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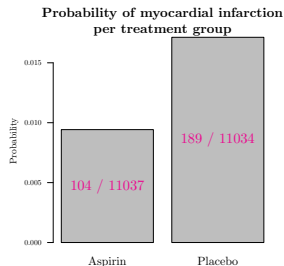
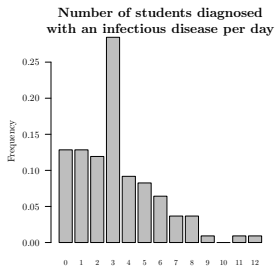
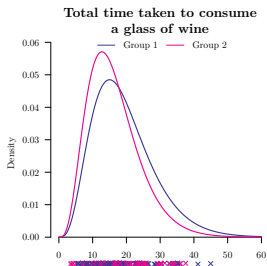
Laboratory of  
Molecular Biology

## Generalised Linear Models (GLM)

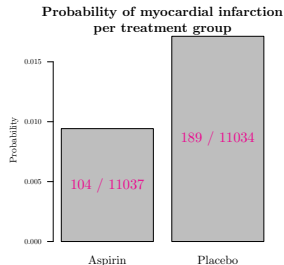
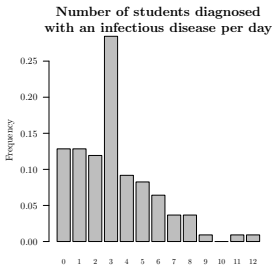
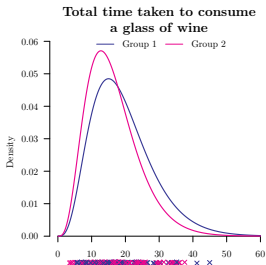
Cancer Research UK – 14<sup>th</sup> of May 2021

D.-L. Couturier / R. Nicholls / M. Fernandes

# Examples of data with non-normal conditional distributions



# Examples of data with non-normal conditional distributions



Linear model not suitable:

► Assumed model:

$$Y_i = \mathbf{x}_i^T \boldsymbol{\beta} + \epsilon_i \text{ where } \epsilon_i \sim N(0, \sigma^2),$$

$$Y_i | (\mathbf{x}_i, \boldsymbol{\beta}) \sim N(\mu_i, \sigma^2).$$

- ▷ theoretical range of  $\epsilon_i = [-\infty, +\infty]$ ,
- ▷  $\mathbf{x}_i^T \boldsymbol{\beta}$  not bounded to  $[0, \infty]$  or  $[0, 1]$ ,
- ▷  $\text{Var}[Y_i]$  independent of  $E[Y_i]$ .

► Solution:

$$Y_i | (\mathbf{x}_i, \boldsymbol{\beta}, \phi) \sim \text{distribution}(\text{function}(\mathbf{x}_i^T \boldsymbol{\beta}), \phi),$$

where *distribution* belongs to the exponential family and *function* is monotonically increasing.

# GLM: conditional distributions

$$Y_i | (\mathbf{x}_i, \boldsymbol{\beta}, \phi) \sim \text{distribution}(\text{function}(\mathbf{x}_i^T \boldsymbol{\beta}), \phi),$$

- Some possible conditional *distributions* :  
statistical probability mass functions & density functions

- Within the exponential family ['classical' GLM framework]

normal  
exponential  
gamma

chi-squared  
beta  
Dirichlet

Bernoulli  
Poisson  
Wishart

Inverse Wishart  
...

- Outside the exponential family ['extended' GLM framework]

Box-Cox power  
exponential  
exponential Gaussian  
generalized beta  
generalized gamma  
generalized inverse

Gaussian  
inverse Gaussian  
logistic  
power exponential  
reverse Gumbel  
skew power exponential

Weibull  
Pareto type I, II, III  
Poisson inverse Gaussian  
...

# GLM: link functions

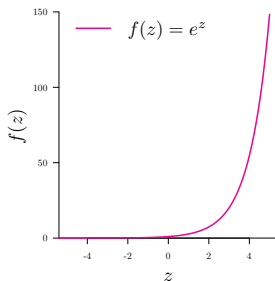
$$Y_i | (\mathbf{x}_i, \boldsymbol{\beta}, \phi) \sim \text{distribution}(\text{function}(\mathbf{x}_i^T \boldsymbol{\beta}), \phi),$$

► Most used link *functions* :

connection between  $Y_i$  and  $\mathbf{x}_i^T \boldsymbol{\beta}$

- to restrict  $f(\mathbf{x}_i^T \boldsymbol{\beta})$  to belong to  $[0, \infty[$ :

▷ log link:  $f(z) = e^z$



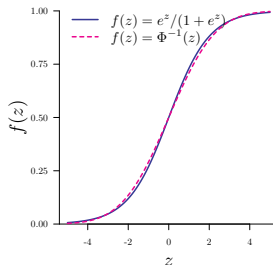
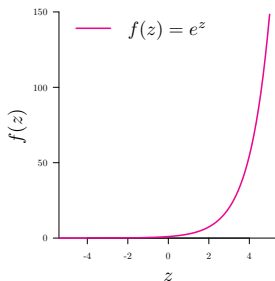
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  - ▷ log link:  $f(z) = e^z$
- to restrict  $f(\mathbf{x}_i^T \boldsymbol{\beta})$  to belong to  $[0, 1]$ :
  - ▷ logit link:  $f(z) = e^z / (1 + e^z) = 1 / (1 + e^{-z})$  where  $z$  is positive
  - ▷ probit link:  $f(z) = \Phi(z)$ , where  $\Phi$  denotes the  $N(0, 1)$ .



# Distribution for dichotomous variates: Bernoulli

## Example:

in Jones (*Unpublished BSc dissertation, University of Southampton, 1975*), the main outcome is the presence/absence of bronchitis:

Sample of 212 men in Cardiff:  $i = 1$     $i = 2$     $i = 3$     $\dots$     $i = 212$

	<del>B</del>	<del>B</del>	B	$\dots$	<del>B</del>
$y_i$	0	0	1	$\dots$	0

If

- ▶  $n$  independent experiments,
- ▶ outcome of each experiment is dichotomous (success/failure),
- ▶ the probability of success  $\pi$  is the same for all experiments,

then, each dichotomous experiment,  $Y_i$ , follows a Bernoulli distribution with parameter  $\pi$ :

$$Y_i \sim \text{Bernoulli}(\pi)$$

$$P(Y_i = 1) = \pi$$

$$P(Y_i = 0) = 1 - \pi$$

# Logistic regression: GLM for dichotomous variates

## Example:

in Jones (*Unpublished BSc dissertation, University of Southampton, 1975*), the main outcome is the presence/absence of bronchitis as a function of the daily number of smoked cigarettes ( $X_1$ ) and level of pollution ( $X_2$ ):

Sample of 212 men in Cardiff:  $i = 1$     $i = 2$     $i = 3$     $\dots$     $i = 212$

	$y_i$	$x_{1i}$	$x_{2i}$
	$\beta$	$\beta$	B
	0	0	1
	...	...	...
	0	0.9	55.4
	5.15	0	2.5
	67.1	66.9	66.7

If

- ▶  $n$  independent experiments,
- ▶ outcome of each experiment is dichotomous (success/failure),
- ▶ the probability of success  $\pi$  is the same for all experiments given the covariates,

then, each dichotomous experiment,  $Y_i$ , follows a Bernoulli distribution with parameter  $\pi_i$ :

$$Y_i \sim \text{Bernoulli}(\pi_i) \text{ where } \pi_i = \frac{e^{\mathbf{x}_i^T \boldsymbol{\beta}}}{1 + e^{\mathbf{x}_i^T \boldsymbol{\beta}}}$$

$$P(Y_i = 1) = \pi_i$$

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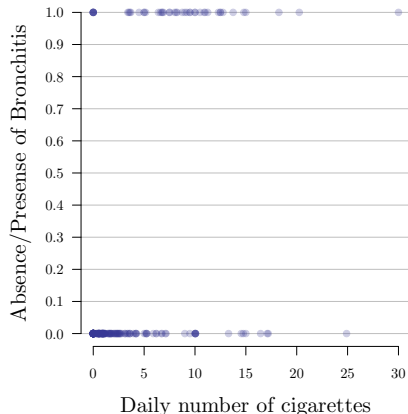


# Logistic regression: predictions and interpretation of $\beta$

## Example:

Model the probability of presence of bronchitis as a function of the daily number of smoked cigarettes ( $X_1$ ):

$$P(Y_i = 1) = \pi_i = \frac{e^{\beta_0 + \beta_1 x_{i1}}}{1 + e^{\beta_0 + \beta_1 x_{i1}}}$$

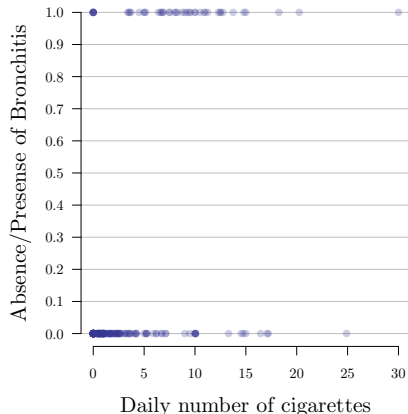


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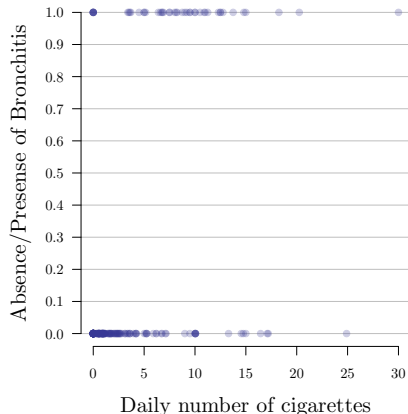
	Estimate	Std. Error	z value	Pr(> z )
(Intercept)	-2.2839832	0.27305505	-8.364552	6.034375e-17
cigs	0.2093618	0.03760466	5.567442	2.585062e-08

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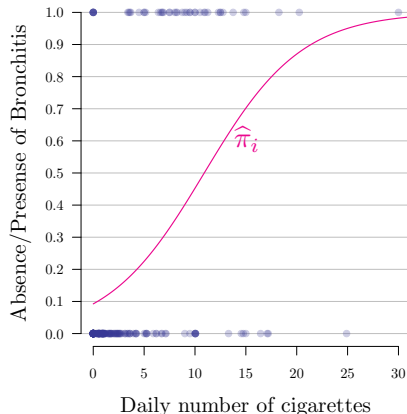
$$\blacktriangleright \hat{\pi}_{0\text{cig}} = \frac{e^{\hat{\beta}_0}}{1 + e^{\hat{\beta}_0}}$$

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$$\pi_{0\text{cig}} = \frac{e^{\hat{\beta}_0}}{1 + e^{\hat{\beta}_0}} \Leftrightarrow \frac{\hat{\pi}_{0\text{cig}}}{1 - \hat{\pi}_{0\text{cig}}} = e^{\hat{\beta}_0}$$

$$\pi_{1\text{cig}} = \frac{e^{\hat{\beta}_0 + \hat{\beta}_1}}{1 + e^{\hat{\beta}_0 + \hat{\beta}_1}} \Leftrightarrow \frac{\hat{\pi}_{1\text{cig}}}{1 - \hat{\pi}_{1\text{cig}}} = e^{\hat{\beta}_0 + \hat{\beta}_1}$$

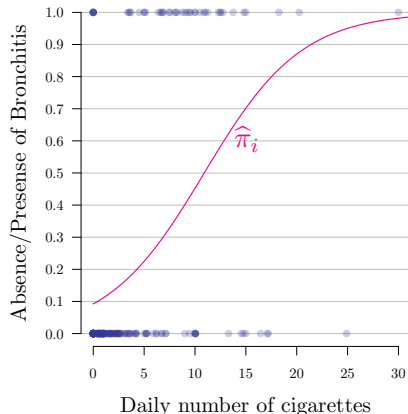
$$\frac{\frac{\hat{\pi}_{1\text{cig}}}{1 - \hat{\pi}_{1\text{cig}}}}{\frac{\hat{\pi}_{0\text{cig}}}{1 - \hat{\pi}_{0\text{cig}}}} = \frac{e^{\hat{\beta}_0 + \hat{\beta}_1}}{e^{\hat{\beta}_0}} = e^{\hat{\beta}_1} \text{ (Odd ratio)}$$

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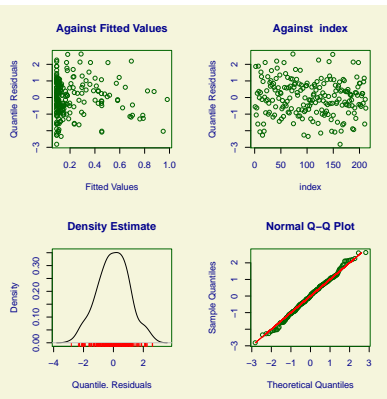
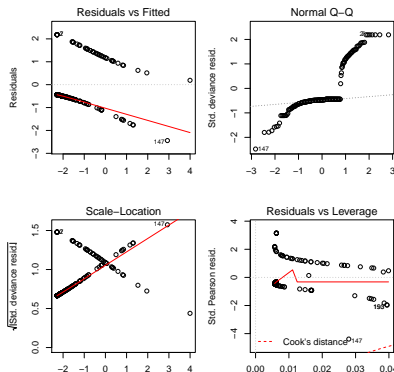
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- $\blacktriangleright \text{H0}_1: \beta_0 = 0 \text{ versus H1}_1: \beta_0 \neq 0$
- $\text{H0}_2: \beta_1 = 0 \text{ versus H1}_2: \beta_1 \neq 0$

# Logistic regression: model check

- ▶ pearson residuals  $(y_i - \hat{\pi}) / \sqrt{\text{Var}(\hat{\pi})}$ ,
- ▶ deviance residuals [Default in R],
- ▶ randomised normalised quantile residuals [Default in package `gamlss()`]



# Distribution for count data: Poisson

## Example:

Interest for the number of high school students diagnosed with an infectious disease

Sample of 115 days:	$t = 1$	$t = 2$	$t = 3$	$\dots$	$t = 115$	
	$y_i$	6	8	12	$\dots$	0

If, during a time interval or in a given area,

- ▶ events occur independently,
- ▶ at the same rate,
- ▶ and the probability of an event to occur in a small interval (area) is proportional to the length of the interval (size of the area),

then,

- ▶ a count occurring in a fixed time interval or in a given area,  $Y$ , may be modelled by means of a Poisson distribution with parameter  $\mu$ :

$$Y \sim \text{Poisson}(\mu) \text{ where } \mu = E[Y] = \text{Var}[Y],$$

- ▶ the probability of observing  $x$  events during a fixed time interval or in a given area is given by

$$P(Y = y|\mu) = \frac{\mu^y e^{-\mu}}{y!}.$$

# Poisson regression: GLM for count data

## Example:

Interest for the number of high school students diagnosed with an infectious disease as a function of the number of days from the initial outbreak

Sample of 115 days:  $t = 1$     $t = 2$     $t = 3$     $\dots$     $t = 115$

$y_t$	6	8	12	$\dots$	0
$t$	1	2	3	$\dots$	115

If, during a time interval or in a given area,

- ▶ events occur independently given the covariates,
- ▶ at the same rate given the covariates,
- ▶ and the probability of an event to occur in a small interval (area) is proportional to the length of the interval (size of the area) given the covariates,

then,

- ▶ each count occurring in a fixed time interval or in a given area,  $Y_t$ , may be modelled by means of a Poisson distribution with parameter  $\mu_t$ :

$$Y_t \sim \text{Poisson}(\mu_t) \text{ where } \mu_t = \mathbb{E}[Y] = \text{Var}[Y] = e^{\mathbf{x}_t^T \boldsymbol{\beta}},$$

- ▶ the probability of observing  $y$  during the fixed time interval or in the given area is given by

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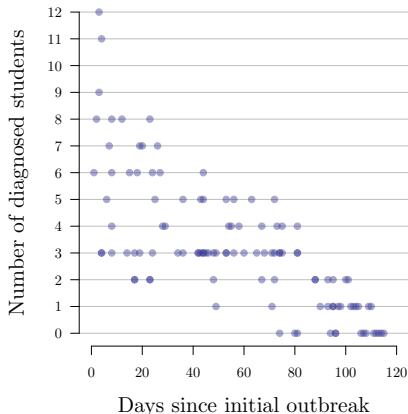


# Poisson regression: predictions and interpretation of $\beta$

## Example:

Model the mean count of diagnosed students,  $\mu_t$ , as a function of the number of days from the outbreak ( $T$ ) :

$$\mu_t = e^{\beta_0 + \beta_1 t}$$

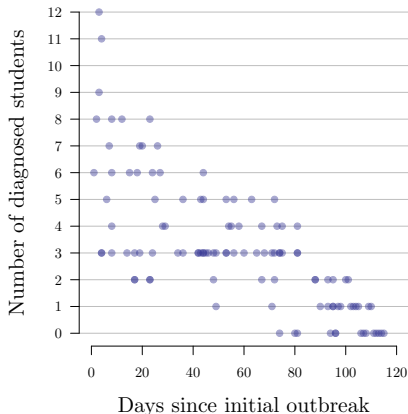


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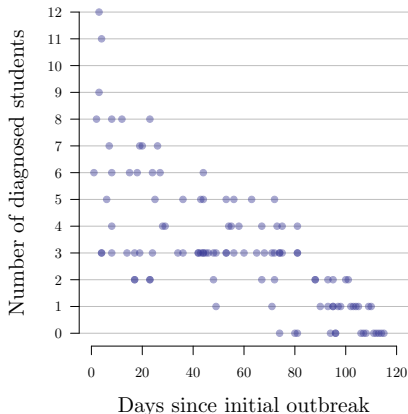
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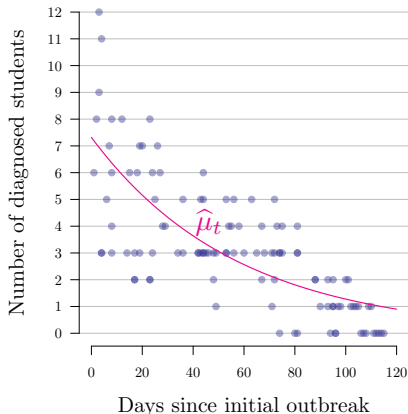
►  $\hat{\mu}_{\text{day}0} = e^{\hat{\beta}_0}$

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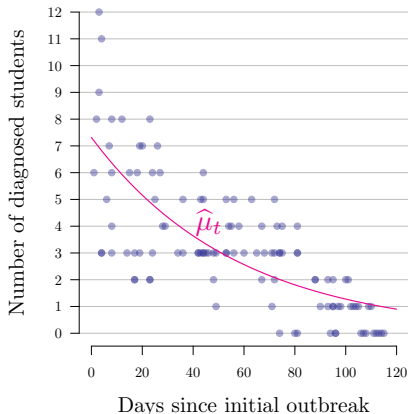
$$\frac{\hat{\mu}_{\text{day1}}}{\hat{\mu}_{\text{day0}}} = \frac{e^{\hat{\beta}_0 + \hat{\beta}_1}}{e^{\hat{\beta}_0}} = e^{\hat{\beta}_1}$$

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- ▶  $\hat{\mu}_{\text{day0}} = e^{\hat{\beta}_0}$
- ▶  $\hat{\mu}_{\text{day1}} = e^{\hat{\beta}_0 + \hat{\beta}_1}$
- ▶  $\frac{\hat{\mu}_{\text{day1}}}{\hat{\mu}_{\text{day0}}} = \frac{e^{\hat{\beta}_0 + \hat{\beta}_1}}{e^{\hat{\beta}_0}} = e^{\hat{\beta}_1}$
- ▶ **H0<sub>1</sub>:**  $\beta_0 = 0$  versus **H1<sub>1</sub>:**  $\beta_0 \neq 0$   
**H0<sub>2</sub>:**  $\beta_1 = 0$  versus **H1<sub>2</sub>:**  $\beta_1 \neq 0$

# Poisson regression: model check

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