.38018 -6.254 4e-10 ***
smokingYes -0.06777 0.27812 -0.244 0.8075
obesityYes 0.69531 0.28509 2.439 0.0147 *
snoringYes 0.87194 0.39757 2.193 0.0283 *
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 '' 1
(Dispersion parameter for binomial family taken to be 1)
```

- Null deviance: 14.1259 on 7 degrees of freedom Residual deviance: 1.6184 on 4 degrees of freedom AIC: 34.537
- Number of Fisher Scoring iterations: 4

- Estimates of the regression coefficients
- Standard errors of same
- Tests for whether each regression coefficient can be assumed to be zero
- Corresponding part of lm output

```
Call:
glm(formula = hyp.tbl ~ smoking + obesity + snoring, family ...
Deviance Residuals:
-0.04344
        0.54145 -0.25476 -0.80051 0.19759 -0.46602
-0.21262
        0.56231
Coefficients:
          Estimate Std. Error z value Pr(>|z|)
smokingYes -0.06777 0.27812 -0.244 0.8075
obesityYes 0.69531 0.28509 2.439 0.0147 *
snoringYes 0.87194
                    0.39757 2.193 0.0283 *
Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 '' 1
(Dispersion parameter for binomial family taken to be 1)
   Null deviance: 14.1259 on 7 degrees of freedom
```

Number of Fisher Scoring iterations: 4

AIC: 34.537

Residual deviance: 1.6184 on 4 degrees of freedom

Residual deviance

- The residual sum of squares (ordinary regression analyses)
 - ▼
- The standard deviation
- The standard deviation of the observations is known.
 (in binomial models)



- AIC (Akaike information criterion)
- ❖ A measure of goodness of fit

Null deviance

- The deviance of a model that contains only the intercept
- The difference from the residual deviance
- Used for a joint test for whether any effects are present in the model

$$14.13 - 1.62 = 12.51$$

❖ *P*-value of approximately 0.6%

Call:

AIC: 34.537

```
glm(formula = hyp.tbl ~ smoking + obesity + snoring, family ...
Deviance Residuals:
-0.04344 0.54145 -0.25476 -0.80051 0.19759 -0.46602
-0.21262 0.56231
Coefficients:
          Estimate Std. Error z value Pr(>|z|)
smokingYes -0.06777 0.27812 -0.244 0.8075
obesityYes 0.69531 0.28509 2.439 0.0147 *
snoringYes 0.87194 0.39757 2.193 0.0283 *
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 '' 1
(Dispersion parameter for binomial family taken to be 1)
   Null deviance: 14.1259 on 7 degrees of freedom
```

Number of Fisher Scoring iterations: 4

Residual deviance: 1.6184 on 4 degrees of freedom

P-value

- ❖ No exact *p*-value
- Only an approximation
- The asymptotic distribution of the residual deviance



❖ The model is wrong (?) → nothing!

Number of Fisher Scoring iterations: 4

Call:

```
glm(formula = hyp.tbl ~ smoking + obesity + snoring, family ...
Deviance Residuals:
-0.04344 0.54145 -0.25476 -0.80051 0.19759 -0.46602
-0.21262 0.56231
Coefficients:
          Estimate Std. Error z value Pr(>|z|)
smokingYes -0.06777 0.27812 -0.244 0.8075
obesityYes 0.69531 0.28509 2.439 0.0147 *
snoringYes 0.87194 0.39757 2.193 0.0283 *
Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 '' 1
(Dispersion parameter for binomial family taken to be 1)
   Null deviance: 14.1259 on 7 degrees of freedom
Residual deviance: 1.6184 on 4 degrees of freedom
AIC: 34.537
```

- ❖ The actual fitting procedure
- Purely technical item
- **❖** No statistical information
- Too large -> too complex to fit (glm function -> halting the fitting procedure)

The Analysis of Deviance Table

- Corresponding ANOVA table for multiple regression analyses
- anova function

```
> glm.hyp <- glm(hyp.tbl~smoking+obesity+snoring,binomial)
> anova(glm.hyp, test="Chisq")
Analysis of Deviance Table

Model: binomial, link: logit
```

Response: hyp.tbl

Terms added sequentially (first to last)

	Df	Deviance	Resid.	Df	Resid. Dev	P(> Chi)
NULL				7	14.1259	
smoking	1	0.0022		6	14.1237	0.9627
obesity	1	6.8274		5	7.2963	0.0090
snoring	1	5.6779		4	1.6184	0.0172
			I			

> glm.hyp <- glm(hyp.tbl~snoring+obesity+smoking,binomial)</pre>

- Differences between models as variables
- $\ \ \, \star \ \ \, \chi \, \, 2$ -distributed with the stated degrees of freedom
- 'snoring' variable -> significant
- 'smoking' variable -> not significant
- ❖ Not be removed -> be rearranged

❖ 'smoking' comes last -> removal

The Analysis of Deviance Table

❖ A test of whether snoring may be removed from a model that also contains obesity

```
> glm.hyp <- glm(hyp.tbl~obesity+snoring,binomial)</pre>
> anova(glm.hyp, test="Chisq")
       Df Deviance Resid. Df Resid. Dev P(>|Chi|)
NULL
                              14.1259
obesity 1 6.8260 6 7.2999 0.0090
snoring 1 5.6218 5 1.6781 0.0177
❖ Alternative model
drop1 function
> drop1(glm.hyp, test="Chisq")
Single term deletions
Model:
hyp.tbl ~ obesity + snoring
       Df Deviance AIC LRT Pr(Chi)
<none> 1.678 32.597
obesity 1 7.337 36.256 5.659 0.01737 *
snoring 1 7.300 36.219 5.622 0.01774 *
```

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 '' 1

Connection to Test for Trend

Tests for comparing relative frequencies

```
prop.test()
prop.trend.test ()
> caesar.shoe
                               > summary(glm(t(caesar.shoe)~shoe.score,binomial))
         4 4.5 5 5.5
     < 4
                          6+
                              Coefficients:
Yes 5 7 6
                          10
                                          Estimate Std. Error z value Pr(>|z|)
No 17 28 36 41
                     46 140
                               (Intercept) -0.87058 0.40506 -2.149 0.03161 *
> shoe.score <- 1:6
                               shoe.score -0.25971 0.09361 -2.774 0.00553 **
> shoe.score
                               Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 '' 1
[1] 1 2 3 4 5 6
                               (Dispersion parameter for binomial family taken to be 1)
                                  Null deviance: 9.3442 on 5 degrees of freedom
                               Residual deviance: 1.7845 on 4 degrees of freedom
                               AIC: 27.616
                               . . .
                               > anova(glm(t(caesar.shoe)~shoe.score,binomial))
                                          Df Deviance Resid. Df Resid. Dev
                                                                   9.3442
                               NULL
                               shoe.score 1 7.5597
                                                                   1.7845
```

Connection to Test for Trend

```
> caesar.shoe.yes <- caesar.shoe["Yes",]</pre>
> caesar.shoe.no <- caesar.shoe["No",]</pre>
> caesar.shoe.total <- caesar.shoe.yes+caesar.shoe.no
> prop.trend.test(caesar.shoe.yes,caesar.shoe.total)
       Chi-squared Test for Trend in Proportions
X-squared = 8.0237, df = 1, p-value = 0.004617
                                                           Generally almost the same
> prop.test(caesar.shoe.yes,caesar.shoe.total)
         6-sample test for equality of proportions without
         continuity correction
X-squared = 9.2874, df = 5, p-value = 0.09814
Warning message:
In prop.test(caesar.shoe.yes, caesar.shoe.total) :
  Chi-squared approximation may be incorrect
```

Likelihood Profiling

Z test Based on Wald approximation

> confint(glm.hyp)

Wald approximation 만약 true values가 estimates와 같다면, parameter estimate의 approximate standard error를 계산하는 것

In large data sets -> no problem
In smaller data sets -> the difference between the Wald tests and the likelihood ratio test can be considerable.



Affecting the calculation of confidence intervals

```
Waiting for profiling to be done...

2.5 % 97.5 %

(Intercept) -3.2102369 -1.718143

obesityYes 0.1254382 1.246788

snoringYes 0.1410865 1.715860

> confint.default(glm.hyp)

2.5 % 97.5 %

(Intercept) -3.12852108 -1.655631

obesityYes 0.13670388 1.254134

snoringYes 0.08801498 1.642902
```

Presentation as Odds-ratio Estimates

Logistic regression using raw data

Prediction

```
predict ()
```

Working for generalized linear models

0.30339158 0.30339158

Chap.14 Survival Analysis

Connection to Test for Trend

The analysis of lifetimes

- ❖ An important topic within biology and medicine
- Often highly nonnormally distributed
- ❖ Not using the standard linear models
- Often censored (the period of observation was cut off before the event of interest occurred.)

Essential concepts					
X	true lifetime				
Т	censoring time	random variable fixed time depending on context noninformative for the method			
The observations -> the minimum of X and T					

S (t)	survival function	probability of being alive at a given time 1 – cumulative distribution function for X (F (t))
h (t)	hazard function or force of mortality	infinitesimal risk of dying within a short interval of time t
f(t)	density of the lifetime distribution	
t	time that the subject is alive	

$$h(t) = f(t) / S(t)$$

more fundamental quantity than the mean or median of survival distribution a basis for modelling

Survival Objects

```
melanom <- read.table("/home/syseo/ISwR/data/melanom.txt", header =TRUE, sep="
  stringsAsFactors=FALSE)
  head (melanom, 30)
    no status days ulc thick sex
   789
                10
                         676
    13
            3
                30
                          65
                35
    97
                         134
    16
                99
                         290
              185
                        1208
   21
               204
   469
                         484
   685
            1 210
                         516
              232
                        1288
   932
            3 232
                         322
10 944
            1 279
                         741
11 558
            1 295
                         419
12 612
            3 355
                          16
    2
               386
                         387
                               1
              426
14 233
                         484
15 418
                         242
                               1
              469
            3 493
                        1256
16 765
17 777
            1 529
                         580
                               2
              621
                         706
   61
   67
               629
                         548
20 819
               659
                         773
   10
            1 667
                        1385
21
   15
            1 718
                         234
   47
            1 752
23
                         419
    9
            1 779
                         404
25 907
              793
                         484
                               2
            1 817
26 758
                          32
    8
              826
                         854
28 400
              833
                         258
29 232
               858
                         356
30 18
               869
                         354
```

The explanation of variables

'status'
Indicator of the patient's status by the end
of the study

1 -> "dead from malignant melanoma"

2 -> "alive on January 1, 1978"

3 -> "dead from other causes"

'days' Observation time in days

'ulc' ulcerated tumor

1 -> present

2 -> absent

2 -> men

'thick' Thickness in 1/100 mm

'sex' Gender of the patient 1 -> women

Survival Objects

```
library (survival)
 attach(melanom)
The following objects are masked from melanom (position 3):
   days, no, sex, status, thick, ulc
 names(melanom)
[1] "no"
            "status" "days"
                             "ulc"
                                      "thick"
                                              "sex"
 Surv(days, status==1)
 [1]
             30+
                  35+
                        99+
                                                                     355+
       10+
                             185
                                   204
                                         210
                                              232
                                                    232+
                                                          279
                                                                295
[13]
      386
            426
                  469
                       493+
                             529
                                   621
                                        629
                                              659
                                                    667
                                                          718
                                                                752
                                                                     779
[25]
                  826+
                       833
                             858
                                   869
                                        872
                                              967
                                                    977
                                                          982
      793
            817
                                                               1041
                                                                    1055
                      1228
                           1252 1271
                                             1427+ 1435
[37] 1062
           1075
                1156
                                       1312
                                                         1499+ 1506
                                                                    1508+
[49] 1510+ 1512+ 1516 1525+ 1542+ 1548
                                       1557+ 1560 1563+ 1584
                                                               1605+ 1621
[61] 1627+ 1634+ 1641+ 1641+ 1648+ 1652+ 1654+ 1654+ 1667 1678+ 1685+ 1690
[73] 1710+ 1710+ 1726 1745+ 1762+ 1779+ 1787+ 1787+ 1793+ 1804+ 1812+ 1836+
[85] 1839+ 1839+ 1854+ 1856+ 1860+ 1864+ 1899+ 1914+ 1919+ 1920+ 1927+ 1933
[97] 1942+ 1955+ 1956+ 1958+ 1963+ 1970+ 2005+ 2007+ 2011+ 2024+ 2028+ 2038+
[109] 2056+ 2059+ 2061 2062
                            2075+ 2085+ 2102+ 2103
                                                  2104+ 2108
[121] 2156+ 2165+ 2209+ 2227+ 2227+ 2256   2264+ 2339+ 2361+ 2387+ 2388
[133] 2426+ 2426+ 2431+ 2460+ 2467  2492+ 2493+ 2521+ 2542+ 2559+ 2565
[157] 3101+ 3144+ 3152+ 3154+ 3180+ 3182+ 3185+ 3199+ 3228+ 3229+ 3278+ 3297+
```

Surv objects

```
Print method that displays the objects in the format above, with a '+' marking censored observations status ==1 -> logical vector, (TRUE = died of malignant melanoma)
```

10+ -> not die from melanoma within 10 days died from other causes

185 -> died from the disease

Kaplan-Meier Estimates

Computation of an estimated survival function in the presence of right-censoring

Product-limit estimator Multiplying together conditional survival curves for intervals in which there are either no censored observations or no deaths

```
Step function Reducing the estimated survival by a factor (1-1/R_t) T: Death time R_t: Still alive and uncensored at that time survfit () Only single argument, Surv object
```

```
> survfit(Surv(days, status==1))
Call: survfit(formula = Surv(days, status == 1))

    n events median 0.95LCL 0.95UCL
205 57 Inf Inf Inf
```

Couple of summary statistics Estimate of the median survival

Not informative Not even interesting <- infinite

Kaplan-Meier Estimates

To see the actual Kaplan–Meier estimate

Using summary on the survfit object

surv.all -> the raw survival function for all patients without regard of patient characteristic

> surv.all <- survfit(Surv(days, status==1))</pre>

```
> summary(surv.all)
Call: survfit(formula = Surv(days, status == 1))
 time n.risk n.event survival std.err lower 95% CI upper 95% CI
  185
         201
                         0.995 0.00496
                                               0.985
                                                             1.000
  204
         200
                         0.990 0.00700
                                               0.976
                                                             1.000
         199
                        0.985 0.00855
  210
                                               0.968
                                                             1.000
         198
                        0.980 0.00985
                                               0.961
  232
                                                             1.000
  279
         196
                        0.975 0.01100
                                               0.954
                                                             0.997
  295
         195
                         0.970 0.01202
                                               0.947
                                                             0.994
                    1
 2565
          63
                         0.689 0.03729
                                               0.620
                                                             0.766
 2782
          57
                        0.677 0.03854
                                               0.605
                                                             0.757
 3042
          52
                         0.664 0.03994
                                               0.590
                                                             0.747
          35
                         0.645 0.04307
                                               0.566
 3338
                    1
                                                             0.735
```

Values of the survival function at the event times

Step function

- 1. Jump points are given in time
- 2. Values right after a jump are given in survival

Kaplan-Meier Estimates_Practice

> plot(surv.all)

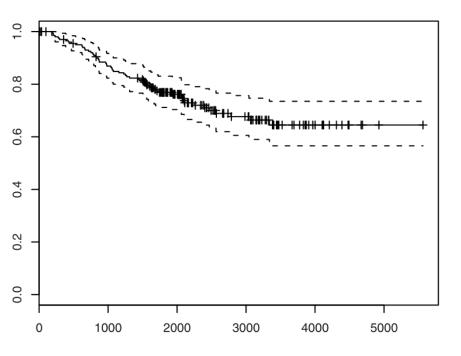


Figure 14.1. Kaplan–Meier plot for melanoma data (all observations).

Markings on the curve -> censoring times Bands -> approximate confidence intervals

Symmetric interval on the log scale

- > surv.bysex <- survfit(Surv(days, status==1)~sex)
- > plot(surv.bysex)

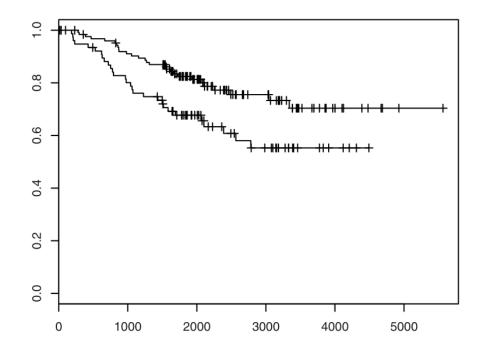


Figure 14.2. Kaplan-Meier plots for melanoma data, grouped by gender.

Splitting by gender

No confidence intervals on the curves

The Log-rank Test

To test whether two or more survival curves are identical Hypothesis test to compare the survival distributions of two samples

Nonparametric test Appropriate to use when the data are right skewed and censored (non-informative)

Establishing the efficacy of a new treatment in comparison with a control treatment

Computing the observed and expected number of events in one of the groups at each observed event time Adding these to obtain an overall summary across all-time points

Comparing estimates of the hazard functions of the two groups at each observed event time

The same test as the score test from the Cox proportional hazard model

survdiff function

The Cox Proportional Hazards Model

Survival models

Analysis of survival data by regression models

Fitted via the maximization of Cox's likelihood

Hazard function How the risk of event per time unit changes over time at baseline levels of covariates

Proportional hazards condition Covariates -> multiplicatively related to the hazard Not restricted to binary predictors

The effect parameters

How the hazard varies in response to explanatory
covariates

Cox partial likelihood
Obtained by using Breslow's estimate of the baseline hazard function
Plugging it into the full likelihood
Observing that the result is a product of two factors.

h(t) =
$$\frac{\text{number of individuals experiencing}}{\text{number of individuals surviving at time } t) \times x \text{ (interval width)}}$$

We therefore consider the following generalisation:

$$h(t, \mathbf{x}) = h_0(t, \boldsymbol{\alpha}) \exp(\boldsymbol{\beta}^T \mathbf{x}),$$

where α are some parameters influencing the baseline hazard function.

Note that we have decomposed the hazard into a product of two items:

- h₀(t, α), a term that depends on time but not the covariates; and
- exp(β^Tx), a term that depends on the covariates but not time.

Thank you for your attention