A Novel Method for Expediting the Development of Patient-Reported Outcome Measures

Lili Garrard, M.S., Ph.D. Candidate

Department of Biostatistics
University of Kansas Medical Center
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Measuring People's Thoughts

Patient-Centered Care

- 2001 IOM – *Crossing the Quality Chasm*
- National priority in the U.S.A
- Patient-reported outcome measures (PROMs)
  - NIH – PROMIS®
  - FDA
  - NQF
  - PCORI

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PROMs Example

- Health-related quality of life (HRQol)
  - Neuro-QoL
- Depression
  - Center for epidemiological studies depression scale (CES-D & CES-D-10)
  - Patient health questionnaire-9 (PHQ-9)
- Cancer
  - PROMIS-Fatigue
  - PROMIS-Pain
- Etc.

Challenges

- Lengthy process
- Small populations or rare diseases
- Limited resources
- Psychometric soundness
  - Reliability - consistency
  - Validity - accuracy

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Reliability

- The extent to which a scale or measure yields reproducible and consistent results
- Goal: “score” or “value” reliability using instruments designed to measure the patient’s or caregiver’s experience under various treatment and/or care conditions
- Estimates of reliability
  - Support the dissemination and use of new instruments in health research
  - Provide one piece of evidence of the psychometric adequacy of an instrument

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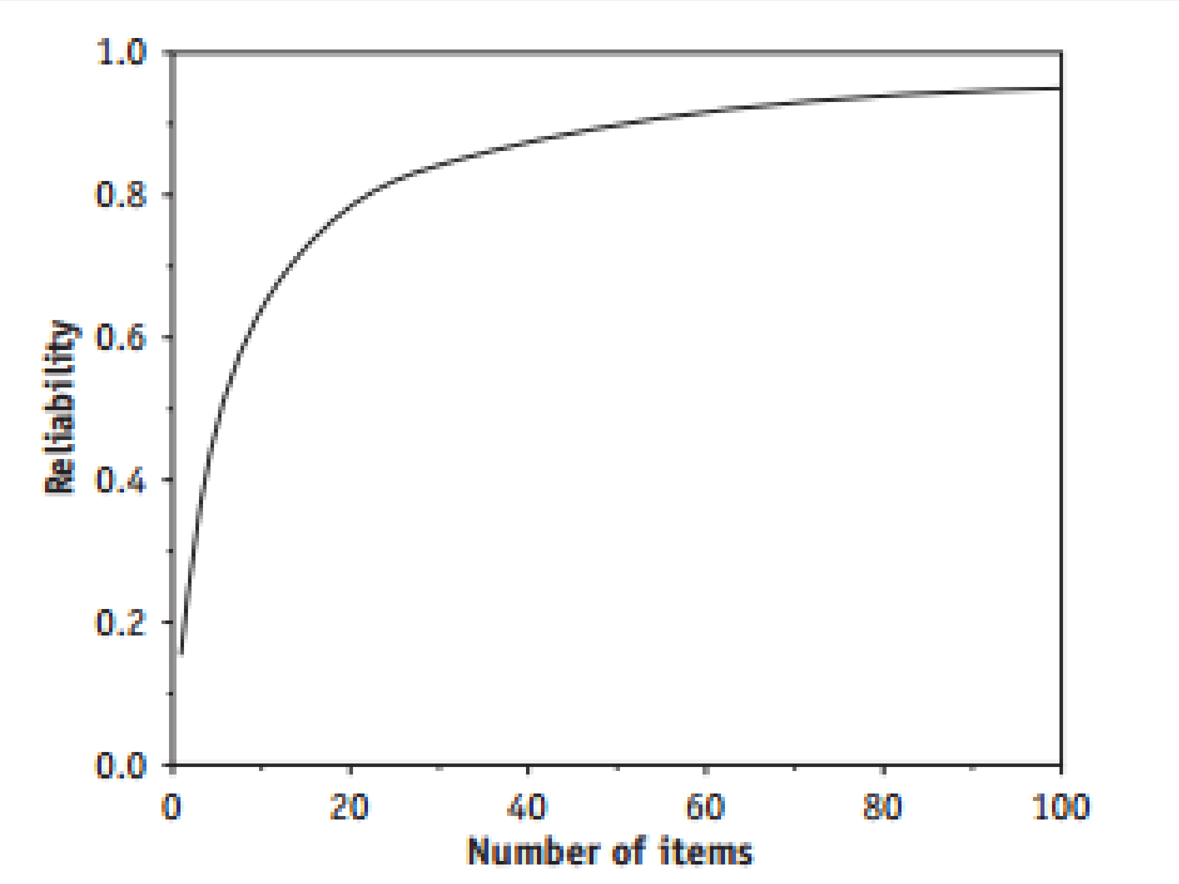
The More Items The Better?



Wainer, H. and Feinberg, R. (2015)

Validity

- The extent to which an instrument measures what it is intended to measure and that it can be useful for its intended purpose
- 3 types:
  - Content validity
  - Construct validity
  - Predictive validity

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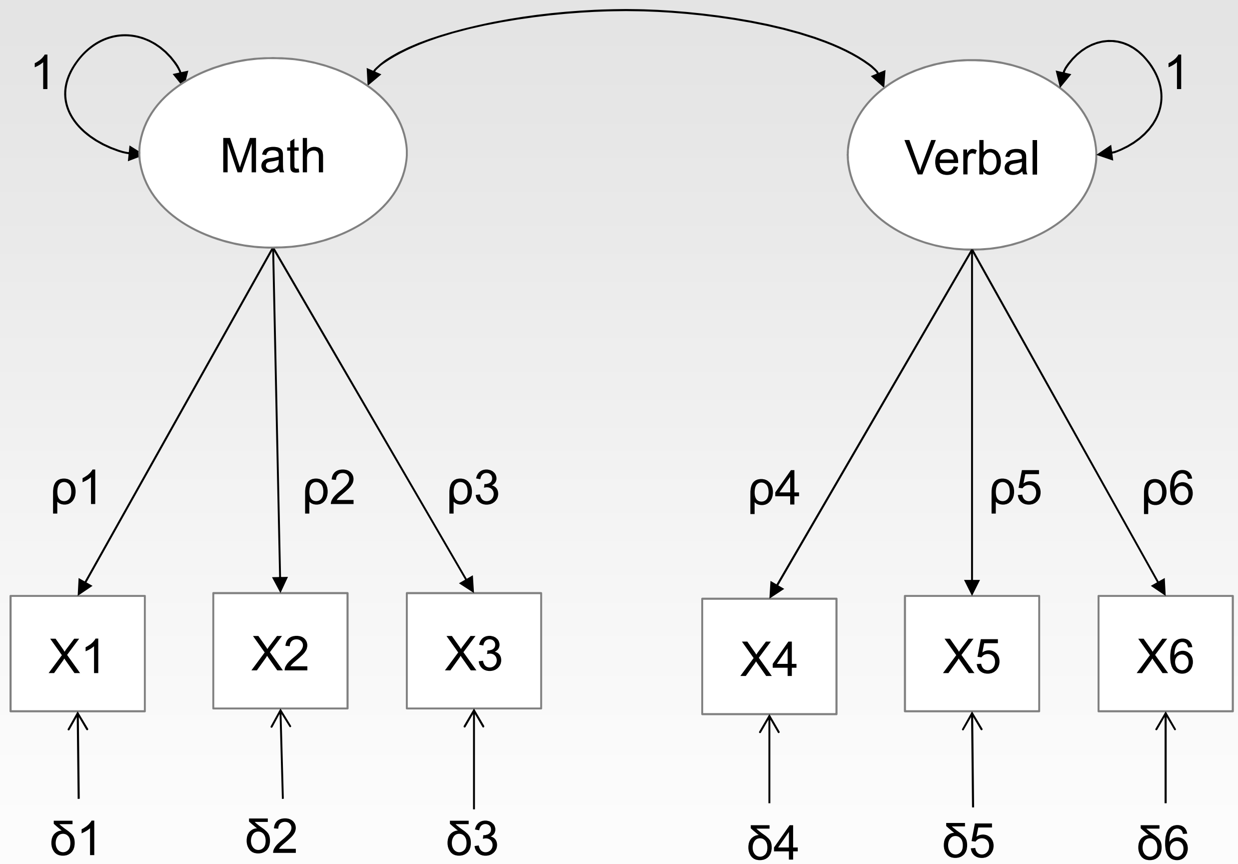
Construct Validity



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Evidence of Construct Validity

- Classical approach: CFA
  - Separate content and construct validity analyses
  - Large sample size requirement
  - Models ordinal data as continuous
    - Ordinal CFA (Mplus; R *lavaan*)
- Bayesian approach: OBID
  - Seamlessly integrates content and construct validity analyses
  - Overcomes small sample size issue
  - Models ordinal data as ordinal
  - Utilizes fast, reliable, and free software

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Study Aims

- Aim 1: to test Ordinal Bayesian Instrument Development (OBID) by comparing its performance to classical instrument development with exact estimation procedures, using simulation data

- Aim 2: to test OBID across a variety of patient populations

- Aim 3: to disseminate Classical and Bayesian Instrument Development (CBID) software for evaluation by investigators in other research communities

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OBID

- Extension of
  - Gajewski et al. (2012): approximate equivalency of relevance scale vs. correlation scale in establishing content validity
  - Gajewski et al. (2013): IACCV
  - Jiang et al. (2014): BID
- Bayesian IRT with a probit link
- Prior elicitation from content experts' data or reference data
  - WinBUGS
- *MCMCpack* (Martin, Quinn and Park, 2011)
  - *MCMCordfactanal* function

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Expert Model

$$x_{jk} = \begin{cases} 1 \text{ "not relevant"} & \text{if } 0.00 \le \rho_{jk} < 0.10 \\ 2 \text{ "somewhat relevant"} & \text{if } 0.10 \le \rho_{jk} < 0.30 \\ 3 \text{ "quite relevant"} & \text{if } 0.30 \le \rho_{jk} < 0.50 \\ 4 \text{ "highly relevant"} & \text{if } 0.50 \le \rho_{jk} \le 1.00 \end{cases}$$

- $k = 1, \dots, K, j = 1, \dots, P$
- ρ_{jk}: *k*th expert's latent item-to-domain correlation for the *j*th item
- ρ_j: item-to-domain correlation based on pooled information from all experts
- Fisher's transformation:

$$\mu_j = g(\rho_j) = \frac{1}{2} log \frac{1+\rho_j}{1-\rho_j} \sim N\left(g(\rho_{0j}), \frac{1}{n_{0j}}\right)$$

- Hierarchical model:

$$g(\rho_{jk}) = g(\rho_j) + e_{jk};\ e_{jk} \sim N(0, \sigma^2)$$

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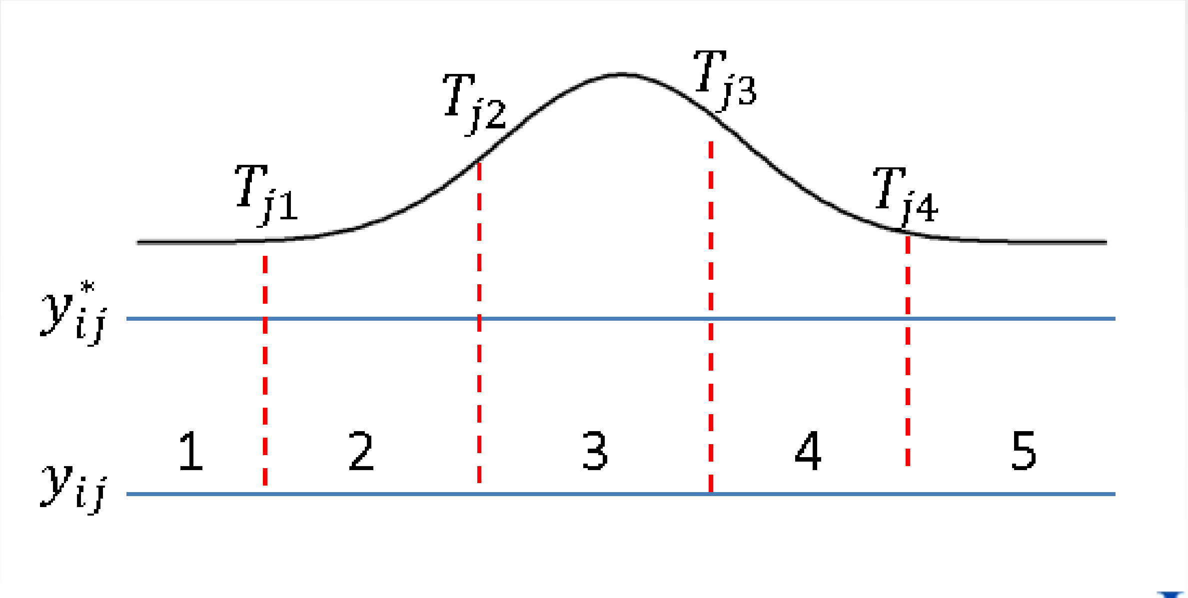
Participant Model

$$y_{ij} = c \text{ if } y^*_{ij} \in \left(T_{j(c-1),} T_{jc}\right]$$

$$y^*_{ij} = \alpha_j + \lambda_j f_i + \varepsilon_{ij} \; ; \; f_i \sim N(0,1), \varepsilon_{ij} \sim N(0,1)$$

$$i = 1, \ldots, N, j = 1, \ldots, P, c = 1, \ldots, C_j$$



Participant Model Cont.

- Likelihood

$$L(y^*|\alpha,\lambda,f)=\prod_{i=1}^{N}\prod_{j=1}^{P}N(y_{ij}^*\,|\alpha_j+\lambda_j f_i\ \ ,1)$$

- Priors

$$\alpha_j\sim N(0,1),\ \lambda_j\sim N\left(\frac{exp\left(2\mu_j\right)-1}{2exp(\mu_j)},\frac{\left(exp\left(2\mu_j\right)+1\right)^2}{4n_{0j}\,exp\left(2\mu_j\right)}\right)$$

$$\mu_j\sim N\left(g\left(\rho_{0j}\right),\frac{1}{n_{0j}}\right),n_{0j}=5K$$

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Aim 1: Simulation Study

Simulation Parameters

- Assume unidimensional model

N (Sample size)	50, 100, 200, 500
P (# of items)	4, 6, 9
C (# of response options)	2, 5, 7
K (# of experts)	2, 3, 6, 16
True ρ^T	Mixture of 0.3, 0.5, 0.7
Unbiased Experts ρ_0	Same as True ρ^T
Moderately Biased Experts ρ_0	Mixture of 0.4, 0.6, 0.8
Highly Biased Experts ρ_0	Mixture of 0.65, 0.75, 0.85

- 144 simulation scenarios for each type of expert ρ_0

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Simulation Strategy

1. Simulate standardized z_{ij}^* based on the classical factor model and convert to y_{ij}^*

$$z_{ij}^* = \rho_j^T f_i^T + e_{ij};\ f_i^T \sim N(0,1),\ e_{ij} \sim N\left(0, 1 - \{\rho_j^T\}^2\right)$$

$$\lambda_j = \frac{\rho_j}{\sqrt{1-\rho_j^2}} \rightarrow \rho_j = \frac{\lambda_j}{\sqrt{1+\lambda_j^2}}$$

2. Convert y_{ij}^* to ordinal responses y_{ij} using percentile-based cut points

$$y_{ij} = c \text{ if } y_{ij}^* \in \left(T_{j(c-1),} T_{jc}\right]$$

- C=2: 50th percentile of standard normal
- C>2: $\left(\frac{1}{C}, \ldots, \frac{C-1}{C}\right)$th percentile of standard normal

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Simulation Strategy Cont.

3. Define priors for the IRT model parameters
4. Select tuning parameters to ensure 20% - 50% acceptance rate (trial and error)
   - N=50: 1.0
   - N=100: 0.7
   - N=200: 0.5
   - N=500: 0.3
5. Fit IRT model via *MCMCpack* on the simulated datasets and estimate ρ_j
6. Fit ordinal CFA model via *lavaan* on the simulated datasets and estimate ρ_j
7. Perform 100 simulations for each of the scenarios defined by the simulation parameters

MSE & Bias

- $\hat{\rho}_j(s)$: OBID posterior mean or CFA parameter estimate of sth iteration for the jth item
- $\bar{\rho}_j = \frac{\sum_{s=1}^{100} \hat{\rho}_j(s)}{100}$
- $MSE(\hat{\rho}_j) = \frac{\sum_{s=1}^{100}\left(\hat{\rho}_j(s)-\rho_j^T\right)^2}{100}$
- $\overline{MSE} = \frac{\sum_{j=1}^{P} MSE(\hat{\rho}_j)}{P}$
- $\left[Bias(\hat{\rho}_j, \rho_j^T)\right]^2 = \left(\bar{\rho}_j - \rho_j^T\right)^2$
- $\overline{Bias^2} = \frac{\sum_{j=1}^{P}\left[Bias(\hat{\rho}_j, \rho_j^T)\right]^2}{P}$

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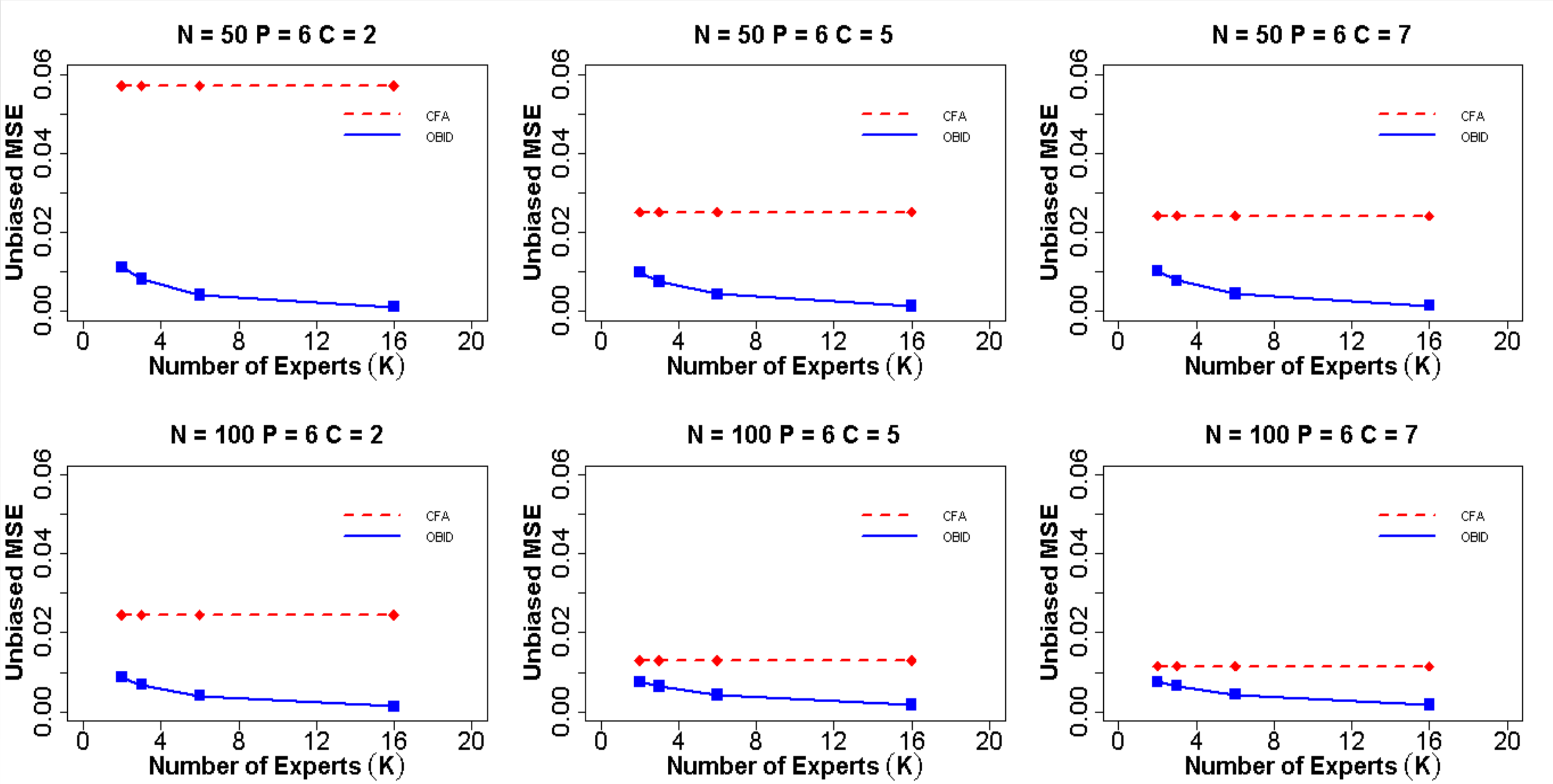
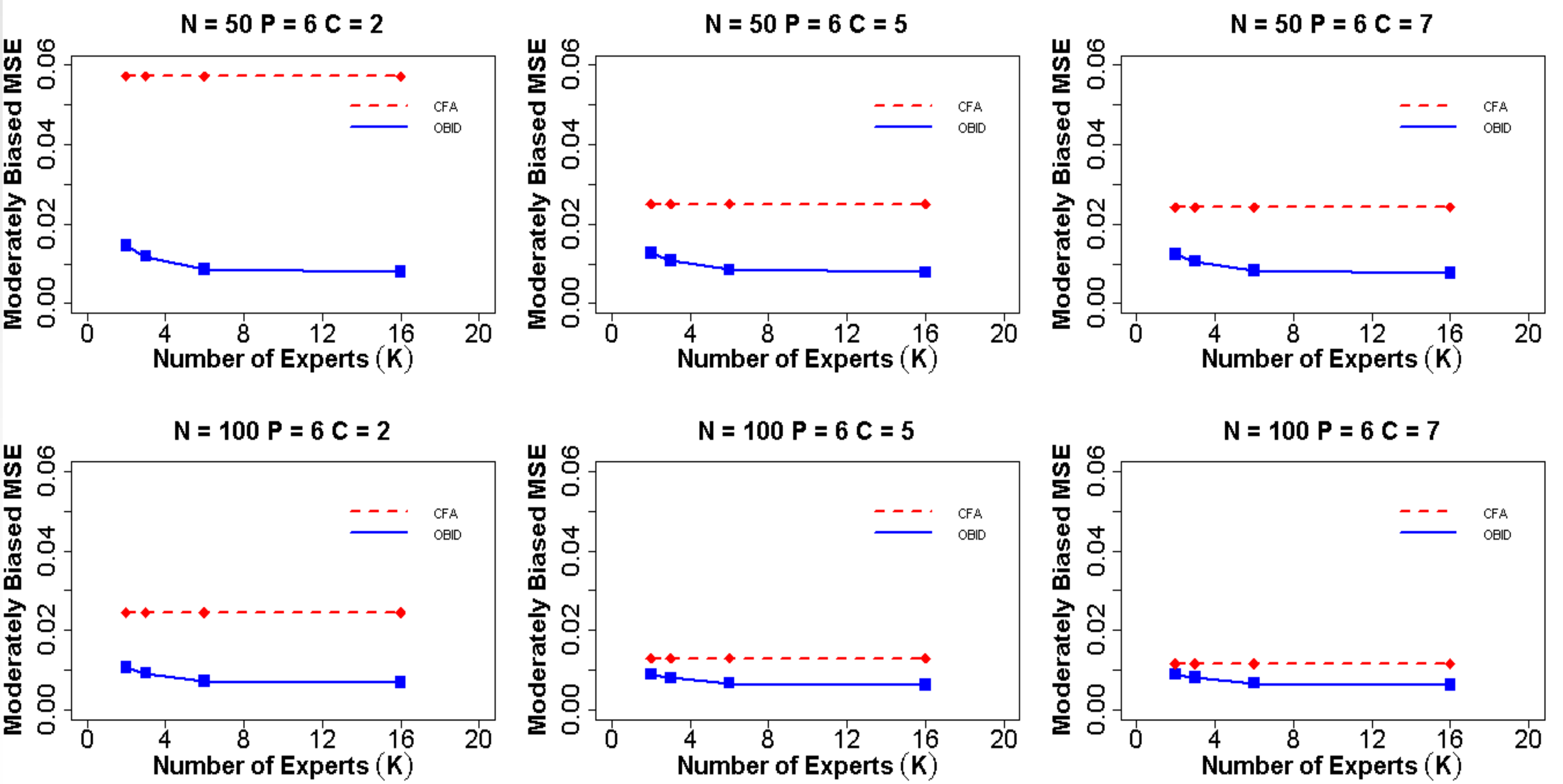
ρ MSE: Unbiased

- ρ_0=(0.3,0.5,0.7,0.7,0.3,0.5)



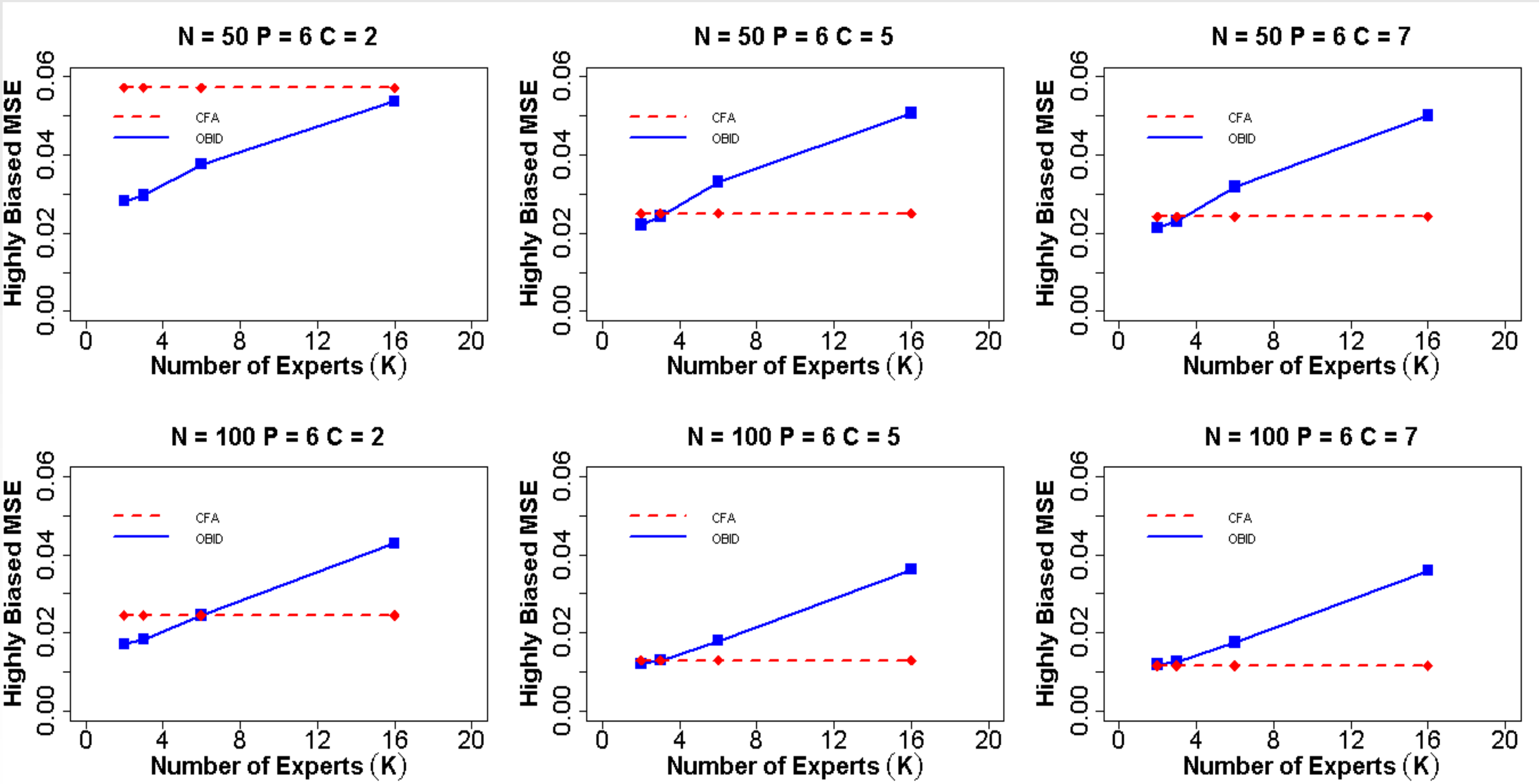
ρ MSE: Moderately Biased

- ρ_0=(0.4,0.6,0.8,0.8,0.4,0.6)



ρ MSE: Highly Biased

- ρ_0=(0.65,0.75,0.85,0.85,0.65,0.75)



Summary

- Overall, OBID outperforms ordinal CFA
  - Use highly biased experts with caution
- Most superior when
  - Smaller sample size: 50 and 100
  - Binary response options
- Trade-off: larger bias, smaller MSEs
- 6 experts will be sufficient (3 if highly biased)

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Discussion: General Prior

- Lack of appropriate content information
- Reliable and relevant external (reference) data available
  - Not necessarily experts
  - Down weigh the prior sample size

- Example: Use adult population as prior for pediatric population PROMs development

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Aim 2: Real Data Application

Model Comparison

- Bayesian model comparison
  - Informative vs. flat prior
  - Predictive model accuracy
- Cross-validation
  - DIC: conditioning on posterior mean—pointwise measure
  - WAIC: averaging over posterior distribution—fully Bayesian
  - Bayesian LOO-CV: asymptotically equal to WAIC
    - Applicable for small *n*

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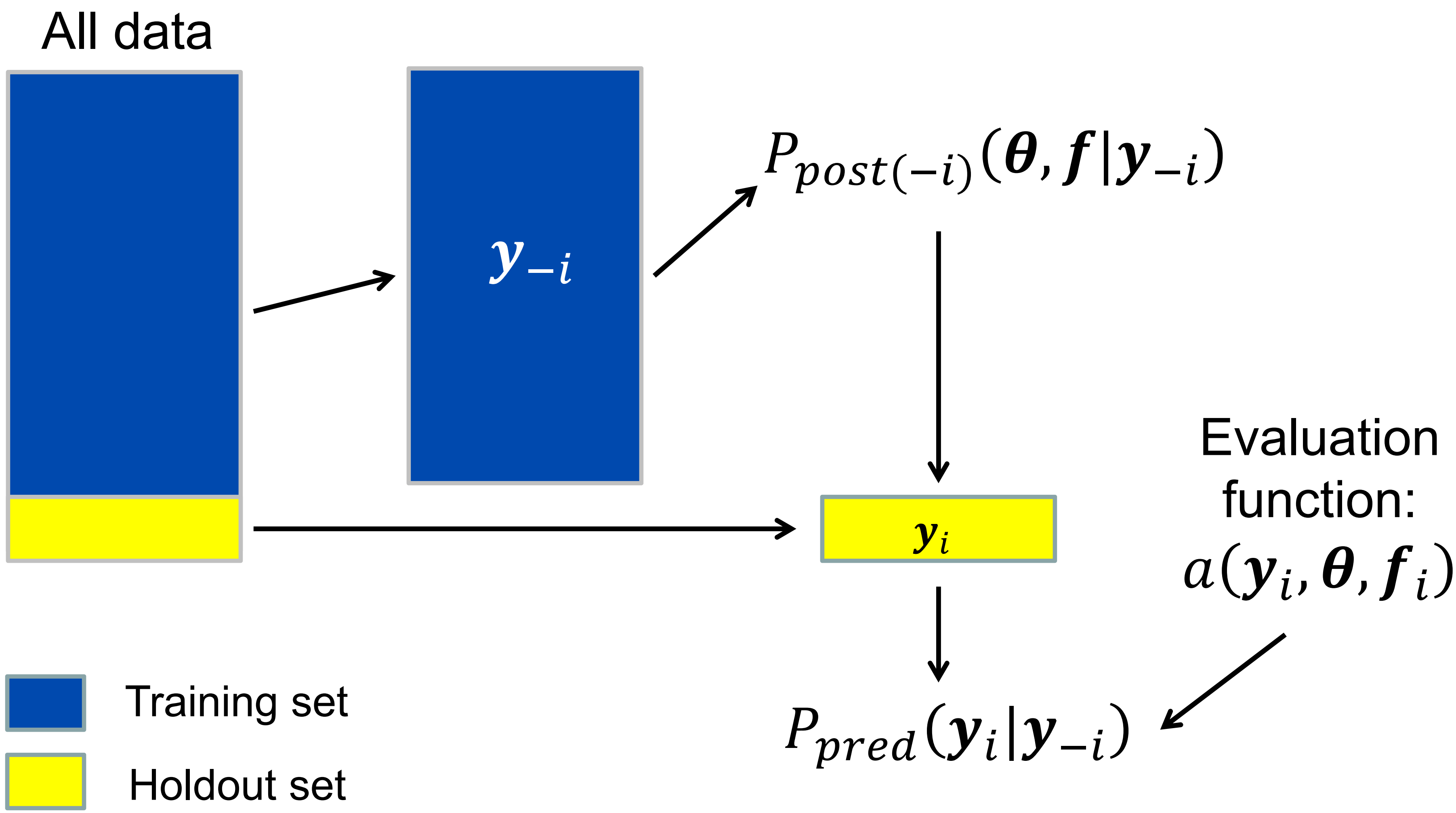
LOO-CV Method



LOO-CV Method Cont.

- CV posterior predictive evaluation

$$E_{post(-i)}\{a(\boldsymbol{y}_i, \boldsymbol{\theta}, \boldsymbol{f}_i)\} = \int a(\boldsymbol{y}_i, \boldsymbol{\theta}, \boldsymbol{f}_i)\, P_{post(-i)}(\boldsymbol{\theta}, \boldsymbol{f} | \boldsymbol{y}_{-i}) d\boldsymbol{\theta} d\boldsymbol{f}$$

- CV posterior predictive density
  - Let $a(\boldsymbol{y}_i, \boldsymbol{\theta}, \boldsymbol{f}_i) = P_{pred}(\boldsymbol{y}_i | \boldsymbol{\theta}, \boldsymbol{f}_i)$

$$P_{pred}(\boldsymbol{y}_i | \boldsymbol{y}_{-i}) = \int P_{pred}(\boldsymbol{y}_i | \boldsymbol{\theta}, \boldsymbol{f}_i)\, P_{post(-i)}(\boldsymbol{\theta}, \boldsymbol{f} | \boldsymbol{y}_{-i}) d\boldsymbol{\theta} d\boldsymbol{f}$$

$$\approx \frac{1}{S} \sum_{s=1}^{S} P_{pred}(\boldsymbol{y}_i | \boldsymbol{\theta}^s, \boldsymbol{f}_i^s)$$

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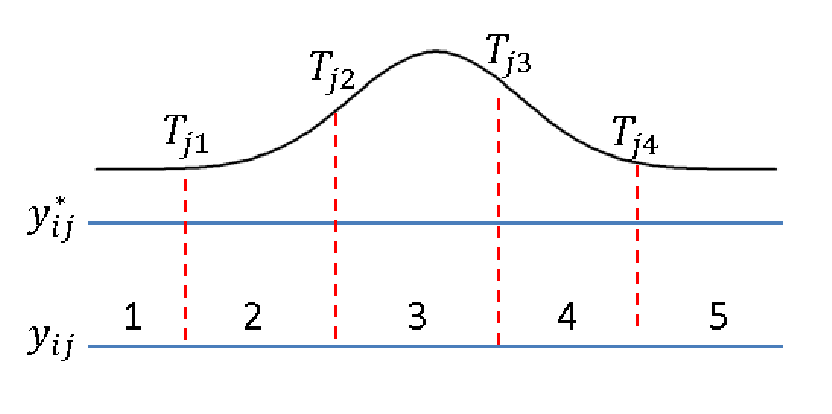
Recall: Participant Model

$$y_{ij} = c \text{ if } y_{ij}^* \in \left(T_{j(c-1),} T_{jc}\right]$$

$$y_{ij}^* = \alpha_j + \lambda_j f_i + \varepsilon_{ij}\ ;\ f_i \sim N(0,1), \varepsilon_{ij} \sim N(0,1)$$

$$i = 1, \ldots, N, j = 1, \ldots, P, c = 1, \ldots, C_j$$



- Likelihood

$$L(y^*|\alpha, \lambda, f) = \prod_{i=1}^{N} \prod_{j=1}^{P} N(y_{ij}^* \,|\alpha_j + \lambda_j f_i\ , 1)$$

LOO-CV Method Cont.

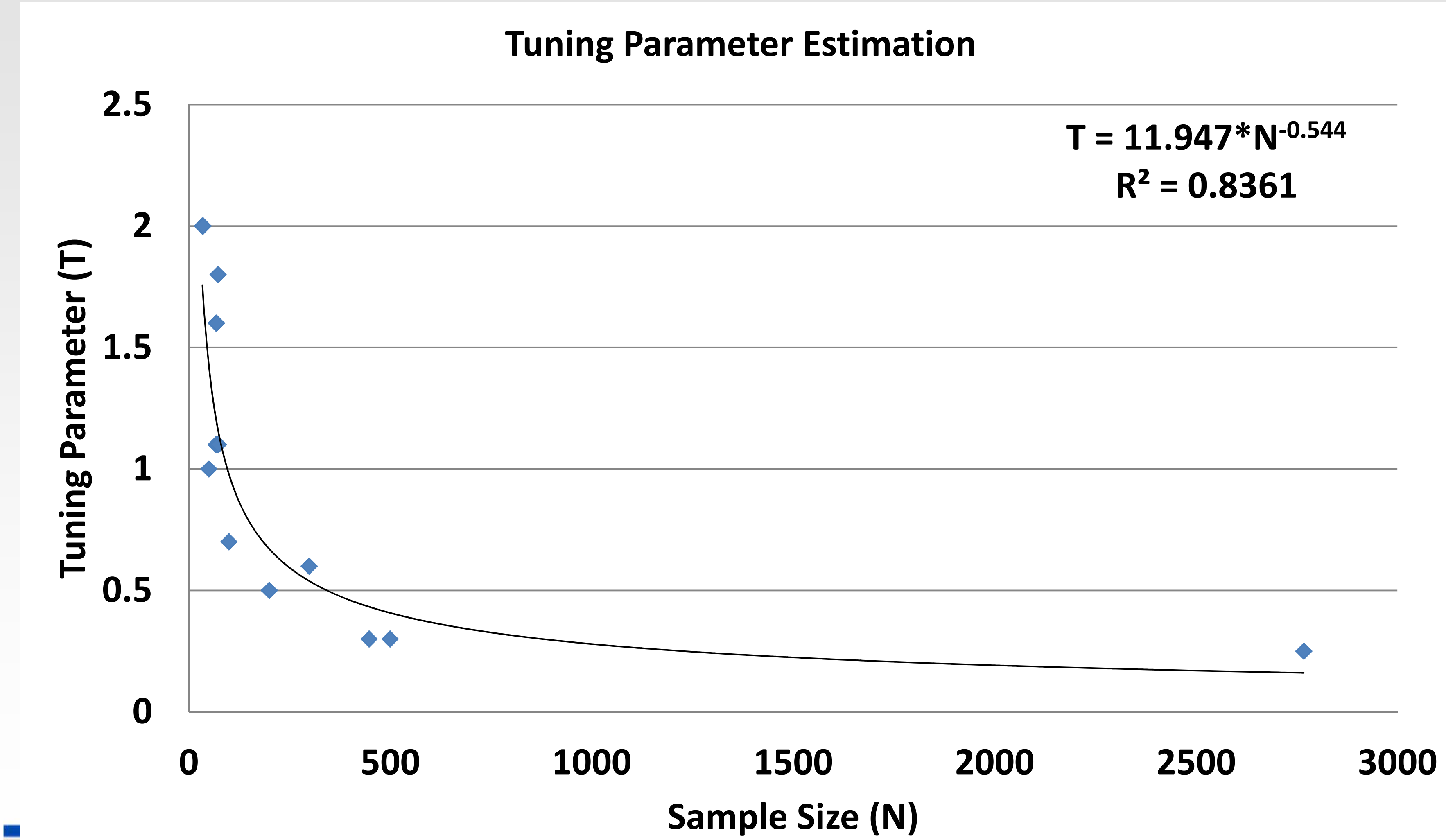
- $\boldsymbol{\theta} = (\boldsymbol{\alpha}, \boldsymbol{\lambda})$
- Predictive density

$$P_{pred}(\boldsymbol{y}_i | \boldsymbol{\alpha}^s, \boldsymbol{\lambda}^s) = \prod_{j=1}^{P} \int_{T_j^s}^{T_j^s} N\left(y_{ij}^* | \alpha_j^s + \lambda_j^s f_i^s, 1\right) dy_{ij}^*$$

- CV information criterion (CVIC)

$$CVIC = -2 \sum_{i=1}^{N} log\left(P_{pred}(\boldsymbol{y}_i | \boldsymbol{y}_{-i})\right)$$

MCMC Tuning Parameter



PAMS Study Background

- Breast cancer related death ranks 2nd among cancer deaths for women in the U.S.
- Routine utilization of mammography
  - Most widely recommended method for breast cancer screening
  - Offers a chance of early detection—critical for overall survival
  - Influenced by patients' decision
    - Prior experiences and satisfaction with mammography

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PAMS Short-Form Survey

- Patient assessment of mammography services (PAMS) survey
  - Single factor, 7 items
  - 5-point Likert scale: 1-poor to 5-excellent
  - Four patient populations
    - American Indian: *N*=299
    - Black: *N*=34
    - Hispanic: *N*=36
    - Non-Hispanic White: *N*=2,768
  - 6 subject experts consulted

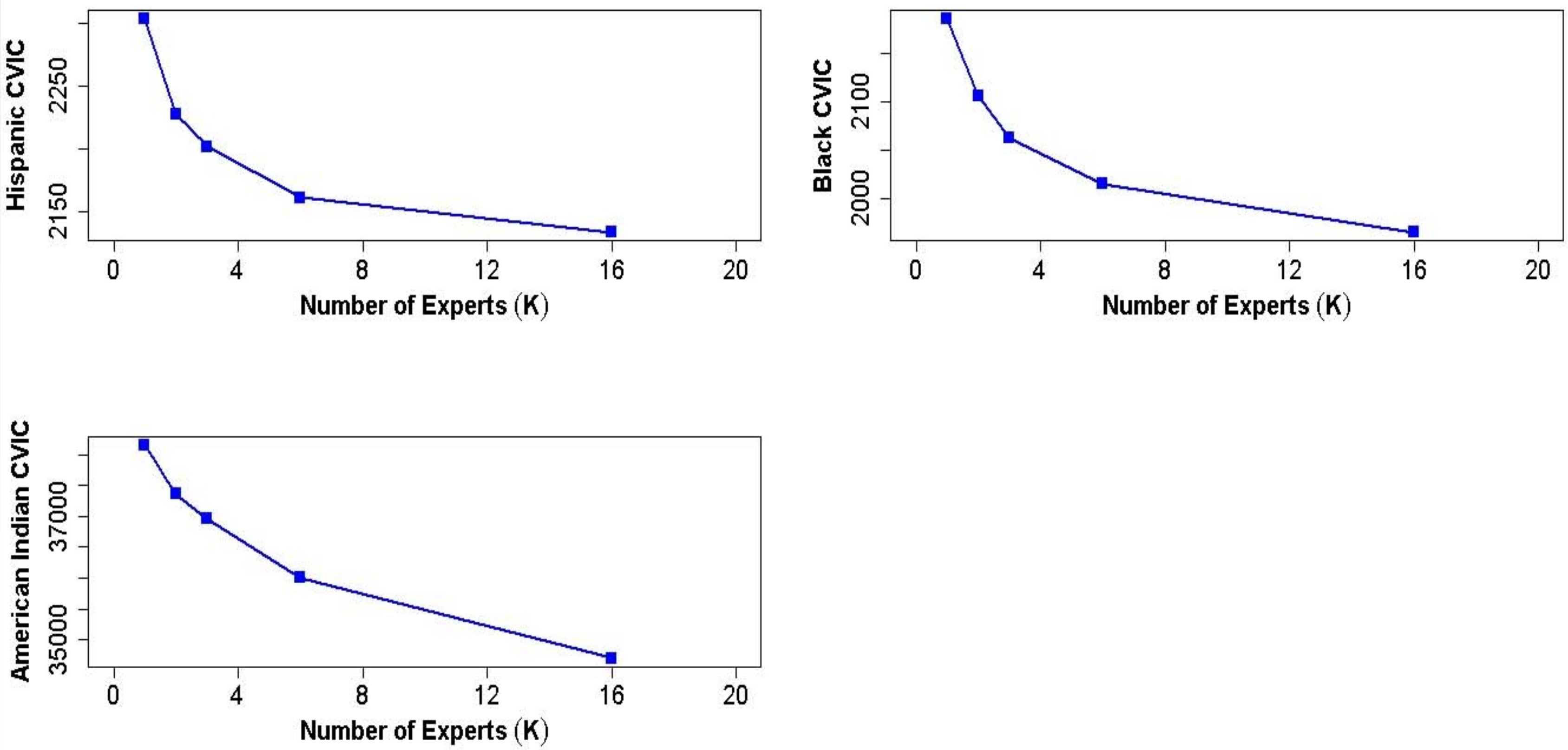
PAMS LOO-CV Results

- Recoding of data
  - Very few respondents selecting “1=poor, 2=fair, 3=good” response options
  - Hispanic & Black: combined poor to good responses
  - American Indian: combined poor to fair responses

	Hispanic	**Black**	**American Indian**
Informative Prior	2154.291	2014.279	36068.882
Flat Prior	2781.639	2489.856	39325.667

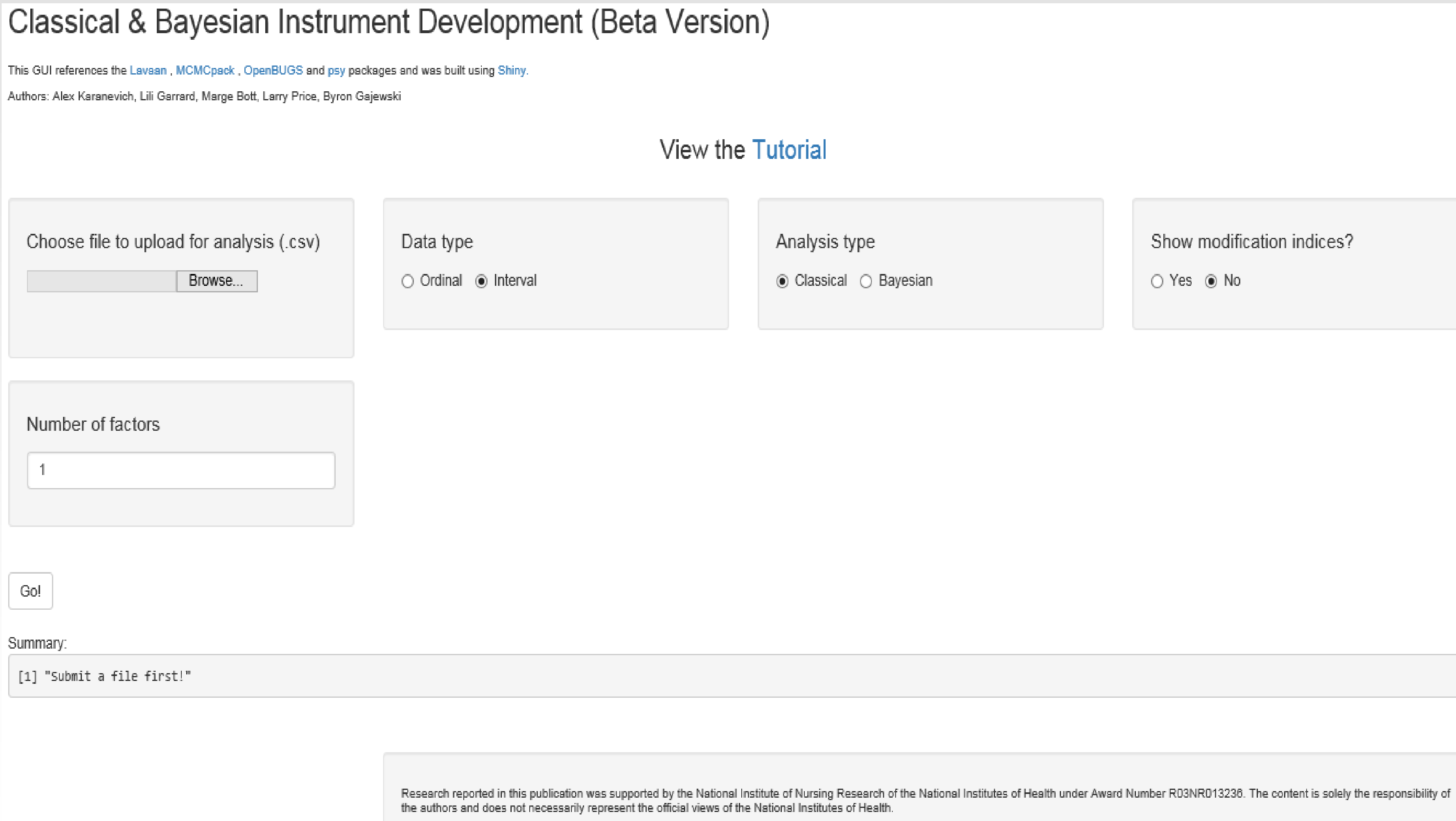
PAMS LOO-CV Results Cont.

- Evaluation of subject expert bias

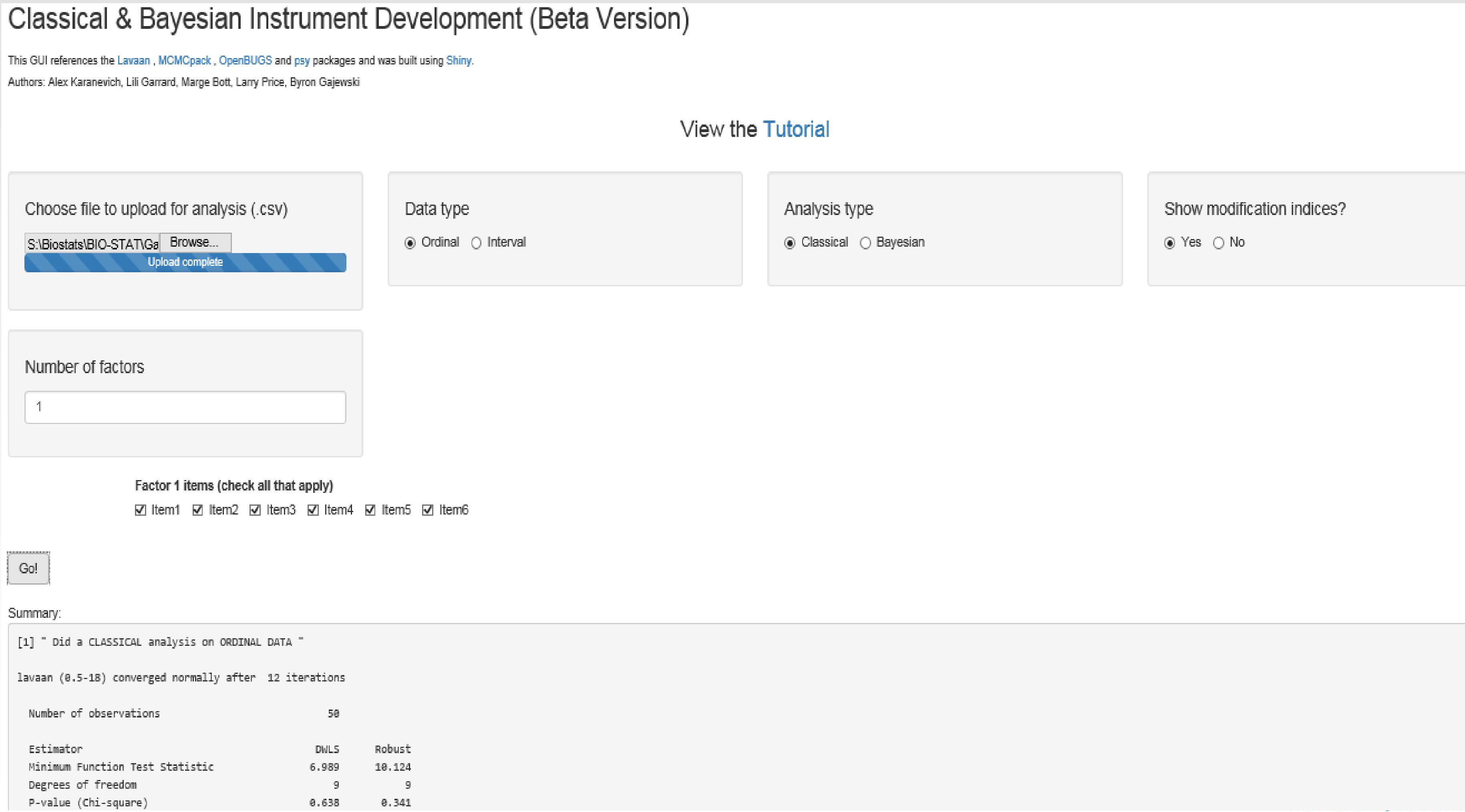


Aim 3: Software Dissemination

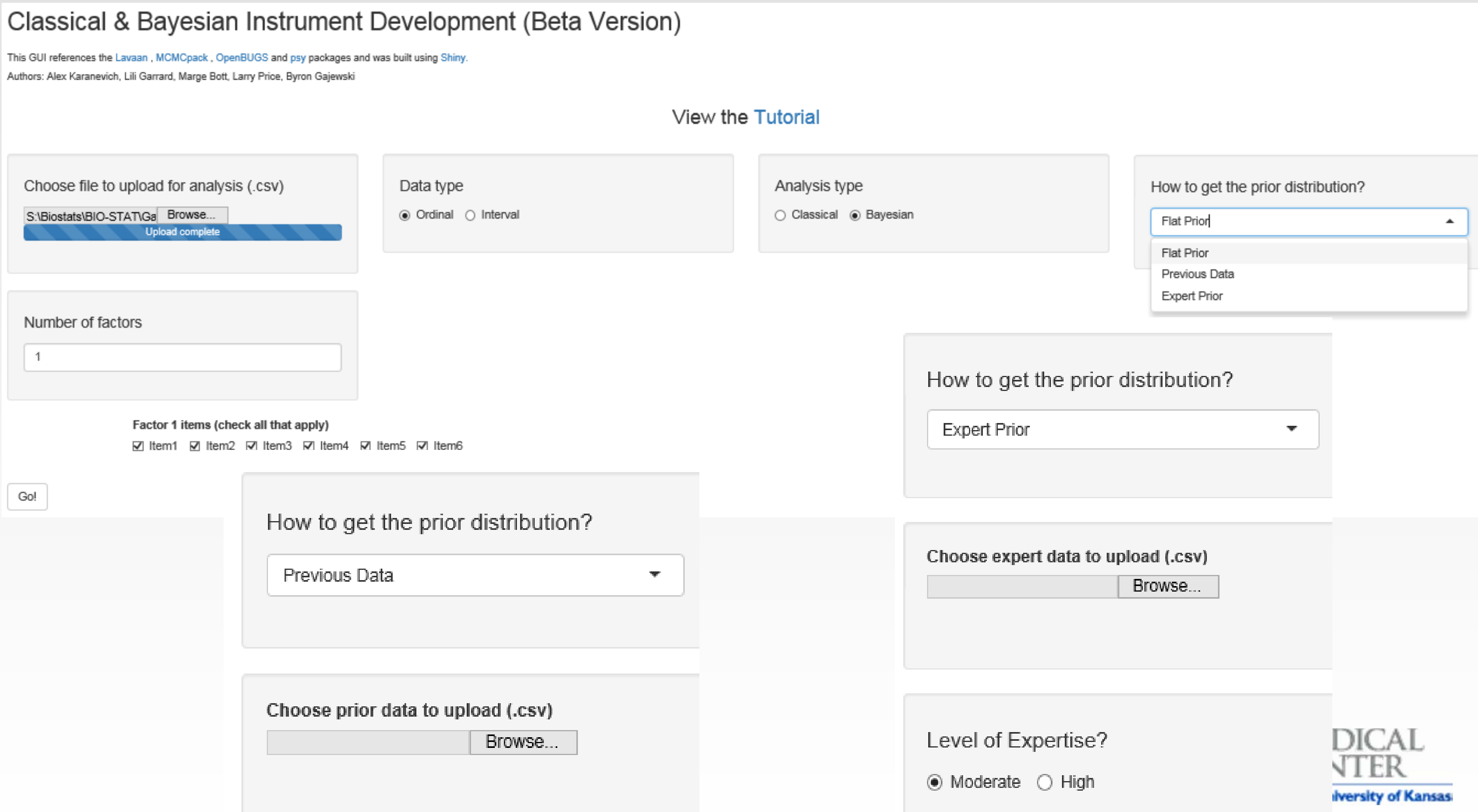
CBID Software



CBID Software - Classical



CBID Software - Bayesian



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Co-authors

- Principal Investigator:
  - Byron J. Gajewski, Ph.D., PStat®
  - Professor, Department of Biostatistics, University of Kansas Medical Center
- Co-Investigator:
  - Marjorie J. Bott, Ph.D., RN
  - Associate Dean for Research, Associate Professor, University of Kansas School of Nursing
- Consultant:
  - Larry R. Price, Ph.D., PStat®
  - Professor – Psychometrics & Statistics, College of Education, Texas State University
- Software Developer (*R Shiny*):
  - Alex Karanevich, M.S.
  - Ph.D. Student, Department of Biostatistics, University of Kansas Medical Center

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Questions and Discussions