COST-EFFECTIVE CHART REVIEW SAMPLING DESIGN TO ACCOUNT FOR PHENOTYPING ERROR IN ELECTRONIC HEALTH RECORDS (EHR) DATA

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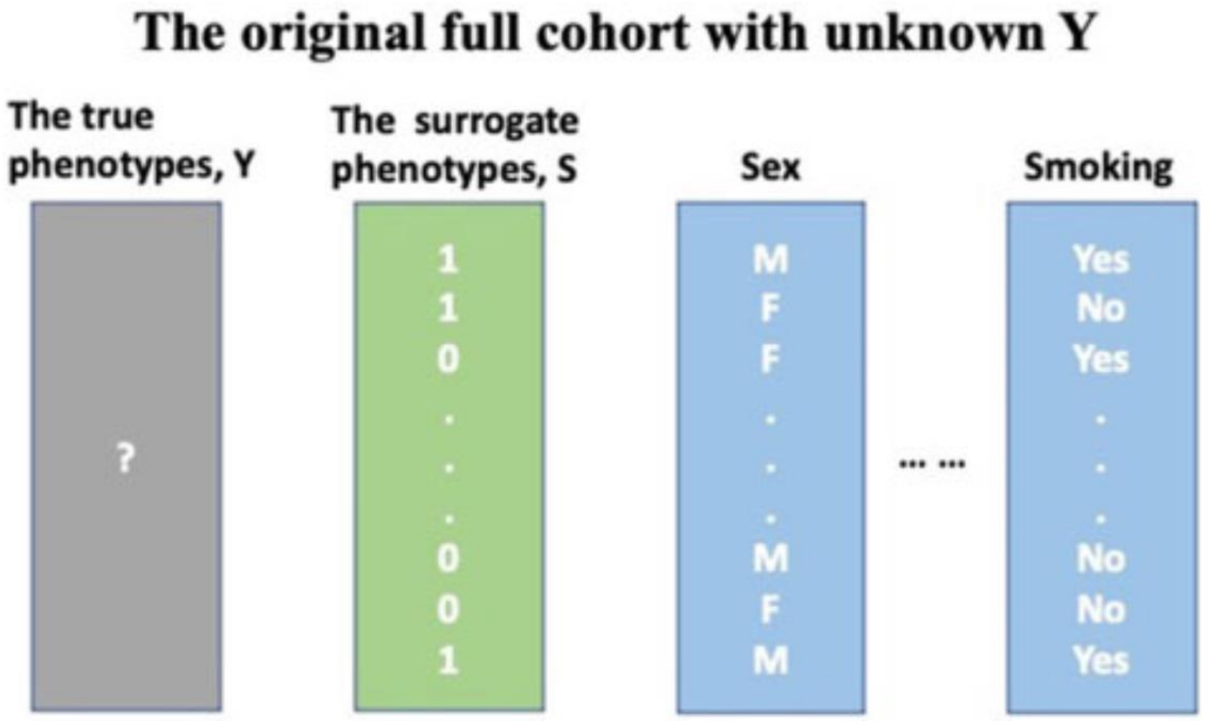
INTRO

Introduction and Motivation

- Electronic health record (EHR) data
  - A digital data system that contains medical history of patients
  - Investigates the association between risk factors and EHR-derived phenotype (binary)
- Problems:
  - EHR-derived phenotypes are likely to be misclassified; a manual chart review is required
  - Chart review can only be conducted for a validation subcohort due to limited resources
  - For rare diseases, positive phenotype patients in full cohort is even fewer
    – chart review may loss efficiency
- Research goal:

  investigate an efficient sampling procedure for association study when there is **a small number of positive phenotype subjects** in the full cohort

EHR Data



The original full cohort with unknown Y

The true phenotypes, Y	The surrogate phenotypes, S	Sex		Smoking
	1	M		Yes
	1	F		No
	0	F		Yes
	.	.		.
?	.	.	… …	.
	.	.		.
	0	M		No
	0	F		No
	1	M		Yes

Relationship between Y and X: $logit\{P(Y_i = 1|\boldsymbol{X_i})\} = \boldsymbol{X_i\beta}$

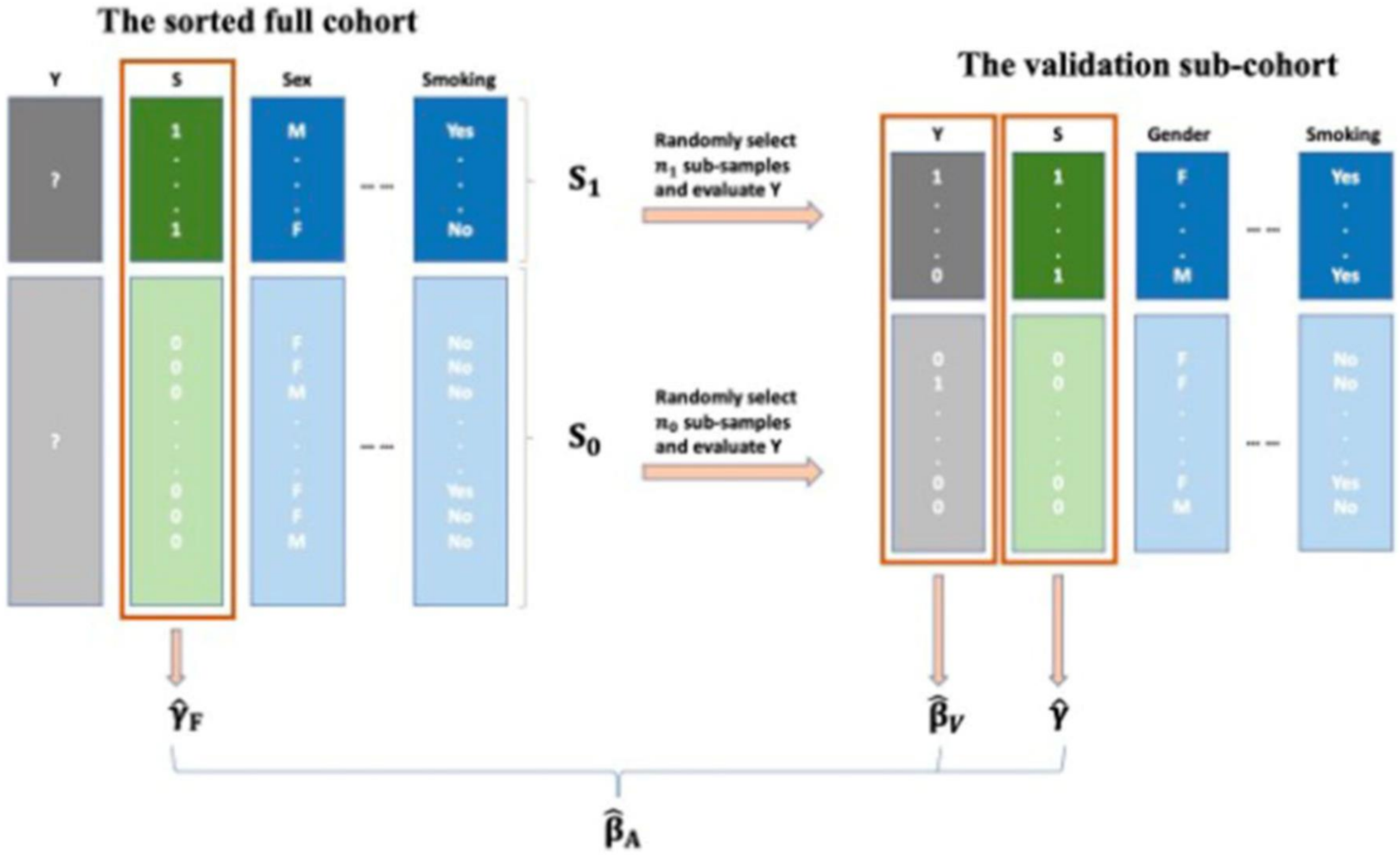
Previous Works

- 1. Original uniform (Ori-Unif) sampling
  - Cannot guarantee a balanced number of positive and negative phenotype patients in the subcohort
- 2. Original biased (Ori-Bias) sampling
  - Only explores the relationship between true phenotype and covariates but fails to take information in surrogate phenotype into account.
- 3. Augmented uniform (Aug-Unif) sampling
  - Introduces information in surrogate phenotype into the estimator
  - But uses a uniform sampling procedure

METHODS

Proposed Method

- Outcome-dependent sampling design for cost-effective chart review with augmented estimation procedure (OSCA)



OSCA

- Assumption: surrogate phenotype and the true phenotype are non-differentially associated
  - Fixed probabilities of making a correct chart review conditional on the observed phenotype

$$p_1 = P(S_i = 1 | Y_i = 1) \text{ and } p_0 = P(S_i = 0 | Y_i = 0).$$

- Improvement of OSCA
  - Fewer subjects are required for chart review to achieve the same statistical power
  - Smaller estimated standard error; higher statistical efficiency

RESULTS

RESULTS

- 3 Simulations

  →Own synthetic data sets

- 1 real data set
  - Real data: Colon cancer recurrence EHR data set in the KPW healthcare system
  - Proved closer estimates to the golden standard

SIMULATION1: DATA GENERATION

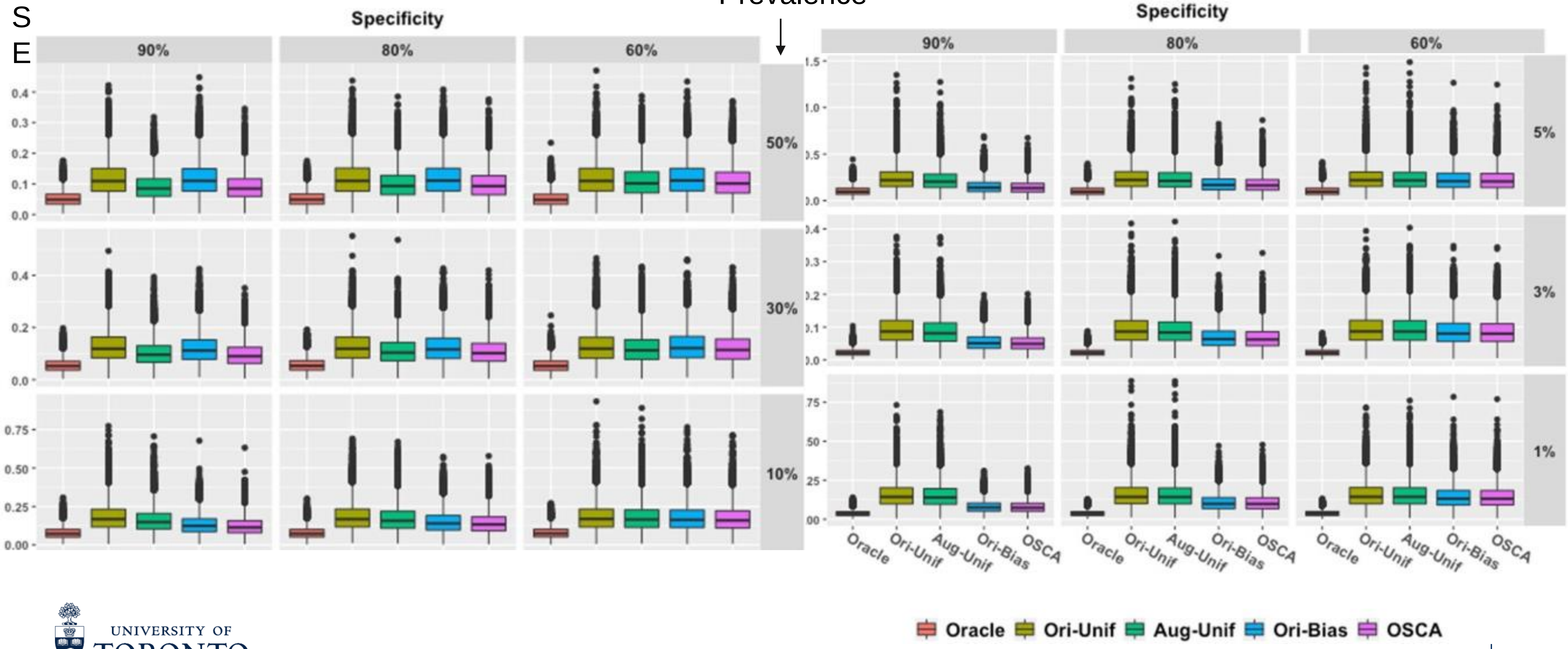
EMPIRICAL COVERAGE PROBABILITIES AND CONFIDENCE INTERVALS

- $\mathrm{logit}\{P(Y_i = 1|X_1, X_2, X_3)\} = b_0 + X_1 + X_2 + X_3$
- Prevalence: {~1%, ~3%, ~5%, ~10%, ~30%, ~50%}
    - For ~5%, ~10%, ~30%, ~50%: N=2000 , n=600
    - For ~1%, ~3%: N=8000 , n=2000

SIMULATION 1: RESULTS

M
S
E

Prevalence



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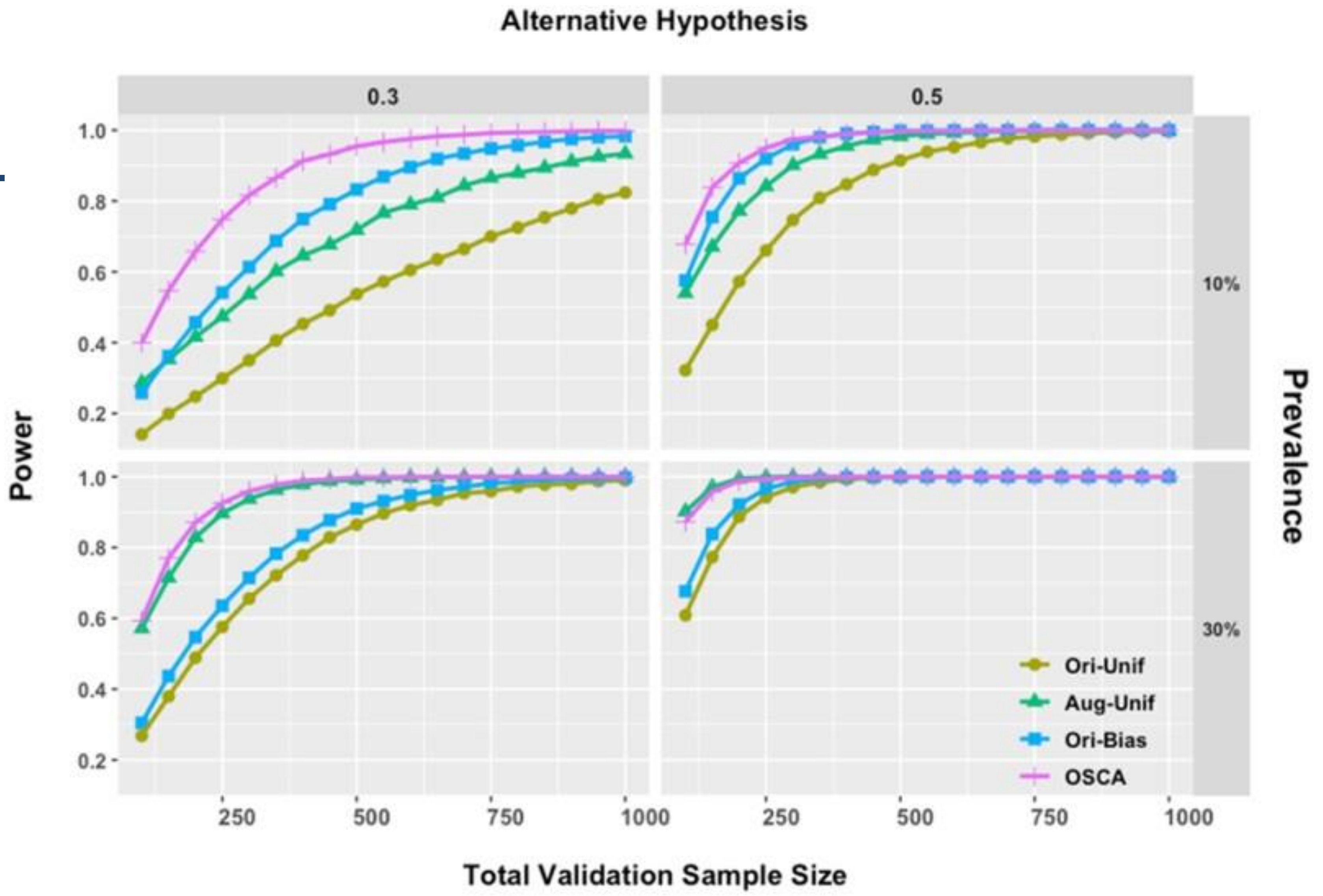
SIMULATION 2:

POWER ANALYSIS

- $\text{logit}\{P(Y_i = 1|X)\} = b_0 + \beta_1 X$

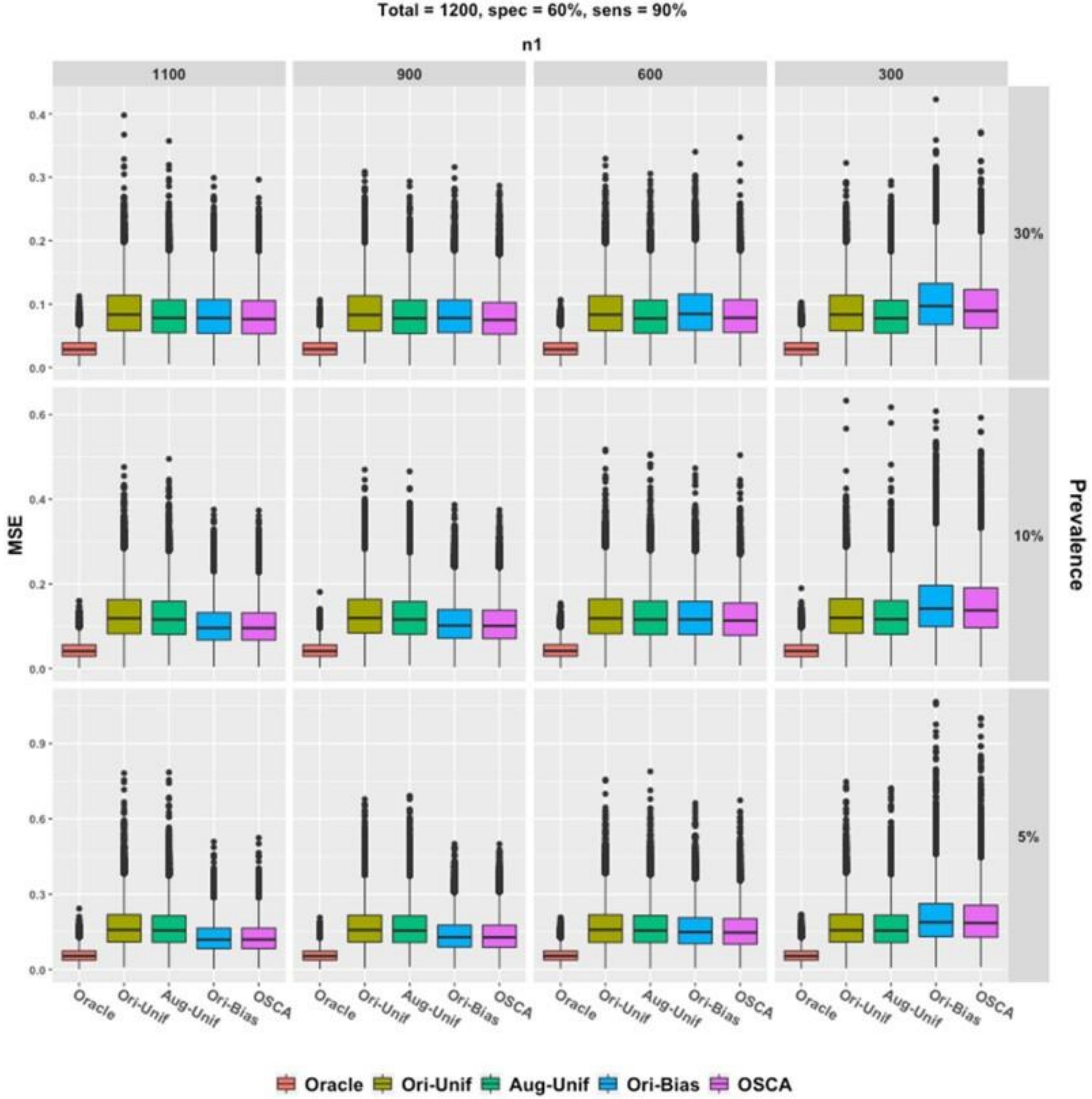
- $H_0\colon\ \beta_1 = 0$

- $H_1\colon \beta_1$ =0.3 or 0.5



SIMULATION 3:

EFFECT OF IMBALANCED SAMPLING



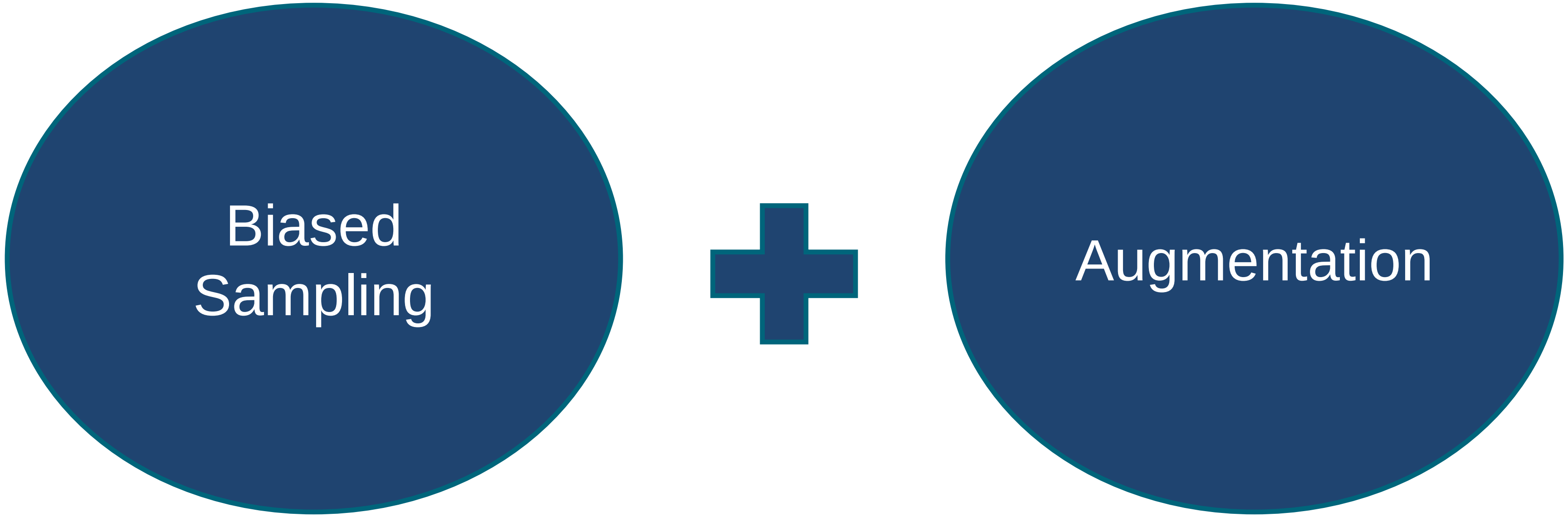
CONCLUSION

PROBLEMS?

- EHR data: an electronic medical records of patients
- phenotyping error in EHR-derived outcomes
  - Systematic bias
- a manual chart review is required
  - Time-consuming

OSCA

the outcome-dependent sampling design for cost-effective chart review with augmented estimation procedure



Biased Sampling

Augmentation

CONCLUSION

- Simulation 1: concentrated MSE box especially when disease is rare
- Simulation 2: Need smaller sub-cohort to reach the same level power
- Simulation 3: validated effectiveness of biased sampling
- In conclusion
    - reduces estimation bias while maintaining low variance
    - Is cost-effective in chart review.

Thank You!