

# Poisson and Binary Regression

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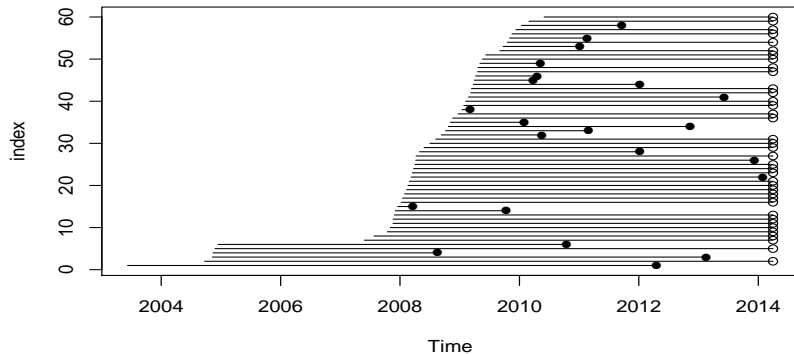
Statistical Practice in Epidemiology (2023, Tartu)

# Points to be covered

- ▶ Incidence rates, rate ratios and rate differences from *follow-up studies* can be computed by fitting *Poisson regression models*.
- ▶ Odds ratios can be computed from binary data by fitting *Logistic regression models*.
- ▶ Both models are special instances of *Generalized linear models*.
- ▶ There are various ways to do these tasks in R.

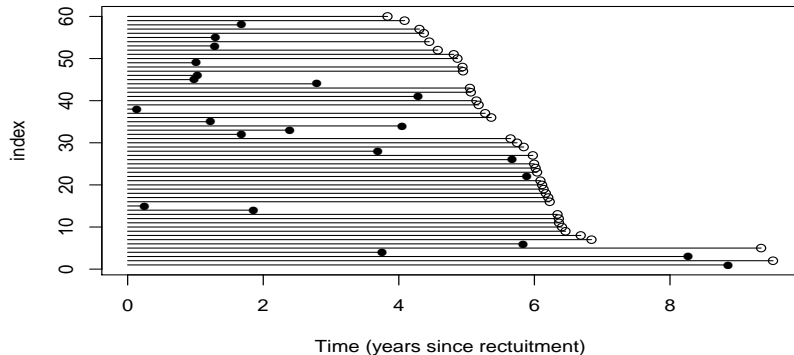
# The Estonian Biobank cohort: survival among the elderly

Follow-up of 60 random individuals aged 75-103 at recruitment, until death (●) or censoring (o) in April 2014 (linkage with the Estonian Causes of Death Registry). (time-scale: calendar time).



# The Estonian Biobank cohort: survival among the elderly

Follow-up time for 60 random individuals aged 75-103 at recruitment (time-scale: time in study).



# Events, dates and risk time

- ▶ Mortality as the outcome:
  - d: indicator for **status** at exit:
    - 1: death observed
    - 0: censored alive

- ▶ Dates:

doe = date of **E**ntry to follow-up,  
dox = date of e**X**it, end of follow-up.

- ▶ Follow-up time (years) computed as:

$$y = (\text{dox} - \text{doe}) / 365.25$$

# Crude overall rate computed by hand and model

Total no. cases, person-years & rate (/1000 y):

```
> D <- sum( d ); Y <- sum(y) ; R <- D/(Y/1000)
> round( c(D=D, Y=Y, R=R), 2)
      D      Y      R
884.00 11678.24  75.70
```

R-implementation of the rate estimation with Poisson regression:

A model with offset term

```
> m1 <- glm( D ~ 1, family=poisson,
             offset=log(Y))
```

```
> coef(m1)
( Intercept )
-2.581
```

A model with poisreg—family (Epi package)

```
> glm(cbind(D, Y) ~1, family=poisreg)
```

```
Coefficients :
( Intercept )
-2.581
```

From the coefficient we get estimate of the rate  $\exp(-2.581) * 1000 = 75.70$

## Constant hazard — Poisson model

Let  $Y \sim \exp(\lambda)$ , then  $f(y; \lambda) = \lambda e^{-\lambda y} I(y > 0)$

Constant rate model:  $\lambda(y) = \frac{f(y; \lambda)}{S(y; \lambda)} = \lambda$  and observed data  $\{(y_i, \delta_i); i = 1, \dots, n\}$ .

The likelihood  $L(\lambda) = \prod_{i=1}^n \lambda^{\delta_i} e^{-\lambda y_i}$  and

$$\log(L) = \sum_{i=1}^n [\delta_i \log(\lambda) - \lambda y_i]$$

Solving the *score equations*:

$$\frac{\partial \log L(\lambda)}{\partial \lambda} = \sum \left[ \frac{\delta_i}{\lambda} - y_i \right] = \frac{D}{\lambda} - Y = 0 \text{ and } D - \lambda Y = 0$$

→ **maximum likelihood estimator** (MLE) of  $\lambda$ :

$$\hat{\lambda} = \frac{D}{Y} = \frac{\text{number of cases}}{\text{total person-time}} = \text{empirical rate!}$$

## offset term — Poisson model

- ▶ Previous model without offset: Intercept  $6.784 = \log(884)$
- ▶ We should use an offset if we suspect that the underlying **population sizes (person-years) differ** for each of the observed counts – For example varying person-years by sex, age, treatment group, ...
- ▶ We need a term in the model that "scales" the likelihood, but does not depend on model parameters ( include a **term with reg. coef. fixed to 1**) – offset term is  $\log(y)$
- ▶ This is all taken care of by family=poisreg – recommend to use

$$\log\left(\frac{\mu}{y}\right) = \beta_0 + \beta_1 x_1$$
$$\log(\mu) = 1 \times \log(y) + \beta_0 + \beta_1 x_1$$



# Comparing rates: The Thorotrast Study

- ▶ Cohort of seriously ill patients in Denmark on whom angiography of brain was performed.
- ▶ Exposure: contrast medium used in angiography,
  1. `thor` = thorotrast (with  $^{232}\text{Th}$ ), used 1935-50
  2. `ctrl` = other medium (?), used 1946-63
- ▶ Outcome of interest: death

`doe` = date of **E**ntry to follow-up,

`dox` = date of **eX**it, end of follow-up.

- ▶ `data(thoro)` in the `Epi` package.

# Tabulating rates: thorotrast vs. control

Tabulating cases, person-years & rates by group

```
> stat.table( contrast ,  
+             list ( N = count(),  
+                   D = sum(d),  
+                   Y = sum(y),  
+                   rate = ratio(d,y,1000) ) )
```

contrast	N	D	Y	rate
ctrl	1236	797.00	30517.56	26.12
thor	807	748.00	19243.85	38.87

# Rate ratio estimation with Poisson regression

- ▶ Include contrast as the explanatory variable (factor).
- ▶ Insert person years in units that you want rates in

```
> m2 <- glm( cbind(d,y/1000) ~ contrast,family = poisreg(link="log") )  
> round( summary(m2)$coef, 4)[, 1:2]
```

	Estimate	Std. Error
( Intercept )	3.2626	0.0354
contrast thor	0.3977	0.0509

- ▶ Rate ratio and CI?

Call function `ci.exp()` in `Epi`

```
> round( ci.exp( m2 ), 3 )  
              exp(Est.)  2.5% 97.5%  
(Intercept)    26.116 24.364 27.994  
contrast thor     1.488  1.347  1.644
```

# Rates in groups with Poisson regression

- ▶ Include contrast as the explanatory variable (factor).
- ▶ Remove the intercept (-1)
- ▶ Insert person-years in units that you want rates in

```
> m3 <- glm( cbind(d,y/1000) ~ factor(contrast)-1,family = poisreg)
> round( summary(m3)$coef, 4)[, 1:2]
```

		Estimate	Std. Error
contrast	ctrl	3.2626	0.0354
contrast	thor	3.6602	0.0366

```
> round( ci.exp( m3 ), 3 )
```

		exp(Est.)	2.5%	97.5%
contrast	ctrl	26.116	24.364	27.994
contrast	thor	38.870	36.181	41.757

# Rate difference estimation with Poisson regression

- The approach with  $d/y$  enables additive rate models too:

```
> contrast<-c(0,1)
> m5 <-glm(cbind(d,y/1000) ~contrast,
            family=poisreg(link="identity") )
> round( ci.exp(m5,Exp=F), 3 )
```

	Estimate	2.5%	97.5%
(Intercept)	26.116	24.303	27.929
contrast thor	12.753	9.430	16.077

## Binary data: Treatment success Y/N

85 diabetes-patients with foot-wounds:

- ▶ Dalterapin (Dal)
- ▶ Placebo (Pl)

Treatment/Placebo given to diabetes patients, the design is prospective and outcome is measured better(Y)/worse(N). Is the probability of outcome more than 15% – yes, then use the risk difference or risk ratio (RR)

	Treatment group	
	Dalterapin	Placebo
Better	29	20
Worse	14	22
Total	43	42

$$\hat{p}_{\text{Dal}} = \frac{29}{43} = 67\% \quad \hat{p}_{\text{Pl}} = \frac{20}{42} = 47\%$$

# Binary data: Crosstabulation analysis of 2x2 table

```
> library(Epi)
> dlt <- rbind( c(29,14), c(20,22) )
> colnames( dlt ) <- c("Better","Worse")
> rownames( dlt ) <- c("Dal","Pl")
> kable(twoby2( dlt ), "latex")
```

2 by 2 table analysis:

	Better	Worse	P(Better)	95% conf. interval
Dal	29	14	0.6744	0.5226 0.7967
Pl	20	22	0.4762	0.3316 0.6249

95% conf. interval

Relative Risk: 1.4163 0.9694 2.0692

Sample Odds Ratio: 2.2786 0.9456 5.4907

Conditional MLE Odds Ratio: 2.2560 0.8675 6.0405

Probability difference: 0.1982 -0.0110 0.3850

Exact P-value: 0.0808

Asymptotic P-value: 0.0665

# Binary regression – estimation of odds ratio

For grouped binary data, the response is a two-column matrix with columns (successes, failures).

```
> library(Epi)
> library(xtable)
> dlt <- data.frame(rbind( c(29,14),c(20,22) ))
> colnames( dlt ) <- c("Better","Worse")
> dlt$trt <- c(1,0)
> b2<-glm(cbind(Better,Worse)~trt,
+         family=binomial(link="logit"),
+         data=dlt)
> xtable(round( ci.exp( b2 ), digits=6 ))
```

	exp(Est.)	2.5%	97.5%
(Intercept)	0.91	0.50	1.67
trt	2.28	0.95	5.49

- ▶ The default parameters in logistic regression are **odds** (the intercept:  $20/22 = 0.9090$ ) and the **odds-ratio** ( $((29/14)/(20/22) = 2.28)$ ).
- ▶ This is **NOT** what you want, because odds ratio is biased estimate of the risk ratio. (recall if  $p > 10\%$   $\frac{p}{1-p} \not\approx p$ )



## Binary regression - Estimation of risk ratio (Relative risk)

```
> library(Epi)
> library(xtable)
> dlt <- data.frame(rbind( c(29,14),c(20,22) ))
> colnames( dlt ) <- c("Better","Worse")
> dlt$trt <- c(1,0)
> b2<-glm(cbind(Better,Worse)~trt,
+         family=binomial(link="log"),
+         data=dlt)
> xtable(round( ci.exp( b2 ), digits=6 ))
```

	exp(Est.)	2.5%	97.5%
(Intercept)	0.48	0.35	0.65
trt	1.42	0.97	2.07

Diabetics with Dalterapin treatment are 1.4 times likely to get better than those treated with placebo

## Binary regression - Estimation of risk difference

```
> library(Epi)
> library(xtable)
> dlt <- data.frame(rbind( c(29,14),c(20,22) ))
> colnames( dlt ) <- c("Better","Worse")
> dlt$trt <- c(1,0)
> b2<-glm(cbind(Better,Worse)~trt,
+         family=binomial(link="identity"),
+         data=dlt)
> xtable(round( ci.exp( b2,Exp=F ), digits=6 ))
```

	Estimate	2.5%	97.5%
(Intercept)	0.48	0.33	0.63
trt	0.20	-0.01	0.40

Twenty percent more of the Diabetics with Dalterapin treatment are getting better compared to Diabetics treated with placebo

## Conclusion: What did we learn?

- ▶ Rates, their ratio and difference can be analysed by Poisson regression
- ▶ In Poisson models the response can be either:
  - ▶ case indicator  $d$  with `offset = log(y)`, or
  - ▶ case and person-years `cbind(d,y)` with `poisreg-family` (Epi-package)
- ▶ Both may be fitted on either grouped data, or individual records.
- ▶ Binary outcome can be modeled with binary regression.