



# Location-adjusted Wald statistics

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Reader in Data Science

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# Outline

- 1 Wald inference
- 2 Location-adjusted Wald statistic
- 3 Wald inference and bias-corrected estimators
- 4 Logistic regression with structural parameters
- 5 Brain lesions
- 6 Recap

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# Wald statistic for scalar parameters

## Data

$$(y_i, x_i^\top) \quad (i = 1, \dots, n)$$

$x_i = (x_{i1}, \dots, x_{ik})^\top \in \mathfrak{R}^k$  is a vector of explanatory variables for  $y_i$

## Model

Independent random variables  $Y_1, \dots, Y_n$  with pdf/pmf  $p_Y(y_i|x_i; \theta)$

Parameter  $\theta \in \Theta \subset \mathfrak{R}^p$  with

$\theta = (\psi, \lambda^\top)^\top$ , where  $\psi \in \mathfrak{R}$  is of interest

## Task

Draw inference about  $\psi$

# Wald statistic

## Log-likelihood<sup>1</sup>

$$l(\theta) = \sum_{i=1}^n \log p_Y(y_i | x_i; \theta)$$

## Wald statistic for testing $\psi = \psi_0$

$$t = \frac{\hat{\psi} - \psi_0}{\kappa(\hat{\theta})} \underset{\text{appr}}{\sim} N(0, 1)$$

## Maximum likelihood estimator (MLE)

$$\hat{\theta} = (\hat{\psi}, \hat{\lambda}^\top)^\top = \arg \max_{\theta \in \Theta} l(\theta)$$

## Standard error

$\kappa(\theta)$  is the square root of the  $(\psi, \psi)$  element of the variance-covariance  $\{i(\theta)\}^{-1}$  of the (asymptotic) null distribution of  $\hat{\theta}$

$i(\theta)$  is typically taken to be the expected information  $E\{\nabla l(\theta)\nabla l(\theta)^\top\}$  or some “robust” variant

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<sup>1</sup>subject to usual regularity conditions; see, Pace and Salvan (1997, §4.3)

# Wald statistic

## Asymptotically equivalent alternatives

Signed root of the likelihood ratio statistic

$$r = \text{sign}(\hat{\psi} - \psi_0) \{l(\hat{\psi}, \hat{\lambda}) - l(\psi_0, \hat{\lambda}_{\psi_0})\}^{1/2} \overset{\text{appr}}{\sim} N(0, 1)$$

Signed root of the score statistic

$$s = \text{sign}(\hat{\psi} - \psi_0) \frac{\partial l(\psi_0, \hat{\lambda}_{\psi_0})}{\partial \psi} \kappa(\psi_0, \hat{\lambda}_{\psi_0}) \overset{\text{appr}}{\sim} N(0, 1)$$

where  $\hat{\lambda}_{\psi_0} = \arg \max_{\lambda} l(\psi_0, \lambda)$  is the constrained MLE for  $\lambda$

## Pros of $t$

Computational convenience

## Cons of $t$

Inferential performance depends on the properties of  $\hat{\theta}$  (bias, efficiency, etc)

z test of coefficients:

	Estimate	Std. Error	z value	Pr(> z )
(Intercept)	-0.37540	0.68957	-0.5444	0.58617
lullyes	1.43237	0.73414	1.9511	0.05105
day2	-0.11394	1.04442	-0.1091	0.91313
day3	-0.58487	1.13343	-0.5160	0.60584
day4	-1.71670	1.31233	-1.3081	0.19083
day5	1.82912	1.30168	1.4052	0.15996
day6	0.24783	0.94155	0.2632	0.79238
day7	0.94994	0.99256	0.9571	0.33854
day8	0.46505	0.96850	0.4802	0.63111
day9	0.88646	1.11872	0.7924	0.42813
day10	1.66815	1.05172	1.5861	0.11271

Lack of reparameterization invariance

# Reading accuracy IQ and dyslexia

## Data

Reading accuracy for 44 nondyslexic and dyslexic Australian children<sup>2</sup>

Ages between 8 years+5 months and 12 years+3 months

## Variables

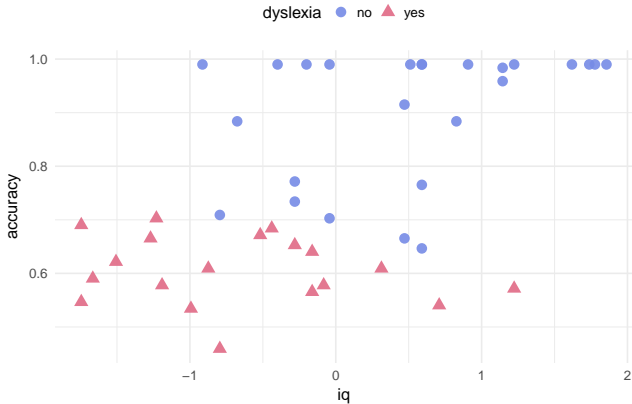
accuracy the score on a reading accuracy test

iq standardized score on a nonverbal intelligent quotient test

dyslexia whether the child is dyslexic or not

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<sup>2</sup>data from Smithson and Verkuilen (2006)



## Aim

Investigate the relative contribution of nonverbal IQ to the distribution the reading scores, controlling for the presence of diagnosed dyslexia



# Reading accuracy IQ and dyslexia

## Model

Score of the  $i$ -th child is from a Beta distribution with mean  $\mu_i$  and variance  $\mu_i(1 - \mu_i)/(1 + \phi_i)$  with

$$\log \frac{\mu_i}{1 - \mu_i} = \beta_1 + \sum_{j=2}^4 \beta_j x_{ij} \quad \text{and} \quad \log \phi_i = \gamma_1 + \sum_{j=2}^3 \gamma_j x_{ij}$$

- $x_{i2}$  takes value  $-1$  if the  $i$ th child is dyslexic and  $1$  if not
- $x_{i3}$  is the nonverbal IQ score, and
- $x_{i4} = x_{i2}x_{i3}$  is the interaction between dyslexia and iq

```
Call:
betareg(formula = accuracy ~ dyslexia * iq | dyslexia + iq, data = ReadingSkills,
        type = "ML")
```

```
Standardized weighted residuals 2:
```

	Min	1Q	Median	3Q	Max
	-2.3900	-0.6416	0.1572	0.8524	1.6446

```
Coefficients (mean model with logit link):
```

	Estimate	Std. Error	z value	Pr(> z )	
(Intercept)	1.1232	0.1428	7.864	3.73e-15	***
dyslexia	-0.7416	0.1428	-5.195	2.04e-07	***
iq	0.4864	0.1331	3.653	0.000259	***
dyslexia:iq	-0.5813	0.1327	-4.381	1.18e-05	***

```
Phi coefficients (precision model with log link):
```

	Estimate	Std. Error	z value	Pr(> z )	
(Intercept)	3.3044	0.2227	14.835	< 2e-16	***
dyslexia	1.7466	0.2623	6.658	2.77e-11	***
iq	1.2291	0.2672	4.600	4.23e-06	***

```
---
```

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

```
Type of estimator: ML (maximum likelihood)
```

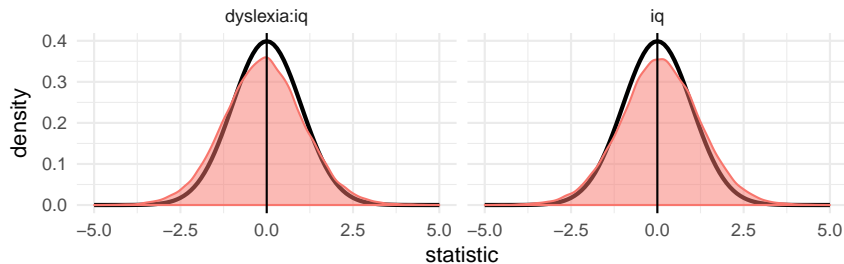
```
Log-likelihood: 65.9 on 7 Df
```

```
Pseudo R-squared: 0.5756
```

```
Number of iterations: 25 (BFGS) + 1 (Fisher scoring)
```

<sup>3</sup>see Grün, Kosmidis, and Zeileis (2012) for a range of modelling strategies and learning methods based on beta regression using the `betareg` R package

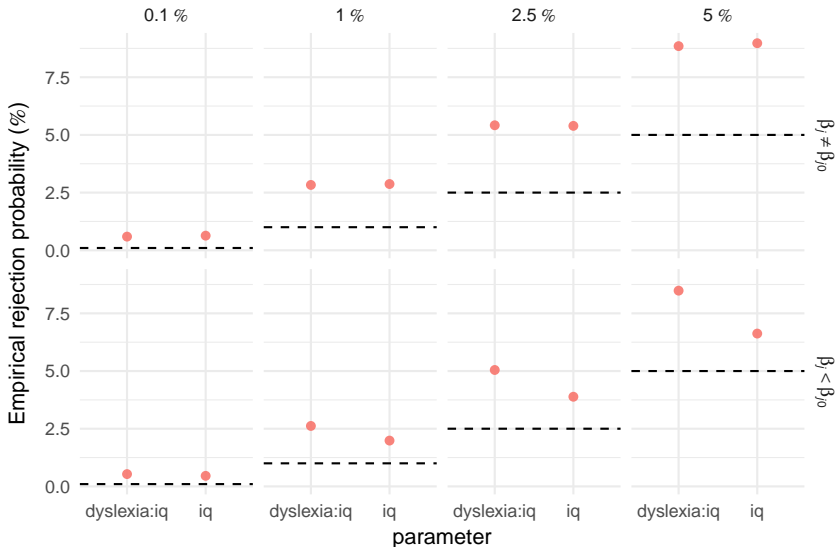
# Null distribution of Wald statistic for $\beta_j = \beta_{0j}$



parameter	mean	sd
dyslexia:iq	-0.09	1.15
iq	0.08	1.15

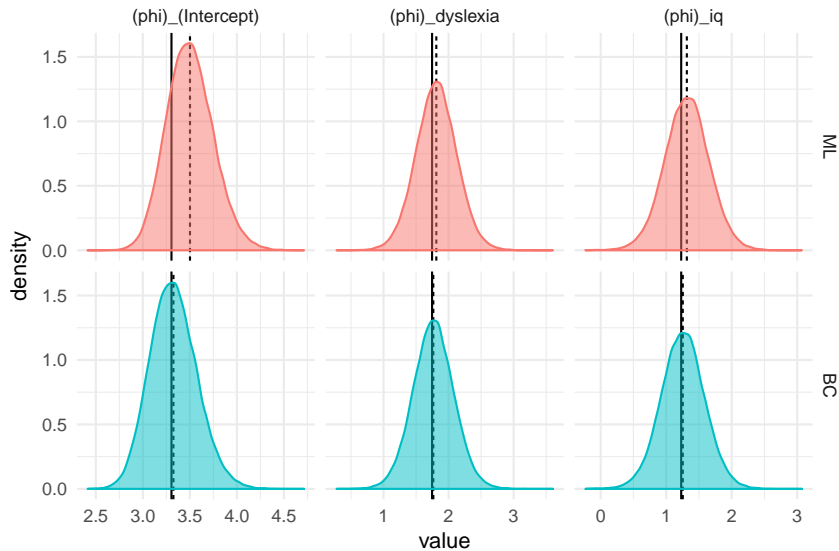
<sup>4</sup>figures based on 50 000 simulated samples under the maximum likelihood fit

# Empirical null rejection probabilities



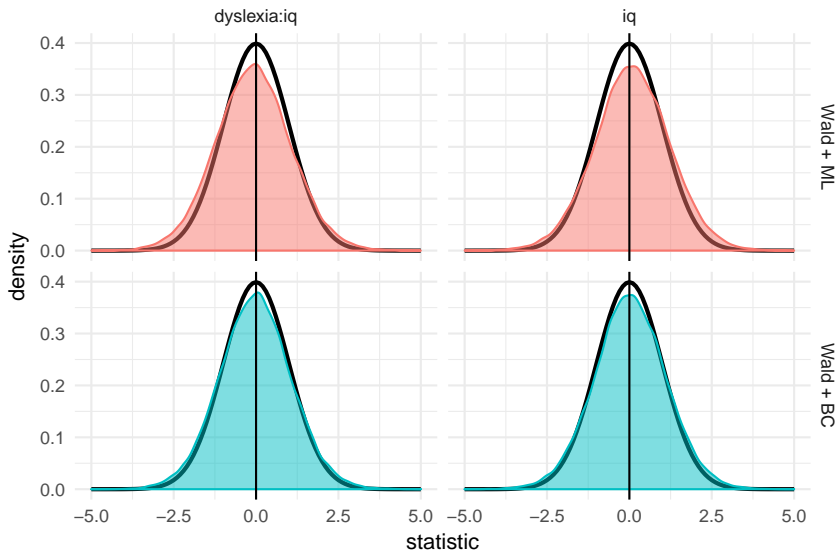
Empirical rejection probabilities are almost double the nominal level

# MLE and bias corrected estimator<sup>5</sup>



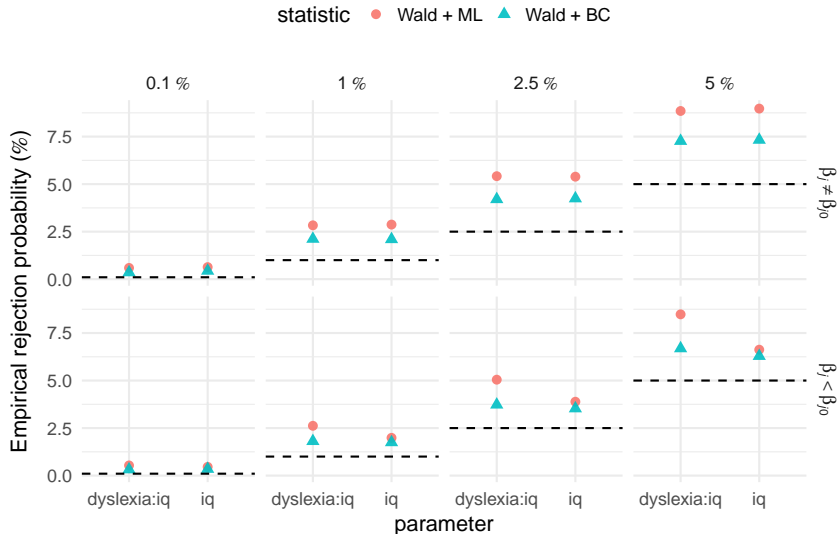
<sup>5</sup>with `type = BC` in the `betareg` call  
see, Grün, Kosmidis, and Zeileis (2012) for details on bias correction

# Null distribution of Wald statistic using BC estimators<sup>6</sup>



<sup>6</sup>Proposed in Kosmidis and Firth (2010)

# Empirical null rejection probabilities



<sup>7</sup>figures based on 50 000 simulated samples under the maximum likelihood fit

# Recap on Wald statistics with improved estimators

Use of improved estimators when forming Wald statistics can improve  $N(0, 1)$  approximation and hence inferential performance<sup>8</sup>

## **But**

Merely an observation, and in a few models

Rather indirect way to improving Wald inference

Better estimators in  $t \not\Rightarrow$  null distribution of  $t$  closer to  $N(0, 1)$

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<sup>8</sup>see, e.g., Kosmidis and Firth (2010)



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# Wald statistic as an estimator

## Wald Transform

$$T(\theta; \psi_0) = \frac{\psi - \psi_0}{\kappa(\theta)}$$



The Wald statistic  
 $t = T(\hat{\theta}; \psi_0)$   
is the MLE of  $T(\theta; \psi_0)$

## Core idea

Bias reduction techniques to bring **asymptotic mean** of  $t$  “closer” to 0

# Bias of $t$

Under regularity conditions<sup>9</sup> it can be shown that

$$E\{T(\hat{\theta}; \psi_0) - T(\theta; \psi_0)\} = B(\theta; \psi_0) + O(n^{-3/2})$$

where

## First-order bias of $t$

$$B(\theta; \psi_0) = b(\theta)^\top \nabla T(\theta; \psi_0) + \frac{1}{2} \text{trace} [\{i(\theta)\}^{-1} \nabla \nabla^\top T(\theta; \psi_0)]$$

## First-order bias of $\hat{\theta}$

$b(\theta)$  such that  $E(\hat{\theta} - \theta) = b(\theta) + o(n^{-1})$

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<sup>9</sup>to guarantee that  $T(\theta, \psi_0)$  is  $> 3$  times differentiable wrt  $\theta$  and  $\hat{\theta}$  is consistent

# Location-adjusted Wald statistic

## Key result

The location-adjusted Wald statistic

$$t^* = T(\hat{\theta}; \psi_0) - B(\hat{\theta}; \psi_0)$$

has null expectation of order  $O(n^{-3/2})$

# Quantities in the bias of $t$

$i(\theta)$  and  $b(\theta)$  are readily available for a wide range of models, including generalized linear and nonlinear models<sup>10</sup>

## Gradient and Hessian of the Wald transform

$$\nabla T(\theta; \psi_0) = \{ \mathbf{1}_p - T(\theta; \psi_0) \nabla \kappa(\theta) \} / \kappa(\theta)$$

$$\nabla \nabla^\top T(\theta; \psi_0) = - \left[ \nabla \kappa(\theta) \{ \nabla T(\theta; \psi_0) \}^\top + \nabla T(\theta; \psi_0) \{ \nabla \kappa(\theta) \}^\top + T(\theta; \psi_0) \nabla \nabla^\top \kappa(\theta) \right] / \kappa(\theta)$$

$\nabla \kappa(\theta)$  and  $\nabla \nabla^\top \kappa(\theta)$  can be computed either analytically, or using automatic or numerical differentiation

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<sup>10</sup>see, for example, Cook et al. (1986); Cordeiro and McCullagh (1991); Cordeiro and Vasconcellos (1997); Cordeiro and Toyama Udo (2008); Kosmidis and Firth (2009); Simas et al. (2010); Grün et al. (2012) etc Ioannis Kosmidis - Location-adjusted Wald statistics 21/45

## Example: Exponential with mean $e^{-\theta}$

Cornish-Fisher expansions (Hall, 1992, § 2.5) of the  $\alpha$ -level quantiles  $q_\alpha$  and  $q_\alpha^*$  of the distribution of  $t$  and  $t^*$  in terms of the corresponding standard normal quantiles  $z_\alpha$  are

$$q_\alpha = z_\alpha + n^{-1/2} \frac{z_\alpha^2 + 2}{6} - n^{-1} \frac{11z_\alpha^3 - 65z_\alpha}{144} + O(n^{-3/2}),$$
$$q_\alpha^* = z_\alpha + n^{-1/2} \frac{z_\alpha^2 - 1}{6} - n^{-1} \frac{11z_\alpha^3 - 65z_\alpha}{144} + O(n^{-3/2}),$$

provided that  $\epsilon < \alpha < 1 - \epsilon$  for any  $0 < \epsilon < 1/2$

→ Quantiles of  $t^*$  are closer to those of  $N(0, 1)$  than  $t$

# Computational complexity and implementation

No extra matrix inversions (beyond  $\{i(\theta)\}^{-1}$ ) or optimisation when computing  $t^*$ ; only extra matrix multiplications

In its analytical form,  $t^*$  has the computational complexity  $O(p^4)$ , whence  $t$  has  $O(p^3)$

Time complexity can be reduced drastically by exploiting sparsity in  $i(\theta)$  in specific models and vectorising operations

Evaluation of  $t^*$  for each of the model parameters can be done post-fit and **in parallel**

# Implementation with numerical derivatives of $\kappa(\theta)$

As implemented in the **waldi** R package

<https://github.com/ikosmidis/waldi><sup>11</sup>

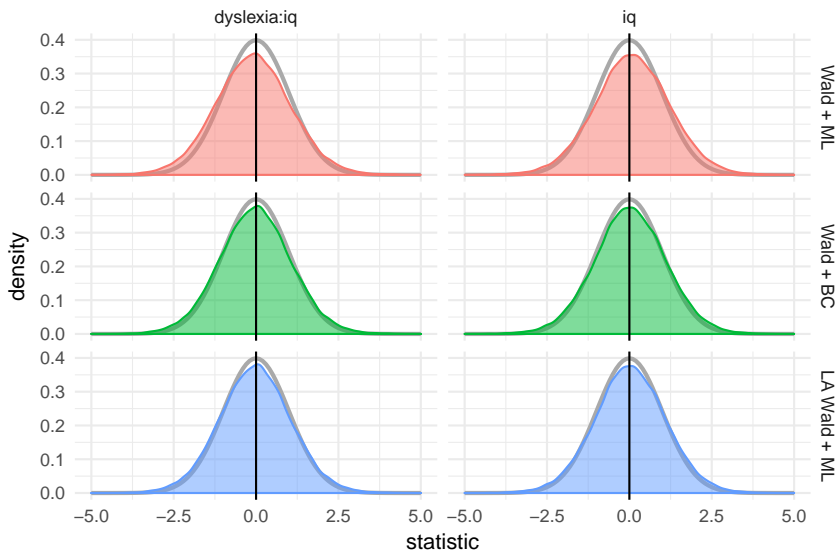
```
R> bias <- enrichwith::get_bias_function(object)
R> info <- enrichwith::get_information_function(object)
R>
R> t <- coef(summary(object))[, "z value"]
R> theta_hat <- coef(object)
R> b <- bias(theta_hat)
R> inverse_i_hat <- solve(info(theta_hat))
R>
R> kappa <- function(theta, j) {
+   inverse_i <- solve(info(theta))
+   sqrt(inverse_i[j, j])
+ }
R>
R> adjusted_t <- function(j) {
+   u <- numDeriv::grad(kappa, theta_hat, j = j)
+   V <- numDeriv::hessian(kappa, theta_hat, j = j)
+   a <- -t[j] * u
+   a[j] <- 1 + a[j]
+   t[j] - sum(a * b)/ses[j] +
+     (sum(inverse_i_hat * (tcrossprod(a, u)))/ses[j] +
+      0.5 * t[j] * sum(inverse_i_hat * V))/ses[j]
+ }
```

---

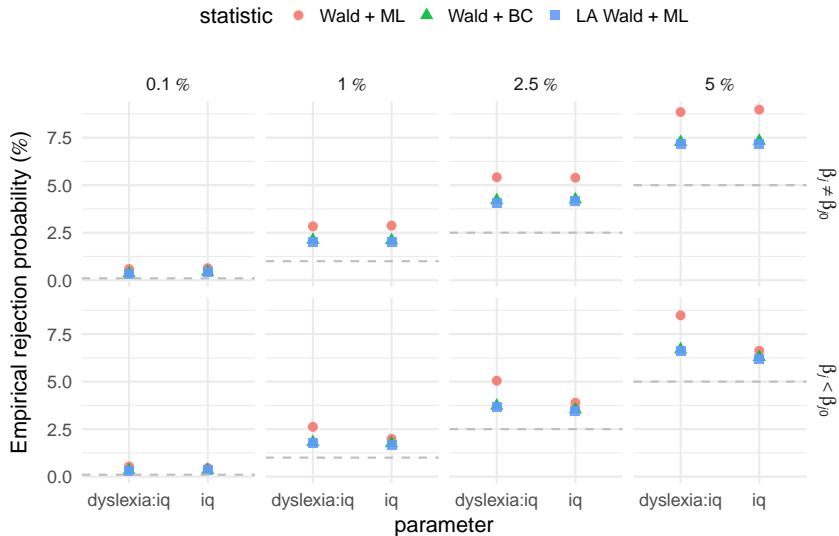
<sup>11</sup>Using R packages `enrichwith` (Kosmidis, 2017) and `numDeriv` (Gilbert and Varadhan, 2016)



# Beta regression: Reading accuracy and dyslexia



# Empirical null rejection probabilities

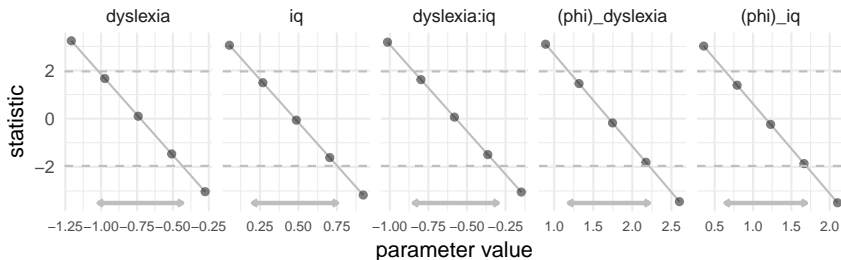


# Confidence intervals based on $t^*$

$100(1 - \alpha)\%$  confidence intervals based on  $t^*$  can be obtained by finding all  $\psi$  such that

$$|T(\hat{\theta}; \psi) - B(\hat{\theta}; \psi)| \leq z_{1-\alpha/2}$$

where  $z_{1-\alpha/2}$  is the  $1 - \alpha/2$  quantile of  $N(0, 1)$



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# Wald statistics with bias-corrected estimators

$$\tilde{t} = T(\tilde{\theta}; \psi_0)$$

with  $\tilde{\theta}$  being a bias-corrected estimator with

$$E(\tilde{\theta} - \theta) = o(n^{-1})$$

## Bias of $\tilde{t}$

$E\{T(\tilde{\theta}; \psi_0) - T(\theta; \psi_0)\} = \tilde{B}(\theta; \psi_0) + o(n^{-1/2})$  with

$$\tilde{B}(\theta; \psi_0) = b(\theta)^\top \nabla T(\theta; \psi_0) + \frac{1}{2} \text{trace} [\{i(\theta)\}^{-1} \nabla \nabla^\top T(\theta; \psi_0)]$$

Use of bias-corrected estimators **eliminates a term**, but bias of Wald statistic is still  $O(n^{-1/2})$

# Models with categorical responses

Location-adjustment of  $\tilde{t}$  is still fruitful

**Categorical response models**, where bias-correction leads to estimates that are **always finite** even in case where the MLE is infinite.

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# Lulling babies

## Data

18 **matched pairs** of binomial observations on the effect of lulling on the crying of babies

Matching is per day and each day pair consists of the number of babies not crying out of a fixed number of control babies, and the outcome of lulling on a single child

Experiment involves 143 babies

## Variables

crying    crying status of the baby (1 not crying; 0 crying)

day        the day of the experiment

lull        has the baby been lulled?

**Aim:** Test the effect of lulling on the crying of children



# Logistic regression: lulling babies

## Model

$Y_{ij}$  is a Bernoulli random variable for the crying status of baby  $j$  in day  $i$  with probability  $\mu_{ij}$  of not crying

$$\log \frac{\mu_{ij}}{1 - \mu_{ij}} = \beta_i + \gamma z_{ij}$$

- $z_{ij}$  is 1 if the  $j$ th child on day  $i$  was lulled, and 0 otherwise

## Task

Test  $\gamma = 0$  accounting for heterogeneity between days

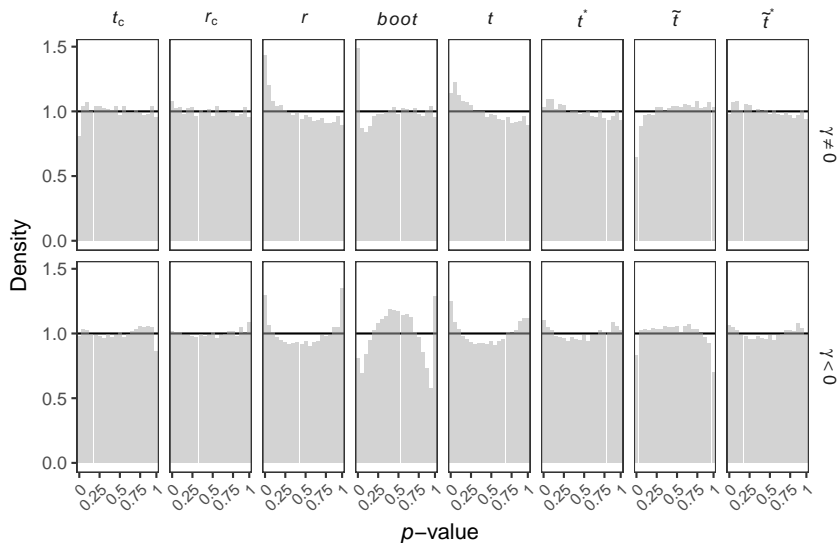
# Testing for $\gamma = 0$

	$t_c$	$r_c$	$r$	$t$	$t^*$	$\tilde{t}$	$\tilde{t}^*$
statistic	1.8307	2.0214	2.1596	1.9511	1.9257	1.7362	1.9064
$p$ -value	0.0671	0.0432	0.0308	0.0510	0.0541	0.0825	0.0566

$t_c$  is the Wald statistic based on the maximum **conditional likelihood estimator**

$r$  and  $r_c$  are the signed roots of the likelihood and conditional likelihood ratio statistics

# Empirical $p$ -value distribution

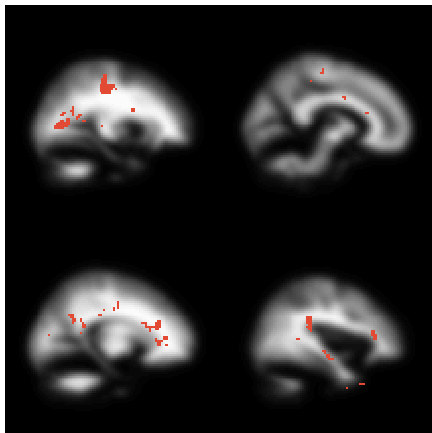


<sup>12</sup>based on 50 000 samples from the mdoel with  $\beta_1, \dots, \beta_{18}$  set to their maximum likelihood estimates and  $\gamma = 0$

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# Mass univariate regression for brain lesions



resolution:  $91 \times 109 \times 91$  (902 629 voxels)

**Aim:** Construct significance maps, highlighting voxels according to the evidence against the null hypothesis of no covariate effect

## Sample

lesion maps for 50 patients<sup>13</sup>

## Patient characteristics

multiple sclerosis type  
(MS)<sup>14</sup>

age

gender

disease duration (DD)

two disease severity measures  
(PASAT and EDSS)

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<sup>14</sup>from the supplementary material of Ge et al. (2014)

<sup>15</sup>0 for relapsing-remitting and 1 for secondary progressive multiple sclerosis

# Voxel-wise probit regressions

**Lesion occurrence in voxel  $j$  for patient  $i$**

$$Y_{ij} \sim \text{Bernoulli}(\pi_{ij})$$

**Lesion probability**

$$\Phi^{-1}(\pi_{ij}) = \beta_{j0} + \beta_{j1}MS_i + \beta_{j2}age_i + \beta_{j3}gender_i + \beta_{j4}DD_i + \beta_{j5}PASAT_i + \beta_{j6}EDSS_i$$

# Results

## Occurrence of infinite estimates

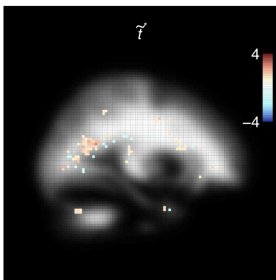
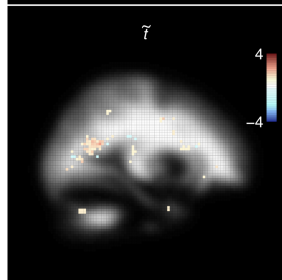
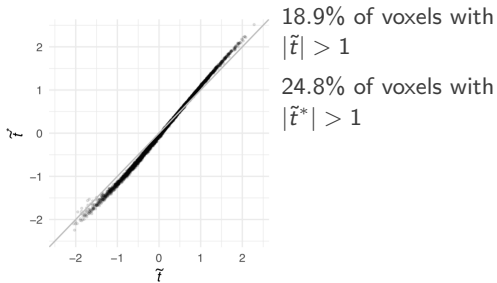
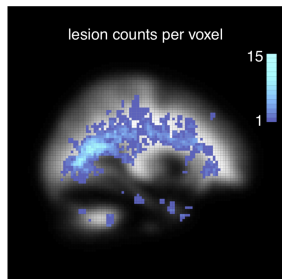
Covariate	Occurrence
MS	75.5%
age	63.7%
gender	78.3%
DD	63.7%
PASAT	63.6%
EDSS	63.2%

## Failures in evaluation of $r$

Covariate	Occurrence
MS	19.2%
age	20.5%
sex	22.4%
DD	18.1%
PASAT	16.8%
EDSS	10.3%

<sup>15</sup>summaries based on voxels with lesion occurrence for at least one lesion across patients

# Significance map for disease duration





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# Recap

Location-adjustment can deliver **substantial improvements** to Wald inference

Extra computational overhead is mainly due to matrix multiplications

Location adjustment with “robust”<sup>16</sup> variance-covariance matrices

Location adjustment with alternative estimators of estimator bias, including bootstrap and jackknife; particularly useful, e.g., for generalized linear mixed effects models

Extensions to other pivotal quantities, including Wald statistics for composite hypotheses, score statistics, or even directly  $p$ -values

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<sup>16</sup>see, for example, MacKinnon and White (1985) Ioannis Kosmidis - Location-adjusted Wald statistics 42/45

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## Location-adjusted Wald statistic



$$t^* = T(\hat{\theta}; \psi_0) - B(\hat{\theta}; \psi_0)$$

### Preprint


Di Caterina C and Kosmidis I (2017). Location-adjusted Wald statistic for scalar parameters. *ArXiv e-prints*. arXiv:1710.11217

### Software

**waldi** R package<sup>17</sup> (soon in CRAN!) for computing  $t^*$  for well-used models, including GLMs (`glm`, `brglm2`) and beta regression (`betareg`)

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<sup>17</sup><https://github.com/ikosmidis/waldi>