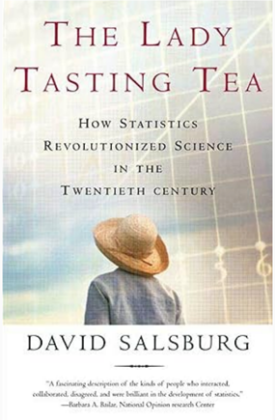
When likelihood goes wrong

Nancy Reid
University of Toronto

October 2 2024

Pfizer Colloquium

UCONN UNIVERSITY OF CONNECTICUT



"by the end of the twentieth century, almost all of science had shifted to using statistical models"

Salsburg, 2001

Outline

1. Models and science: a haphazard selection
2. Models and parameters
3. What's special about likelihood?
4. Some approaches to misspecification
5. Example
6. Conclusion

Models and science: a haphazard selection

Clim. Past, 20, 1387–1399, 2024
https://doi.org/10.5194/cp-20-1387-2024

Climate of the Past
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600 years of wine must quality and April to August temperatures in western Europe 1420–2019

Christian Pfister[1], Stefan Brönnimann[2], Andres Altwegg[3], Rudolf Brázdil[4], Laurent Litzenburger[5], Daniele Lorusso[6], and Thomas Pliemon[7]

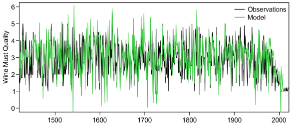

Figure 4. Observed series of wine quality (average; black) from 1420 to 2019 and series obtained with a statistical model calibrated in 1781–1800 (green). The model is explained in Sect. 3.

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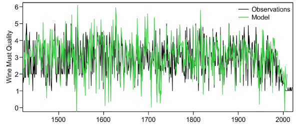

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Scientific question: Can historical records of wine quality be used as temperature proxies?

observational data

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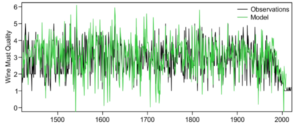

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Statistical model: "we used a statistical [linear regression] model for wine quality based on local temperature and precipitation"

yes, if used carefully

Income supplements

Vivalt et al 2024

NBER WORKING PAPER SERIES

THE EMPLOYMENT EFFECTS OF A GUARANTEED INCOME: EXPERIMENTAL EVIDENCE FROM TWO U.S. STATES

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Working Paper 32719
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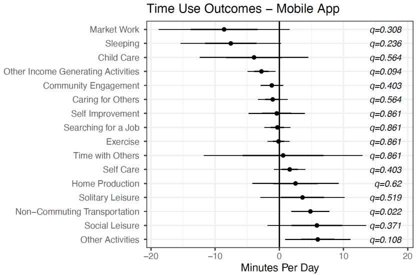
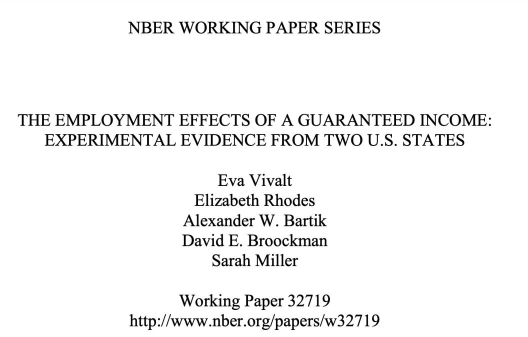
Figure 5: Time Use Results: Mobile App

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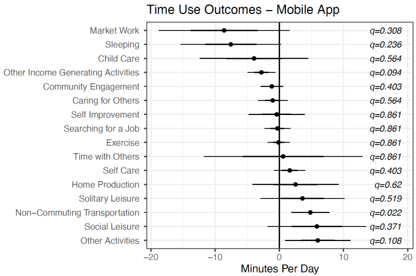

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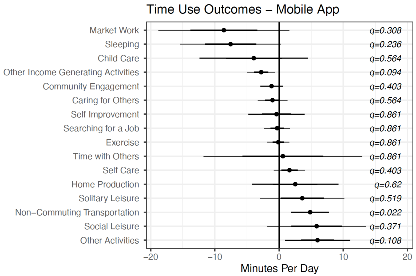

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Statistical model: $Y_i = \alpha + \beta Treated_i + \gamma^{\mathrm{T}} X_i + \epsilon_i$

"support for both sides of this debate"

Breast cancer mortality

Giannakeas et al 2024

JAMA Oncology | Original Investigation

Bilateral Mastectomy and Breast Cancer Mortality

Vasily Giannakeas, PhD, MPH; David W. Lim, MDCM, MEd, PhD; Steven A. Narod, MD

IMPORTANCE The benefit of bilateral mastectomy for women with unilateral breast cancer in terms of deaths from breast cancer has not been shown.

OBJECTIVES To estimate the 20-year cumulative risk of breast cancer mortality among women with stage 0 to stage III unilateral breast cancer according to the type of initial surgery performed.

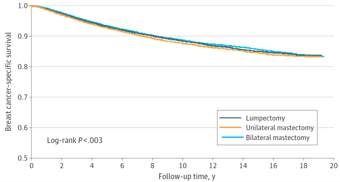
DESIGN, SETTINGS, AND PARTICIPANTS This cohort study used the Surveillance, Epidemiology, and End Results (SEER) Program registry database to identify women with unilateral breast cancer (invasive and ductal carcinoma in situ) who were diagnosed from 2000 to 2019. Three closely matched cohorts of equal size were generated using 1:1:1 matching according to surgical approach. The cohorts were followed up for 20 years for contralateral breast cancer and for breast cancer mortality. The analysis compared the 20-year cumulative risk of breast cancer mortality for women treated with lumpectomy vs unilateral mastectomy vs bilateral mastectomy. Data were analyzed from October 2023 to February 2024.

EXPOSURES Type of breast surgery performed (lumpectomy, unilateral mastectomy, or bilateral mastectomy).

Editorial

Supplemental content

C 20-y Breast cancer-specific survival



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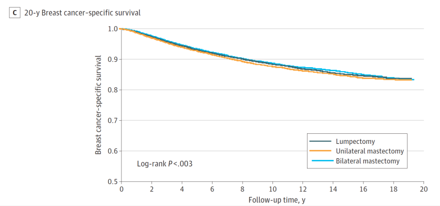

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matched case-cohort study

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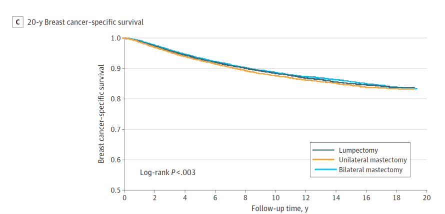

Scientific question: Does bilateral mastectomy for unilateral breast cancer improve 20-year survival?

matched case-cohort study

Statistical model: “We used the Kaplan-Meier method to estimate survival”

“preemptive surgery did not appear to reduce the risk of death”

Article

https://doi.org/10.1038/s41550-023-01983-1

Variability of extragalactic X-ray jets on kiloparsec scales

Received: 17 May 2022

Accepted: 27 April 2023

Published online: 29 May 2023

Eileen T. Meyer[1], Aamil Shaik[1], Yanbo Tang[2], Nancy Reid[3], Karthik Reddy[1,4], Peter Breiding[5], Markos Georganopoulos[1], Marco Chiaberge[5,6], Eric Perlman[7], Devon Clautice[7], William Sparks[8,9], Nat DeNigris[1,10] & Max Trevor[1,11]

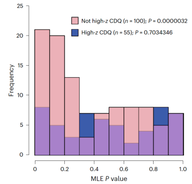

Fig. 3 | Histogram of the single-region P values from the directional test, not adjusted for multiple comparison. In pink, the subset of sources that

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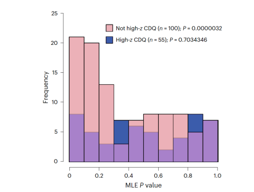

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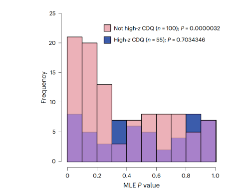

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Statistical model: compare background and source counts using Poisson distribution:

$$x_i \sim Po(a_i\beta_i), \quad y_i \sim Po(b_i\beta_i + b_i f_i \mu_i), \quad H_0 : \mu_i \equiv 0$$

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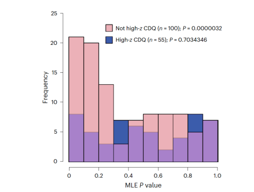

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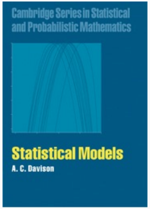
"variability in the *X*-ray emission is not compatible with current theory"

Models and parameters

Why these models?

- standard in the literature of that field — income
- standard in the publications of that lab — breast cancer
- follow some prescription:
  - binary response — use logistic regression
  - time to event — use PH model
  - time series — use ARMA — wine
  - repeated measures — use random effects
  - ...
- motivated by theory: economic, physical, ... — *X*-ray jets

Some guidance from the experts



- the key feature of a statistical model is that variability is represented using probability distributions

- the art of modelling lies in finding a balance that enables the questions at hand to be answered or new ones posed

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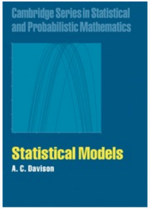

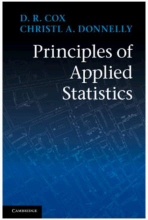

- the key feature of a statistical model is that variability is represented using probability distributions
- the art of modelling lies in finding a balance that enables the questions at hand to be answered or new ones posed
- probability models as an aid to the interpretation of data
- perturbations of no intrinsic interest distort an otherwise exact measurement
- substantial natural variability in the phenomenon under study

Statistical Science
1990, Vol. 5, No. 2, 160–168

Model Specification: The Views of Fisher and Neyman, and Later Developments

E. L. Lehmann

Role of Models in Statistical Analysis

D. R. Cox

Abstract. A number of distinct roles are identified for probability models used in the analysis of data. Examples are outlined. Some general issues arising in the formulation of such models are discussed.

empirical, or predictive models, contrasted with explanatory models

indirect models

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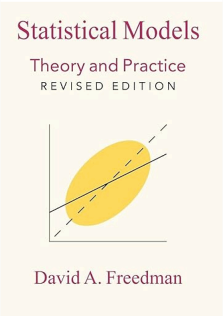

The emphasis throughout is on the connection
– or lack of connection –
between the models and the real phenomena.

The role of parameters

- probability models very likely be parameterized
- thus defining a class of models $\{f(y;\theta);\theta \in \Theta\}$
- parameters may be finite- or infinite-dimensional parametric vs nonparametric

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for the application at hand

- other parameters complete the specification
- the meaning of various parameters varies with the application

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The Annals of Statistics
2002, Vol. 30, No. 5, 1225–1310

WHAT IS A STATISTICAL MODEL?[1]

BY PETER MCCULLAGH
University of Chicago

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"Probability theory alone is insufficient to describe statistical methods" – Salsburg

What’s special about likelihood?

The likelihood function

- it puts the emphasis on the model: $L(\theta; y) \propto f(y; \theta)$ — inverse problem
- provides a convenient way to compare parameter values — e.g. $L(\theta)/L(\hat{\theta})$

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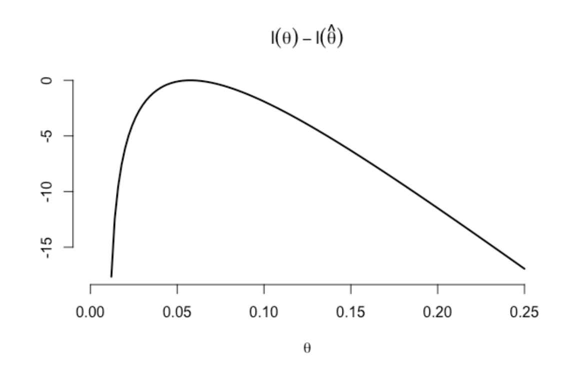

Pfizer vaccine

$Bin(162 + 8, \theta)$ via 2 Poissons

The likelihood function

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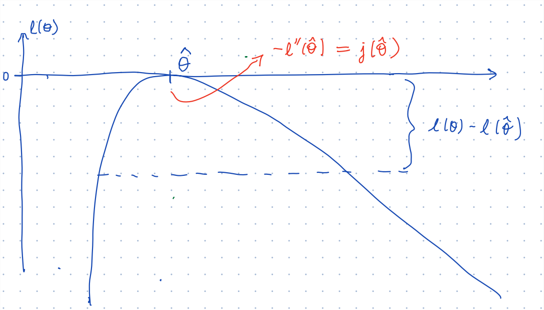
- provides a convenient way to compare parameter values — e.g. $L(\theta)/L(\hat{\theta})$
- provides reliable summary measures



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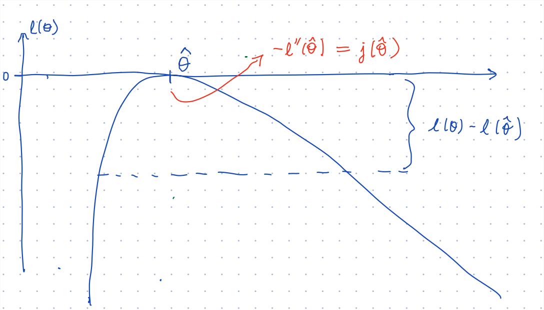

- can be converted to a probability, given a prior probability for θ

Inference

- Data and model: $y = y_1, \ldots, y_n$ independent; $\quad Y \sim f(y; \theta), \quad \theta \in \mathbb{R}^p$ $\qquad y \in \mathbb{R}^n$
- Likelihood function: $L(\theta; y) \propto f(y; \theta) = \prod_{i=1}^n f(y_i; \theta)$
- Log-likelihood function: $\ell(\theta; y) = \log L(\theta; y) = \sum_{i=1}^n \log f(y_i; \theta)$

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- Maximum likelihood estimator: $\hat{\theta} = \hat{\theta}(y) = \arg\sup_\theta \ell(\theta; y)$ $\qquad \ell'(\hat{\theta}) = 0$

- Score function $\ell'(\theta; y) = \Sigma_{i=1}^n \partial \ell(\theta; y_i)/\partial \theta^{\mathrm{T}}$ $\quad i(\theta) = \mathrm{var}\{\partial \ell(\theta; Y)/\partial \theta^{\mathrm{T}}\}$ $\qquad$ CLT

- observed Fisher information $\qquad j(\theta) = -\partial^2 \ell(\theta; y)/\partial \theta \partial \theta^{\mathrm{T}}$ $\qquad \mathrm{E}\{j(\theta)\} = i(\theta)$

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- observed Fisher information $\qquad j(\theta) = -\partial^2\ell(\theta; y)/\partial\theta\partial\theta^{\mathrm{T}}$ $\qquad \mathrm{E}\{j(\theta)\} = i(\theta)$
- in “large samples”

$$\ell'(\theta) \dot\sim N_p\{0, i(\theta)\}, \quad \hat\theta \dot\sim N_p\{\theta, j^{-1}(\hat\theta)\}, \quad 2\{\ell(\hat\theta) - \ell(\theta)\} \dot\sim \chi^2_p$$

Too much notation!

CLT:

$$\frac{1}{\sqrt{n}}\ell'(\theta) \xrightarrow{d} N\{0, i_1(\theta)\}$$

large-sample approx:

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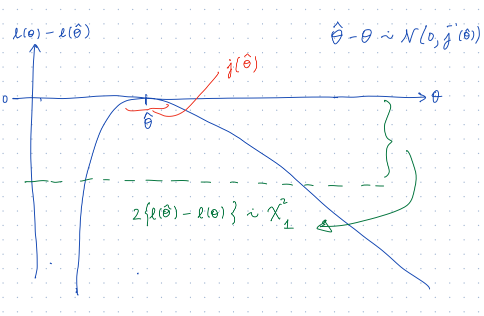
```
Coefficients:
             Estimate Std. Error z value Pr(>|z|)
(Intercept)    -3.079      0.987   -3.12   0.0018 **
aged1          -0.292      0.754   -0.39   0.6988
stage1          1.373      0.784    1.75   0.0799 .
grade1          0.872      0.816    1.07   0.2850
xray1           1.801      0.810    2.22   0.0263 *
acid1           1.684      0.791    2.13   0.0334 *
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 40.710  on 22  degrees of freedom
Residual deviance: 18.069  on 17  degrees of freedom
```



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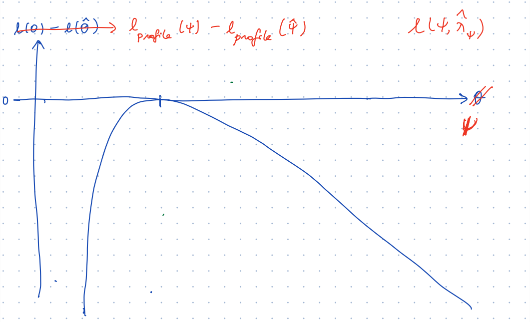
- results above used profile log-likelihood function $\quad \ell_{\text{profile}}(\psi) = \ell(\psi, \hat{\lambda}_\psi)$



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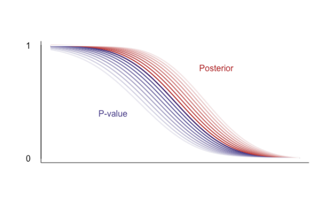

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Some approaches to misspecification

- true model $m(\boldsymbol{y})$ fitted model $f(\boldsymbol{y};\theta)$

$$\boldsymbol{y} = (y_1, \ldots, y_n)$$

$$\ell(\theta;\boldsymbol{y}) \equiv \log f(\boldsymbol{y};\theta)$$

- maximum likelihood estimator $\widehat{\theta}$

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KL-divergence

$$\theta_m^{\circ} = \arg\min_\theta \int m(\boldsymbol{y}) \log\{\frac{m(\boldsymbol{y})}{f(\boldsymbol{y};\theta)}\} d\boldsymbol{y}$$

1. Classical

Cox 1961,2; Huber 1967; White 1982

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$$\text{a.var. } (\widehat{\theta}) = G^{-1}(\theta_m^{\mathrm{o}}), \qquad G(\theta) = J(\theta)I^{-1}(\theta)J(\theta)$$

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"we used robust standard errors "

2. More flexible inference functions

Composite likelihood

- true model $m(\boldsymbol{y}_i) = f(\boldsymbol{y}_i;\theta), \boldsymbol{y}_i \in \mathbb{R}^d$ fitted model $\prod_{A \in \mathcal{A}} f(y_{iA};\theta)$ subsets A

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- Example: pairwise likelihood $\boldsymbol{y} = (\boldsymbol{y}_1,\ldots,\boldsymbol{y}_n)$

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interpretation of θ

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- Example pseudo-likelihood in spatial models condition on near neighbours; Besag 74

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Quasi-likelihood and generalized estimating equations

$$g\{\mathrm{E}(y_i \mid \boldsymbol{x}_i)\} = g(\mu_i) = \boldsymbol{x}_i^{\mathrm{T}}\boldsymbol{\beta}, \quad \mathrm{var}(y_i \mid \boldsymbol{x}_i) = \sigma^2 V(\mu_i)$$

- estimating equation for $\boldsymbol{\beta}$

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Quadratic inference functions

Qu, Lindsay, Li 2000; Hector 2023

- replace $V^{-1}(\mu_i)$ above with an expansion in basis functions
- apply generalized method of moments

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- does parameter of interest have a stable interpretation — model assumption

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Example

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- survival times for n matched pairs (y_{1i}, y_{2i})

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- consider modelling nuisance parameters λ_i as random effects

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- random effects model: $\lambda_i \sim \text{Gamma}(\alpha, \beta)$ shape, rate
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can this be generalized?

1. for pair (y_{1i}, y_{2i})

$$L(\psi, \alpha, \beta; y_{1i}, y_{2i}) = \frac{\Gamma(\alpha+2)}{\Gamma(\alpha)} \frac{\beta^{\alpha}}{(y_{1i}/\psi + \psi y_{2i} + \beta)^{\alpha+2}}$$

2. orthog

$$\frac{\partial^2}{\partial\psi\partial\alpha} \log L(\psi, \alpha, \beta; y_{1i}, y_{2i}) = \frac{y_{2i} - y_{1i}/\psi^2}{y_{2i}\psi + y_{1i}/\psi + \beta}$$

3.

$$\mathrm{E}_m \left\{ \frac{y_{2i} - y_{1i}/\psi^2}{y_{2i}\psi + y_{1i}/\psi + \beta} \right\} = 0$$

4. for Gamma random effects, but also for any random effects distribution

interpretation of α, β when not Gamma

Towards a formalisation

- true model $m(\boldsymbol{y})$ with parameter ψ and true value ψ_*
- fitted model $f(\boldsymbol{y}; \psi, \lambda)$ same parameter of interest, (many) nuisance parameters

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- can be easier to show $\mathrm{E}_m\{\partial \ell(\psi_*, \lambda)/\partial \psi\} = 0 \quad \forall \lambda$ (2)

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- fitted model $f(\boldsymbol{y};\psi,\lambda)$ same parameter of interest, (many) nuisance parameters

  interpretation of ψ is stable
- maximum likelihood estimates $(\hat{\psi},\hat{\lambda}) \xrightarrow{p} (\psi_m^0,\lambda_m^0)$ KL divergence
- assume no value of $\lambda \in \Lambda$ gives back $m(\cdot)$ misspecified
- Does $\widehat{\psi} \xrightarrow{p} \psi_*$? need $\mathrm{E}_m\{\partial\ell(\psi_*,\lambda_m^0)/\partial\psi\} = 0$ (1) λ_m^0 unknown
- can be easier to show $\mathrm{E}_m\{\partial\ell(\psi_*,\lambda)/\partial\psi\} = 0 \quad \forall\lambda$ (2)
- **Result :** (1) $\equiv$ (2) $\iff$ ψ_* is *m*-orthogonal to Λ: $\forall\lambda \quad \mathrm{E}_m\left\{\frac{\partial^2\ell(\psi,\lambda)}{\partial\psi\partial\lambda}\right\} = 0$

... towards a formalisation

Battey & R 2024

- true model $m(\boldsymbol{y})$ with parameter ψ and true value ψ_*
- fitted model $f(\boldsymbol{y}; \psi, \lambda)$
- Result : orthogonal parameters lead to consistent estimate — m-orthogonal
- Some weaker conditions will suffice for m-orthogonality, hence consistency
- Result : if the parametrization of f has a particular symmetry, then ψ_* is m-orthogonal to nuisance, hence consistency
- Example: generalized scale model — $f(y; \sigma) = (1/\sigma) f_0(y/\sigma)$

$$f(y; \psi\lambda) = \frac{1}{\psi} f_0\left(\frac{y}{\psi}; \lambda\right), \quad f(y; \lambda/\psi) = \psi f_0(\psi y; \lambda)$$

Tentative conclusions, further work

- Results above only establish consistency
- asymptotic variance is much more difficult

although estimating it might be okay

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- effectively assuming an arbitrary (nonparametric) mixing distribution
- less efficient when the random effects model is correct

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- orthogonality under assumed model $\mathrm{E}_\theta\{-\partial^2\ell(\theta)/\partial\theta\partial\theta^{\mathrm{T}}\} = 0$ — $\theta = (\psi, \lambda)$
- *m*-orthogonality under true model $\mathrm{E}_m\{-\partial^2\ell(\theta)/\partial\theta\partial\theta^{\mathrm{T}}\} = 0$
- connection to Neyman orthogonality? — decorrelated score

$$\partial\ell(\psi,\lambda)/\partial\psi - w^{\mathrm{T}}\partial\ell(\psi,\lambda)/\partial\lambda, \quad w = I_{\psi\lambda}I_{\lambda\lambda}^{-1}$$

- extension to general estimating equations important in 2-debiased ML

Chernozhukov et al 2018, Ning et al 2017, Jorgensen & Knudsen 2004

Conclusion

What can go wrong?

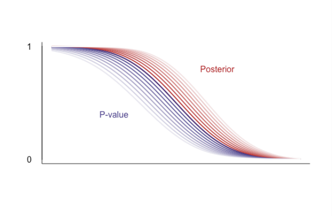
- too many parameters
- weird parameter space
- computational intractability
- $\boxed{\text{model is misspecified}}$
- likelihood is not a probability

$p \sim n, \quad p/n \to C, \quad p/n \to \infty$

$pf(y;\theta_1) + (1-p)f(y;\theta_2), \quad 0 \le p \le 1$

$L(\theta,\tau;y) = \int_{\mathbb{R}^k} f(y \mid z;\theta) f(z;\tau) dz$

$\boxed{\text{true } Y \sim m(y), \quad \nexists\theta_* \text{ w. } f(\cdot;\theta_*) = m(\cdot)}$

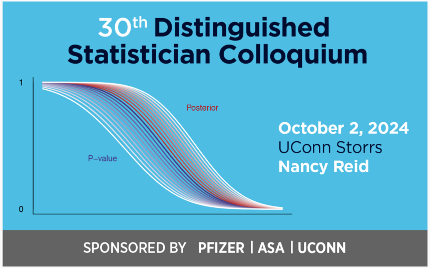


... what can go wrong?

• too many parameters	new asymptotic theory ($p \sim n$) regularization ($p > n$)	Sur & Candès 19; Zhao et al 22 Lasso, SCAD, MCP
• weird parameter space	different asymptotic theory, e.g. $\chi^2_D \to \Sigma \lambda_j \chi^2_{1j}$	Battey & McCullagh 24
• computational intractability	composite likelihood	Genton et al 15
• likelihood is not a probability	priors can be very influential	

... and so much more!

Thank you!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