Prediction in Multilevel Logistic Regression

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Outline

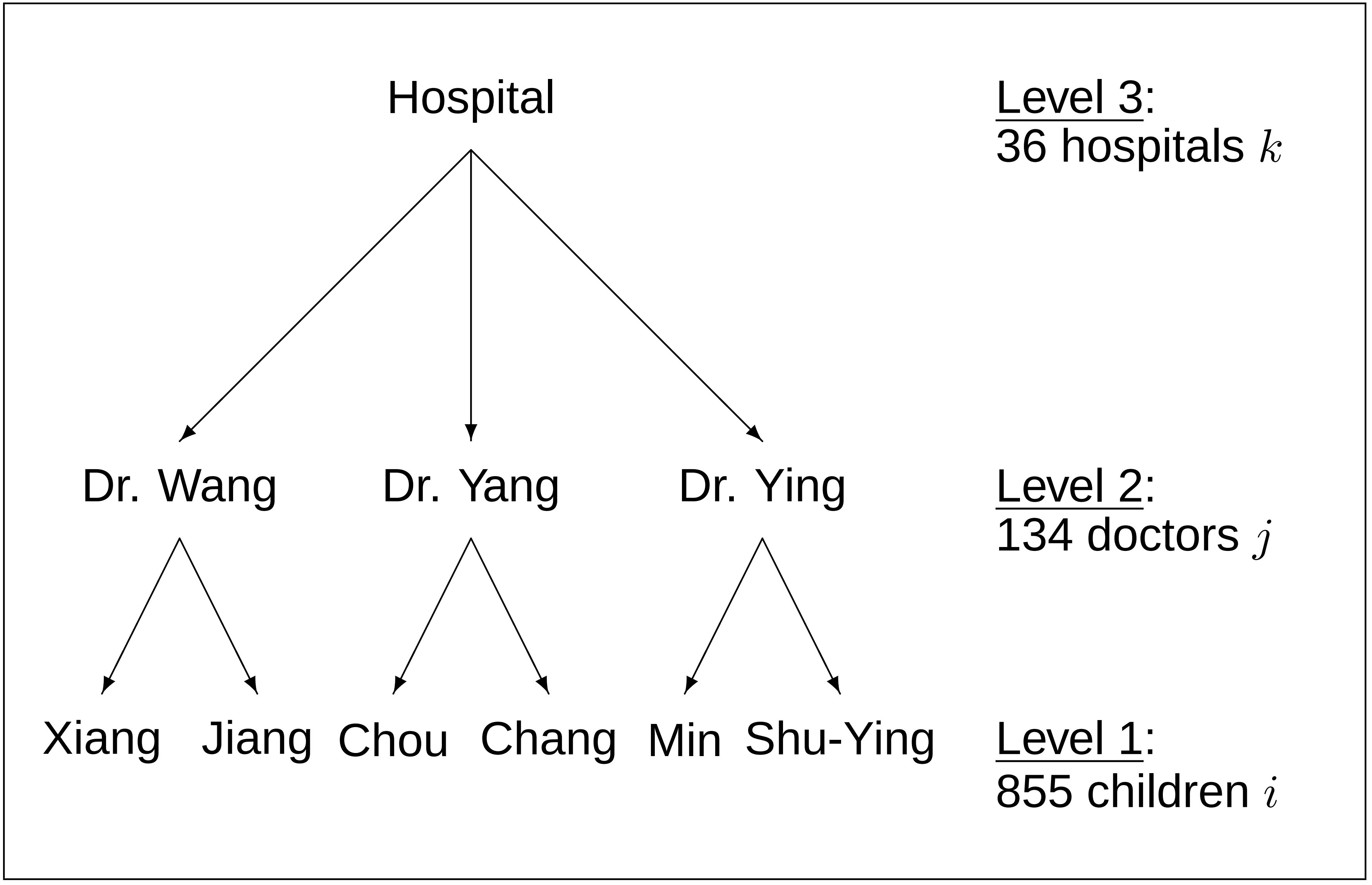
- Application: Abuse of antibiotics in China
- Three-level logistic regression model
- Prediction of random effects
  - Empirical Bayes (EB) prediction
  - Standard errors for EB prediction and approximate CI
- Prediction of response probabilities
  - Conditional response probabilities
  - Posterior mean response probabilities (different types)
  - Population-averaged response probabilities
- Concluding remarks

Abuse of antibiotics in China

- Acute respiratory tract infection (ARI) can lead to pneumonia and death if not properly treated
- Inappropriate frequent use of antibiotics was common in China in 1990's, leading to drug resistance
- In the 1990's the WHO introduced a program of case management for children under 5 with ARI in China
- Data collected on 855 children i (level 1) treated by 134 doctors j (level 2) in 36 hospitals k (level 3) in two counties (one of which was in the WHO program)
- **Response variable:** Whether antibiotics were prescribed when there were no clinical indications based on medical files

Reference: Min Yang (2001). *Multinomial Regression*. In Goldstein and Leyland (Eds). *Multilevel Modelling of Health Statistics*, pages 107-123.

Three-level data structure



Variables

- Response variable y_{ijk}
  - Antibiotics prescribed without clinical indications (1: yes, 0: no)
- 7 covariates $\mathbf{x}_{ijk}$
  - Patient level i
    - [Age] Age in years (0-4)
    - [Temp] Body temperature, centered at 36°C
    - [Paymed] Pay for medication (yes=1, no=0)
    - [Selfmed] Self medication (yes=1, no=0)
    - [Wrdiag] Failure to diagnose ARI early (yes=1, no=0)
  - Doctor level j
    - [DRed] Doctor's education
      (6 categories from self-taught to medical school)
  - Hospital level k
    - [WHO] Hospital in WHO program (yes=1, no=0)

Three-level random intercept logistic regression

- Logistic regression with random intercepts for doctors and hospitals

$$\text{logit}[\Pr(y_{ijk} = 1|\mathbf{x}_{ijk}, \zeta_{jk}^{(2)}, \zeta_{k}^{(3)})] = \mathbf{x}'_{ijk}\boldsymbol{\beta} + \zeta_{jk}^{(2)} + \zeta_{k}^{(3)}$$

  - Level 3: $\zeta_k^{(3)}|\mathbf{x}_{ijk} \sim N(0, \psi^{(3)})$
    independent across hospitals
    $\psi^{(3)}$ is residual between-hospital variance
  - Level 2: $\zeta_{jk}^{(2)}|\mathbf{x}_{ijk}, \zeta_k^{(3)} \sim N(0, \psi^{(2)})$
    independent across doctors, independent of $\zeta_k^{(3)}$
    $\psi^{(2)}$ is residual between-doctor, within-hospital variance

- `gllamm` command:

```
gllamm abuse age temp Paymed Selfmed Wrdiag DRed WHO, ///
   i(doc hosp) link(logit) family(binom) adapt
```

Maximum likelihood estimates

	No covariates		Full model		
Parameter	Est	(SE)	Est	(SE)	(OR)
β_0 [Cons]	0.87	(0.14)	1.52	(0.46)	
β_1 [Age]			0.14	(0.07)	1.15
β_2 [Temp]			−0.72	(0.10)	0.49
β_3 [Paymed]			0.38	(0.30)	1.46
β_4 [Selfmed]			−0.65	(0.21)	0.52
β_5 [Wrdiag]			1.97	(0.20)	7.18
β_6 [DRed]			−0.20	(0.10)	0.82
β_7 [WHO]			−1.26	(0.32)	0.28
$\psi^{(2)}$	0.20		0.14		
$\psi^{(3)}$	0.36		0.19		
Log-likelihood	−512.14		−415.76		

using `gllamm` with adaptive quadrature

Distributions of random effects and responses

- Vector of all random intercepts for hospital k

$$\boldsymbol{\zeta}_{k(3)} \equiv (\zeta_{1k}^{(2)}, \ldots, \zeta_{J_k k}^{(2)}, \zeta_k^{(3)})'$$

- Random effects distribution [Prior distribution]

$$\varphi(\boldsymbol{\zeta}_{k(3)}), \quad \varphi(\zeta_{jk}^{(2)}), \quad \varphi(\zeta_k^{(3)}), \quad \text{all (multivariate) normal}$$

- Conditional response distribution of all responses $\mathbf{y}_{k(3)}$ for hospital k, given all covariates $\mathbf{X}_{k(3)}$ and all random effects $\boldsymbol{\zeta}_{k(3)}$ for hospital k [Likelihood]

$$f(\mathbf{y}_{k(3)}|\mathbf{X}_{k(3)}, \boldsymbol{\zeta}_{k(3)}) = \prod_{\substack{\text{all docs } j \\ \text{in hosp } k}} \; \prod_{\substack{\text{all patients } i \\ \text{of doc } j}} f(y_{ijk}|\mathbf{x}_{ijk}, \zeta_{jk}^{(2)}, \zeta_k^{(3)})$$

Posterior distribution

- Use Bayes theorem to obtain posterior distribution of random effects given the data:

$$\omega(\boldsymbol{\zeta}_{k(3)}|\mathbf{y}_{k(3)},\mathbf{X}_{k(3)}) = \frac{\varphi(\boldsymbol{\zeta}_{k(3)})f(\mathbf{y}_{k(3)}|\mathbf{X}_{k(3)},\boldsymbol{\zeta}_{k(3)})}{\int\varphi(\boldsymbol{\zeta}_{k(3)})f(\mathbf{y}_{k(3)}|\mathbf{X}_{k(3)},\boldsymbol{\zeta}_{k(3)})\mathrm{d}\boldsymbol{\zeta}_{k(3)}}$$

$$\propto \varphi(\zeta_k^{(3)})\prod_j \varphi(\zeta_{jk}^{(2)})\prod_i f(y_{ijk}|\mathbf{x}_{ijk},\zeta_{jk}^{(2)},\zeta_k^{(3)})$$

- Denominator, marginal likelihood contribution for hospital k, simplifies

$$\int\varphi(\zeta_k^{(3)})\prod_j\left[\int\varphi(\zeta_{jk}^{(2)})\prod_i f(y_{ijk}|\mathbf{x}_{ijk},\zeta_{jk}^{(2)},\zeta_k^{(3)})\,\mathrm{d}\zeta_{jk}^{(2)}\right]\mathrm{d}\zeta_k^{(3)}$$

Empirical Bayes prediction of random effects

- Empirical Bayes (EB) prediction is mean of posterior distribution

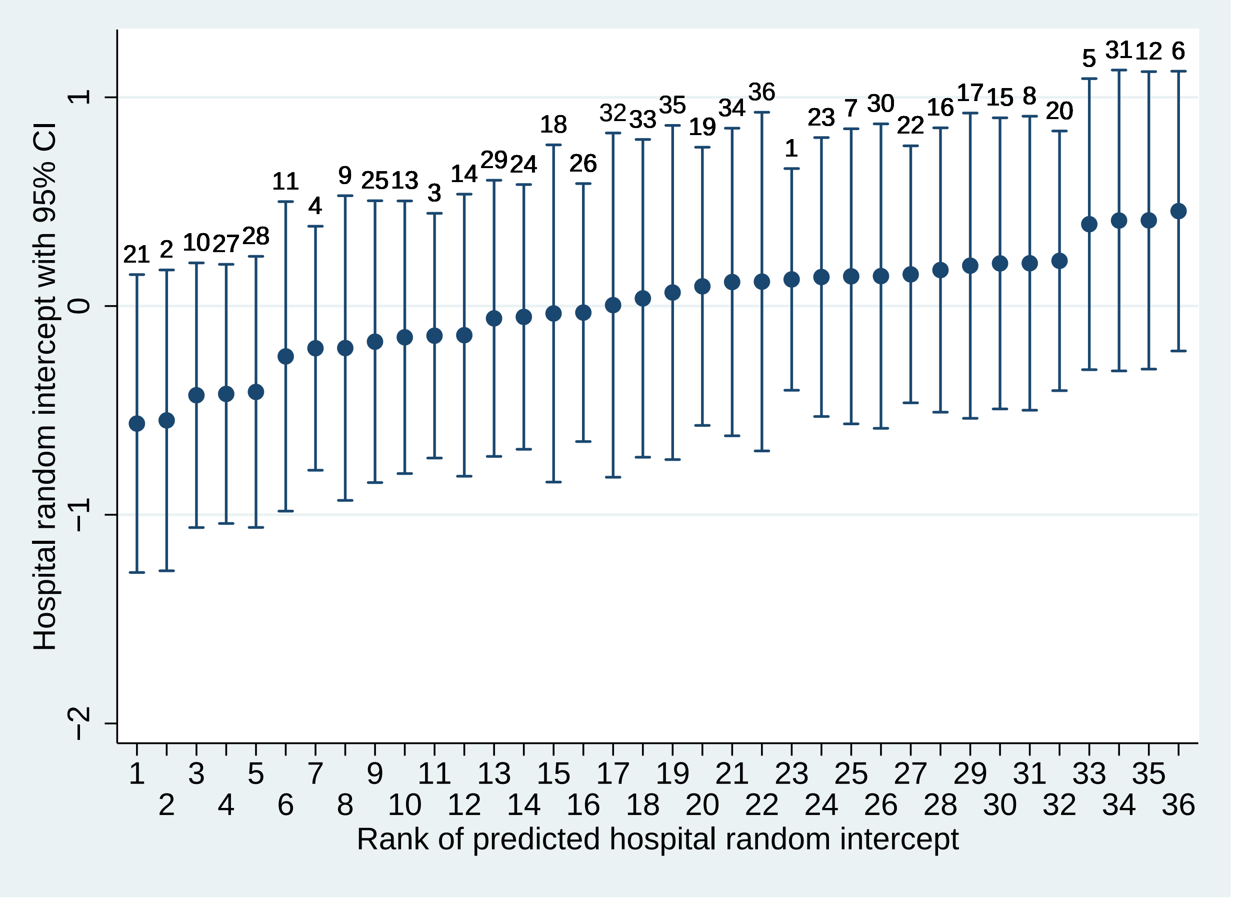
$$\widetilde{\boldsymbol{\zeta}}_{k(3)} = \int \boldsymbol{\zeta}_{k(3)}\, \omega(\boldsymbol{\zeta}_{k(3)}|\mathbf{y}_{k(3)}, \mathbf{X}_{k(3)})\, \mathrm{d}\boldsymbol{\zeta}_{k(3)}$$

- Standard error of EB is standard deviation of posterior distribution
- Using `gllapred` with the u option

```
gllapred eb, u
```

  - `ebm1` contains $\widetilde{\zeta}_{jk}^{(2)}$
  - `ebs1` contains SE($\widetilde{\zeta}_{jk}^{(2)}$)
  - `ebm2` contains $\widetilde{\zeta}_{k}^{(3)}$
  - `ebs2` contains SE($\widetilde{\zeta}_{k}^{(3)}$)
- For approximately normal posterior, use Wald-type interval, e.g., for hospital k, 95% CI is $\widetilde{\zeta}_{k}^{(3)} \pm 1.96$ SE($\widetilde{\zeta}_{k}^{(3)}$)

Confidence intervals for hospital random effects



- $\widetilde{\zeta}_k^{(3)} \pm 1.96\,\text{SE}(\widetilde{\zeta}_k^{(3)})$
- Identify the good and bad with caution

Predicted probability for patient of hypothetical doctor

- Predicted **conditional probability** for hypothetical values $\mathbf{x}^0$ of the covariates and ζ^0 of the random intercepts

$$\widehat{\text{Pr}}(y = 1|\mathbf{x}^0, \boldsymbol{\zeta}^0) \;=\; \frac{\exp(\mathbf{x}^{0\prime}\widehat{\boldsymbol{\beta}} + \zeta^{(2)0} + \zeta^{(3)0})}{1 + \exp(\mathbf{x}^{0\prime}\widehat{\boldsymbol{\beta}} + \zeta^{(2)0} + \zeta^{(3)0})}$$

- If $\zeta^{(2)0} + \zeta^{(3)0} = 0$, median of distribution for $\zeta_{jk}^{(2)} + \zeta_{k}^{(3)}$, then predicted conditional probability is median probability
  - Analogously for other percentiles
- Using `gllapred` with `mu` and `us()` option:

```
replace age = 2 /* etc.: change covariates to x⁰ */
generate zeta1 = 0
generate zeta2 = 0
gllapred probc, mu us(zeta)
```

Predicted probability for new patient of existing doctor in existing hospital

- **Posterior mean probability** for new patient of existing doctor j in hospital k

$$\widetilde{\text{Pr}}_{jk}(y=1|\mathbf{x}^0) = \int \widehat{\text{Pr}}(y=1|\mathbf{x}^0, \boldsymbol{\zeta}_{k(3)})\, \omega(\boldsymbol{\zeta}_{k(3)}|\mathbf{y}_{k(3)}, \mathbf{X}_{k(3)})\, \mathrm{d}\boldsymbol{\zeta}_{k(3)}$$

  - Invent additional patient i^*jk with covariate values $\mathbf{x}_{i^*jk} = \mathbf{x}^0$
  - Make sure that invented observation does not contribute to posterior $\omega(\boldsymbol{\zeta}_{k(3)}|\mathbf{y}_{k(3)}, \mathbf{X}_{k(3)})$

$$\omega(\boldsymbol{\zeta}_{k(3)}|\mathbf{y}_{k(3)}, \mathbf{X}_{k(3)}) \propto \varphi(\zeta_k^{(3)}) \prod_j \varphi(\zeta_{jk}^{(2)}) \prod_{i \neq i^*} f(y_{ijk}|\mathbf{x}_{ijk}, \zeta_{jk}^{(2)}, \zeta_k^{(3)})$$

  - Cannot simply plug in EB prediction $\widetilde{\boldsymbol{\zeta}}_{k(3)}$ for $\boldsymbol{\zeta}_{k(3)}$

$$\widetilde{\text{Pr}}_{jk}(y=1|\mathbf{x}^0) \;\neq\; \widehat{\text{Pr}}(y=1|\mathbf{x}^0, \boldsymbol{\zeta}_{k(3)} = \widetilde{\boldsymbol{\zeta}}_{k(3)})$$

Prediction dataset: One new patient per doctor

Data (ignore gaps)

id	doc	hosp	abuse
1	1	1	0
2	1	1	1
3	2	2	0
4	3	2	1
5	3	2	1

Data with invented observations

id	doc	hosp	abuse
1	1	1	0
2	1	1	1
.	1	1	.
3	2	2	0
.	2	2	.
4	3	2	1
5	3	2	1
.	3	2	.

- Response variable **abuse** must be missing for invented observations
- Use required value of **doc**
- Can invent several patients per doctor

Prediction dataset:
One new patient per doctor (continued)

Data with invented observations

				terms for posterior		
id	**doc**	**hosp**	**abuse**	hospital	doctor	patient
1	**1**	**1**	**0**	$\varphi(\zeta_1^{(3)})$	$\varphi(\zeta_{11}^{(2)})$	$f(y_{111}\|\zeta_1^{(3)}, \zeta_{11}^{(2)})$
2	**1**	**1**	**1**			$f(y_{211}\|\zeta_1^{(3)}, \zeta_{11}^{(2)})$
.	**1**	**1**	**.**			1
3	**2**	**2**	**0**	$\varphi(\zeta_2^{(3)})$	$\varphi(\zeta_{22}^{(2)})$	$f(y_{322}\|\zeta_2^{(3)}, \zeta_{22}^{(2)})$
.	**2**	**2**	**.**			1
4	**3**	**2**	**1**		$\varphi(\zeta_{32}^{(2)})$	$f(y_{432}\|\zeta_2^{(3)}, \zeta_{32}^{(2)})$
5	**3**	**2**	**1**			$f(y_{532}\|\zeta_2^{(3)}, \zeta_{32}^{(2)})$
.	**3**	**2**	**.**			1

- Using `gllapred` with `mu` and `fsample` options:

```
gllapred probd, mu fsample
```

Predicted probability for new patient of new doctor in existing hospital

- Posterior mean probability for new patient of new doctor in existing hospital k

$$\widetilde{\Pr}_k(y=1|\mathbf{x}^0) = \int \widehat{\Pr}(y=1|\mathbf{x}^0, \boldsymbol{\zeta}^*_{k(3)})\, \omega(\boldsymbol{\zeta}^*_{k(3)}|\mathbf{y}_{k(3)}, \mathbf{X}_{k(3)})\, \mathrm{d}\boldsymbol{\zeta}^*_{3(k)}$$

  - Invent additional observation i^*j^*k with covariates in $\mathbf{x}_{i^*j^*k} = \mathbf{x}^0$
  - $\boldsymbol{\zeta}^*_{k(3)} = (\zeta^{(2)}_{j^*k}, \boldsymbol{\zeta}'_{k(3)})'$
  - Make sure that invented doctor **but not invented patient** contribute to posterior $\omega(\boldsymbol{\zeta}^*_{k(3)}|\mathbf{y}_{k(3)}, \mathbf{X}_{k(3)})$

$$\omega(\boldsymbol{\zeta}^*_{k(3)}|\mathbf{y}_{k(3)}, \mathbf{X}_{k(3)}) \propto \overbrace{\varphi(\zeta^{(2)}_{j^*k})}^{\text{Prior}}\, \omega(\boldsymbol{\zeta}_{k(3)}|\mathbf{y}_{k(3)}, \mathbf{X}_{k(3)})$$

Prediction dataset: One new doctor and patient per hospital

Data (ignore gaps)

id	doc	hosp	abuse
1	1	1	0
2	1	1	1
3	2	2	0
4	3	2	1
5	3	2	1

Data with invented observations

id	doc	hosp	abuse
1	1	1	0
2	1	1	1
.	0	1	.
3	2	2	0
4	3	2	1
5	3	2	1
.	0	2	.

- Response variable **`abuse`** must be missing for invented observations
- Use unique (for that hospital) value of **`doc`**
- Can invent several new docs which can all have the same value of **`doc`**

Prediction dataset: One new doctor and patient per hospital (continued)

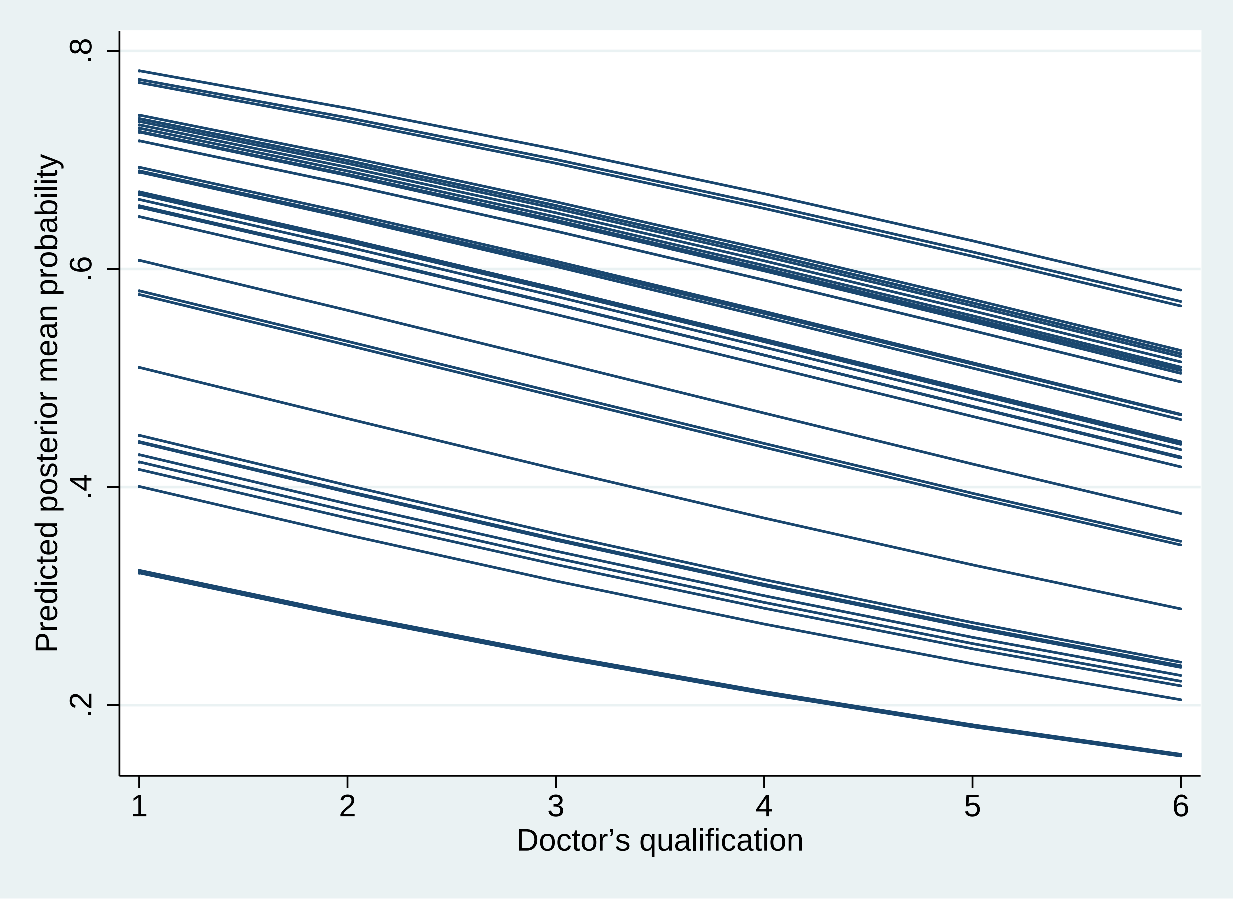
Data with invented observations

				terms for posterior		
id	**doc**	**hosp**	**abuse**	hospital	doctor	patient
1	**1**	**1**	**0**	$\varphi(\zeta_1^{(3)})$	$\varphi(\zeta_{11}^{(2)})$	$f(y_{111}\|\zeta_1^{(3)}, \zeta_{11}^{(2)})$
2	**1**	**1**	**1**			$f(y_{211}\|\zeta_1^{(3)}, \zeta_{11}^{(2)})$
.	**0**	**1**	**.**		$\varphi(\zeta_{01}^{(2)})$	1
3	**2**	**2**	**0**	$\varphi(\zeta_2^{(3)})$	$\varphi(\zeta_{22}^{(2)})$	$f(y_{322}\|\zeta_2^{(3)}, \zeta_{22}^{(2)})$
4	**3**	**2**	**1**		$\varphi(\zeta_{32}^{(2)})$	$f(y_{432}\|\zeta_2^{(3)}, \zeta_{32}^{(2)})$
5	**3**	**2**	**1**			$f(y_{532}\|\zeta_2^{(3)}, \zeta_{32}^{(2)})$
.	**0**	**2**	**.**		$\varphi(\zeta_{02}^{(2)})$	1

- Using `gllapred` with `mu` and `fsample` options:

```
gllapred probh, mu fsample
```

Example: Predicted probability for new patient of new doctor in existing hospital

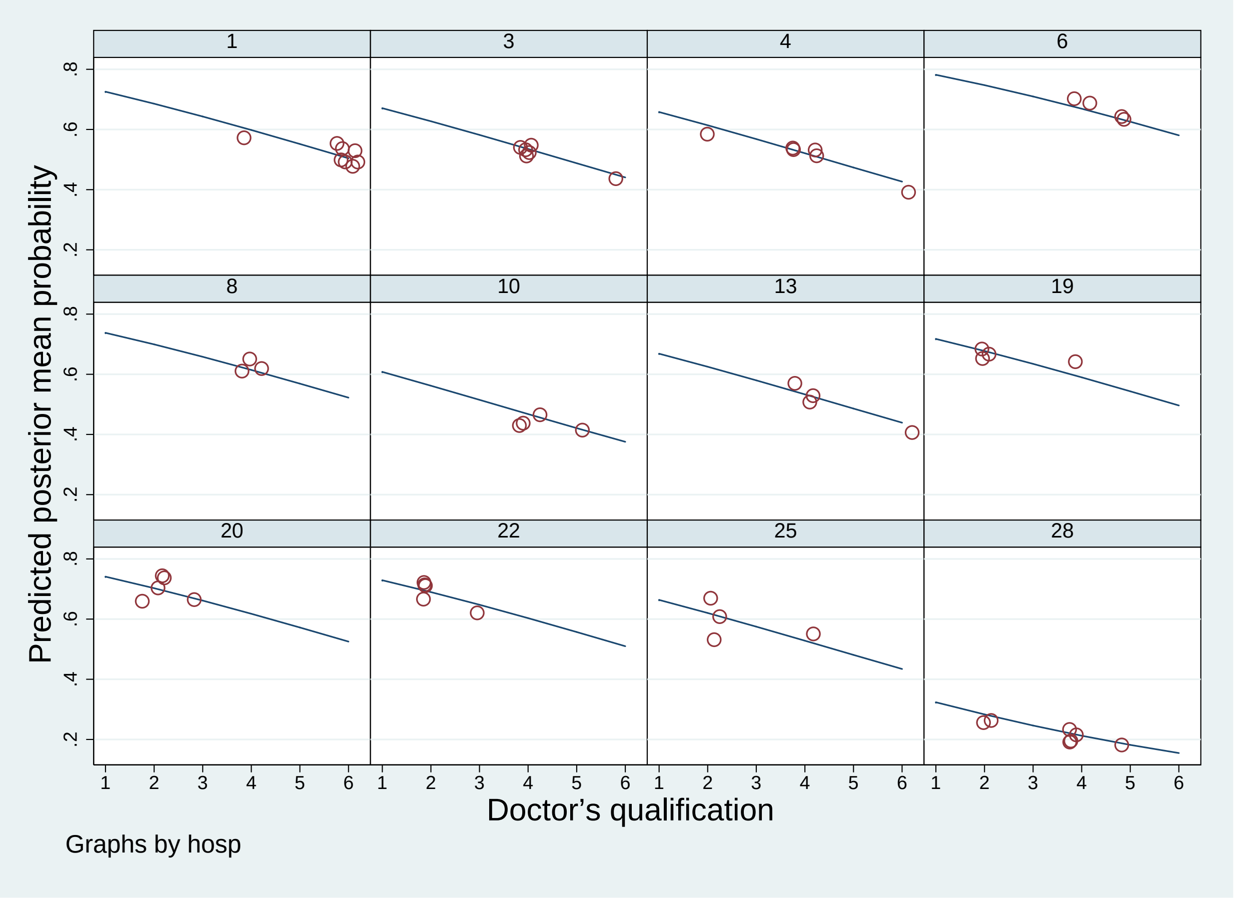


- Each curve represents a hospital

  For each hospital: 6 new doctors with [DRed] $= 1, 2, 3, 4, 5, 6$

  For each doctor: 1 new patient with [Age] $= 2$, [Temp] $= 1$ ($37°C$), [Paymed] $= 0$, [Selfmed] $= 0$, [Wrdiag] $= 0$

Example: Predicted probability for new patient of existing doctor in existing hospital



- 12 of the hospitals, with curves as in previous slide
- Dots represent doctors with [DRed] as observed

  For each doctor: predicted probability for 1 new patient with [Age] $= 2$, [Temp] $= 1$, [Paymed] $= 0$, [Selfmed] $= 0$, [Wrdiag] $= 0$

Predicted probability for new patient of new doctor in new hospital

- Population-averaged or **marginal probability**:

$$\overline{\text{Pr}}(y=1|\mathbf{x}^0) \quad = \quad \int \widehat{\text{Pr}}(y=1|\mathbf{x}^0, \zeta_{jk}^{(2)}, \zeta_k^{(3)})\, \varphi(\zeta_{jk}^{(2)}), \varphi(\zeta_k^{(3)})\, \mathrm{d}\zeta_{jk}^{(2)} \mathrm{d}\zeta_k^{(3)}$$

- Cannot plug in means of random intercepts

$$\overline{\text{Pr}}(y=1|\mathbf{x}^0) \quad \neq \quad \widehat{\text{Pr}}(y=1|\mathbf{x}^0, \zeta_{jk}^{(2)}=0, \zeta_k^{(3)}=0)$$

mean ≠ median

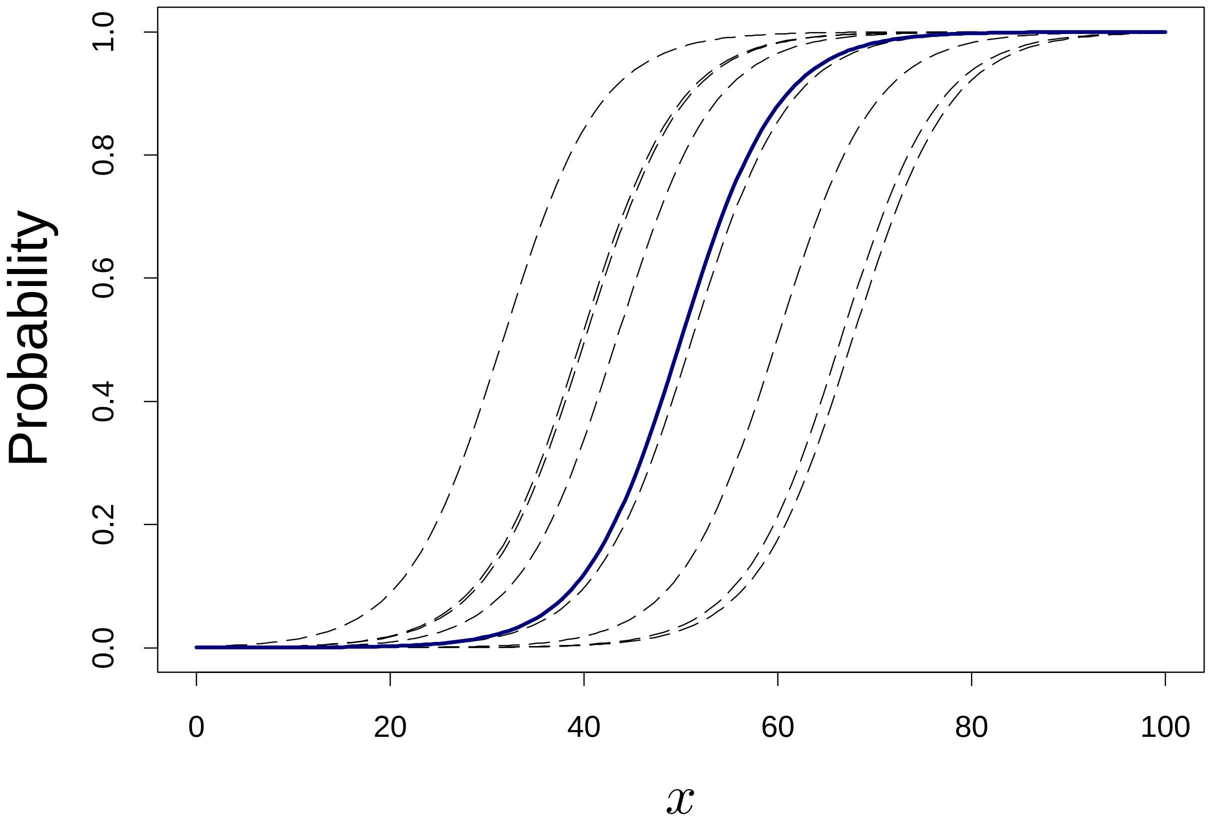
- Using `gllapred` with the `mu` and `marg` options:

```
gllapred prob, mu marg fsample
```

- Confidence interval, by sampling parameters from the estimated asymptotic sampling distribution of their estimates

```
ci_marg_mu lower upper, level(95) dots
```

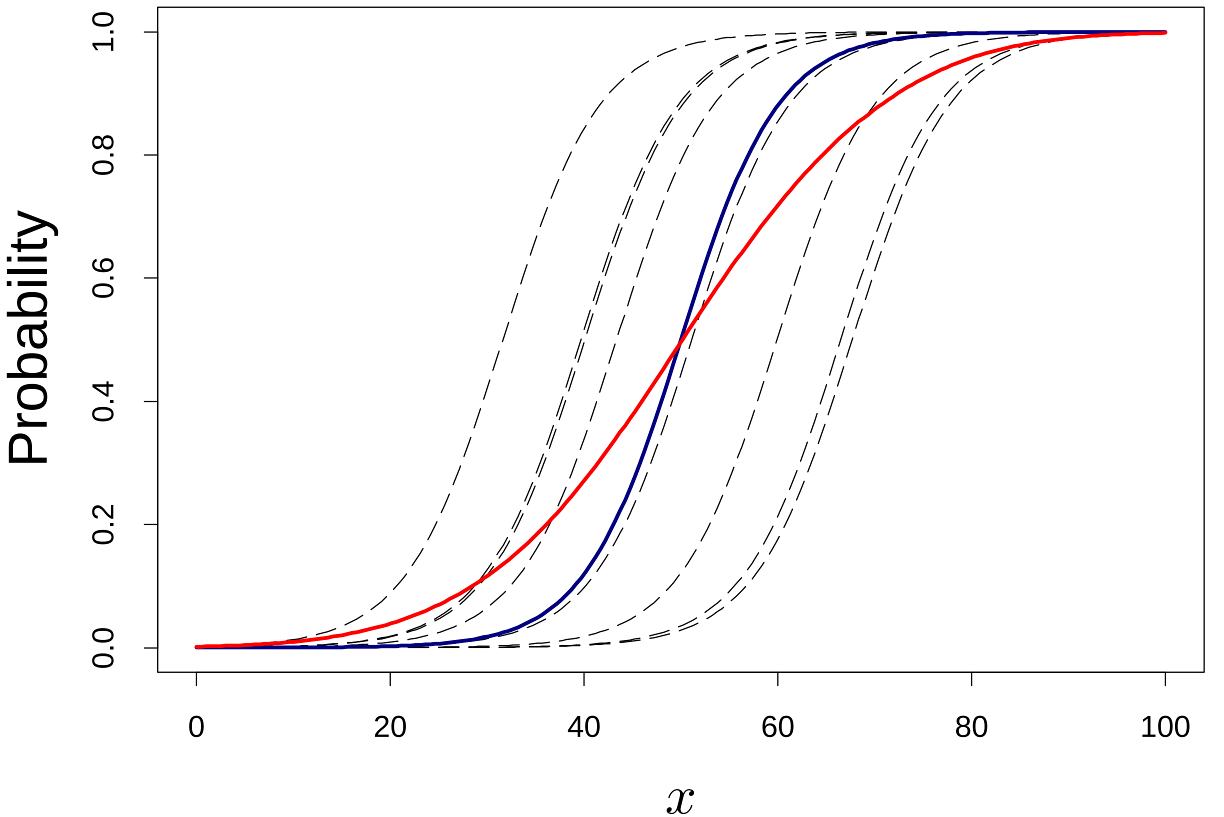
Illustration Cluster-specific: versus population averaged probability



- - - - - cluster-specific (random sample)

——— median

Illustration Cluster-specific: versus population averaged probability

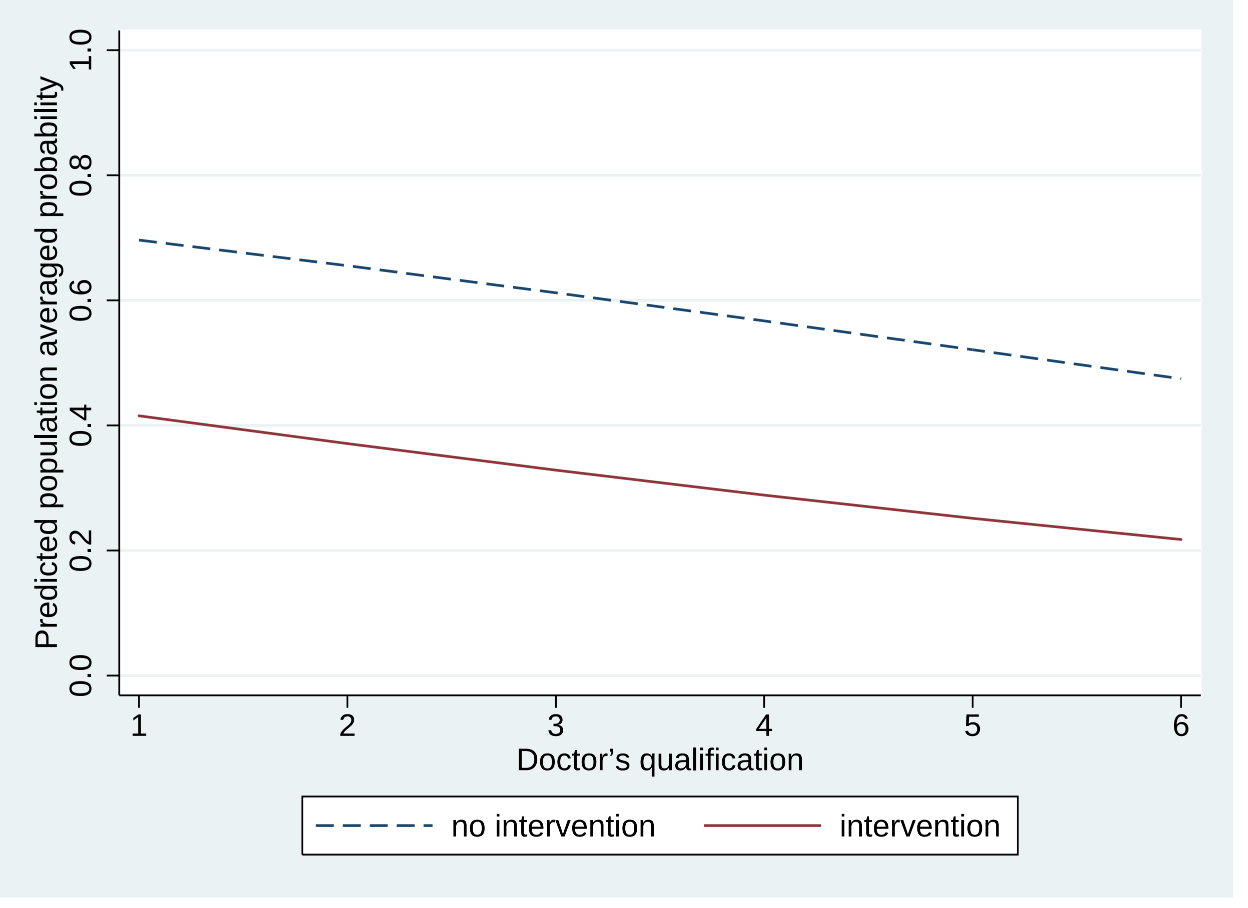


- - - - - cluster-specific (random sample)

—— median

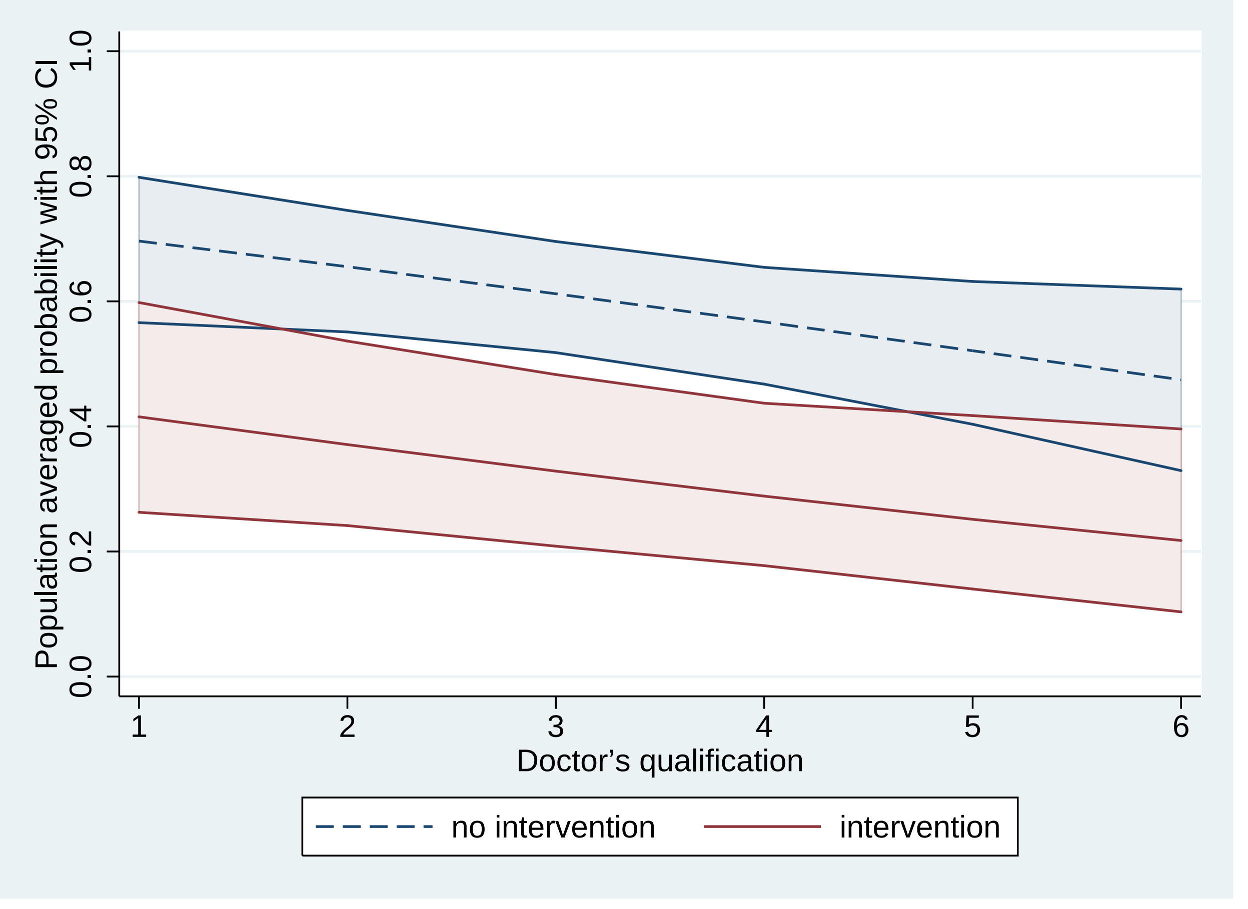
—— population averaged

Example: Predicted probability for new patient of new doctor in new hospital



- Same patient covariates as before
-

Example: Predicted probability for new patient of new doctor in new hospital

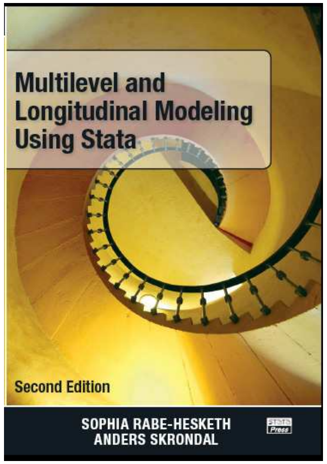


- Same patient covariates as before
- Confidence bands represent parameter uncertainty

Concluding remarks

- Discussed:
  - Empirical Bayes (EB) prediction of random effects and CI using `gllapred`, ignoring parameter uncertainty
  - Prediction of different kinds of probabilities using `gllapred` after careful preparation of prediction dataset
  - Simulation-based CI for predicted marginal probabilities using new command `ci_marg_mu`
- Methods work for any GLLAMM model, including random-coefficient models and models for ordinal, nominal or count data
- Assumed normal random effects distribution
  - EB predictions not robust to misspecification of distribution
  - Could use nonparametric maximum likelihood in `gllamm`, followed by same `gllapred` and `ci_marg_mu` commands

References

- 

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