High Dimensional Feature Selection algorithms with Interactions on Time-to-Event Outcome

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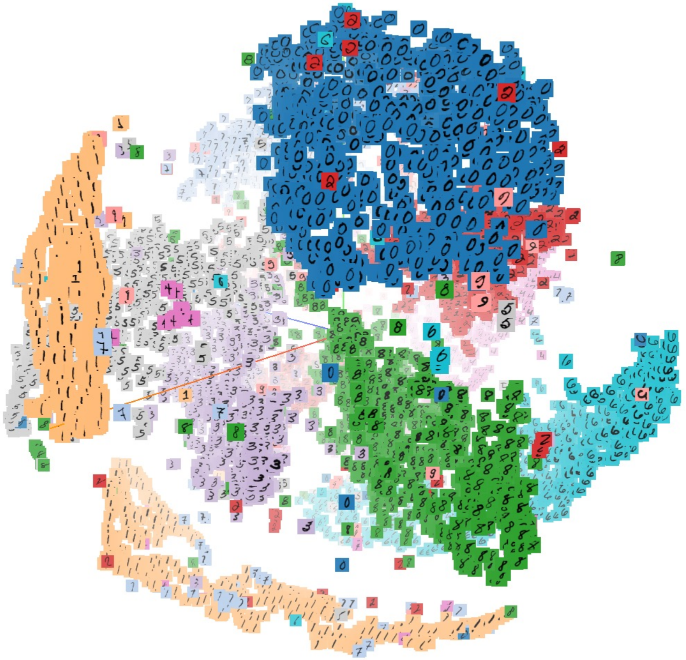
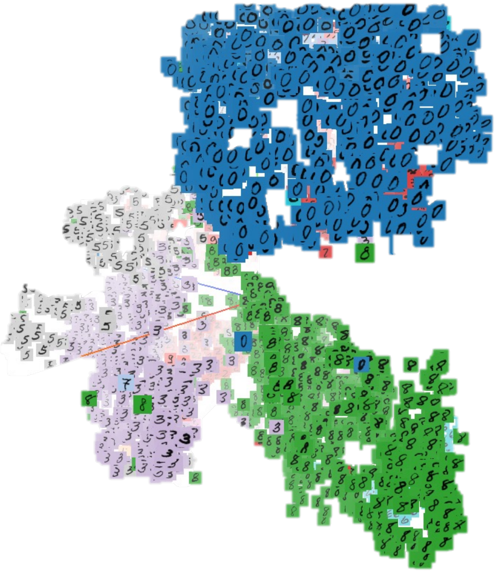
Background: Challenges of High Dimensional Data



Feature selection (e.g., LASSO, Ridge)

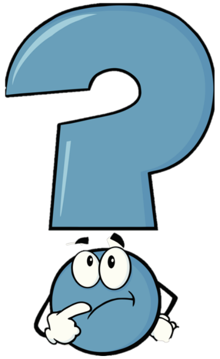


High dimensional data:
model overfitting, generalizability

Low dimensional data

Image copyright: Visualize high dimensional data. (pinterest.com)

Research Question and Objective



Interactive effects not considered

Existing methods:

HDSI algorithms[1,2,3] for continuous and binary cases

Research question: Is HDSI/RHDSI Robust? Can it be extended to different types of data?

Objective: Develop feature selection algorithm with **interactions** for **time-to-event outcome**

1. Jain R, Xu W. HDSI: High dimensional selection with interactions algorithm on feature selection and testing. PLOS ONE.
2. Jain R, Xu W. RHDSI: A novel dimensionality reduction based algorithm on high dimensional feature selection with interactions. Inf Sci. 2021 Oct 1;574:590–605.
3. Zhuang Z, Xu W, Jain R. High Dimensional Selection with Interactions Algorithm on Feature Selection for Binary Outcome.

Method Pipeline

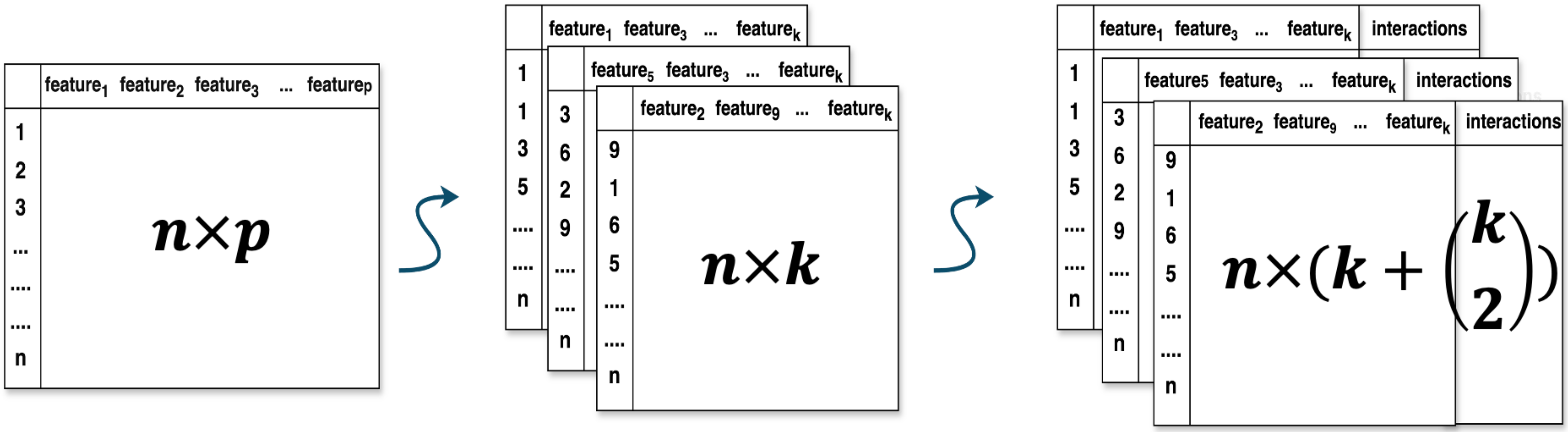
1: Develop algorithms for model building and hyper parameters tuning

2: Conduct simulations with high dimensional features with both marginal and interactive effects

3: Implement the proposed algorithms into real clinical study

Method: Development of the HDSI-LASSO and HDSI-Ridge Algorithms

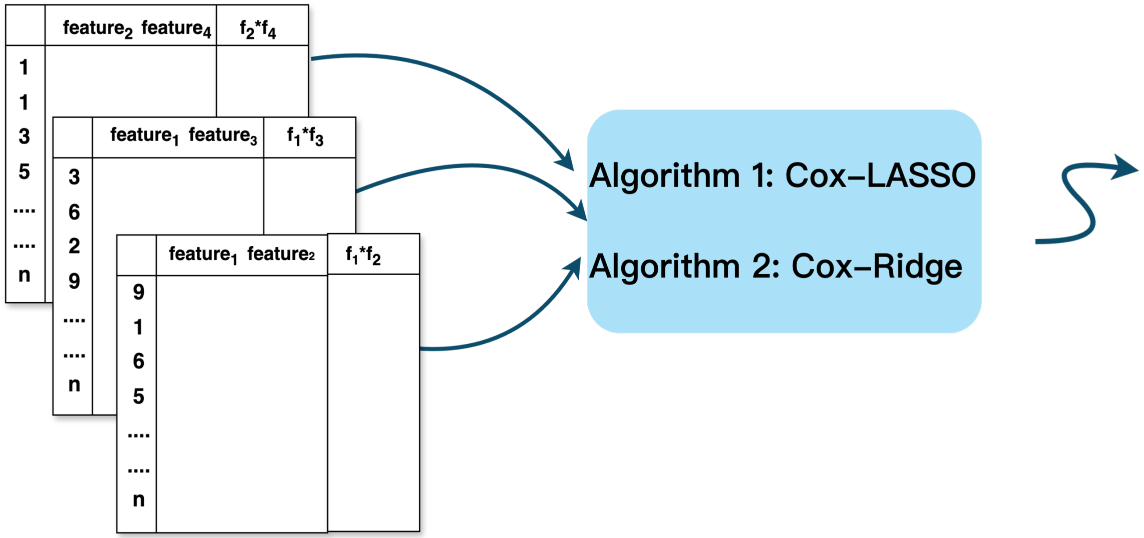
Step 1: Prepare Bootstrap Sets



B Bootstrap datasets with interactions

Method: Development of the HDSI-LASSO and HDSI-Ridge Algorithms

Step 2: Build model and select features



Input

Feature Selection Algorithm

bootstrap set 1 output		
X_1	X_2	X_{1*2}
$\hat{\beta}_1^1$	$\hat{\beta}_2^1$	$\hat{\beta}_{1*2}^1$
C_1^1	C_2^1	C_{1*2}^1

...

bootstrap set B output		
X_2	X_4	X_{2*4}
$\hat{\beta}_2^3$	$\hat{\beta}_4^3$	$\hat{\beta}_{2*4}^3$
C_2^3	C_4^3	C_{2*4}^3

Output:
- **Coef. estimates($\hat{\beta}$)**
- **C-index(C)**

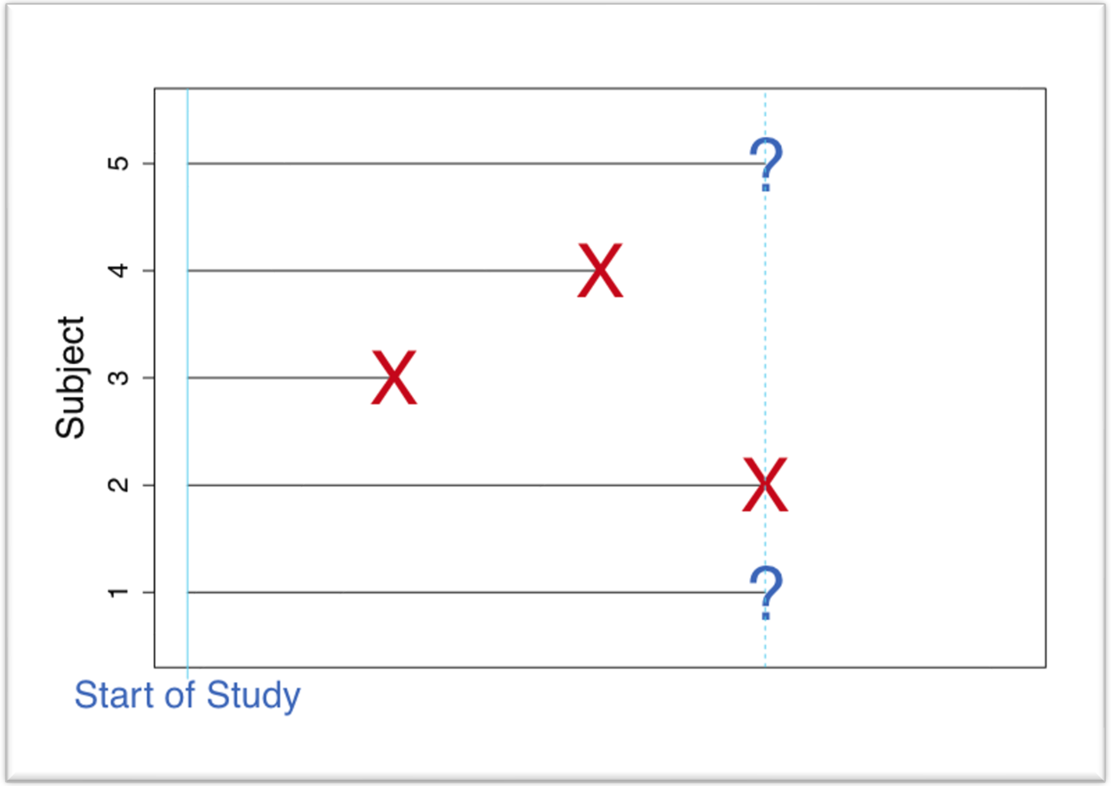
Pooled results:

- $\hat{\beta}_j = \text{avg}(\hat{\beta}_j^1, \hat{\beta}_j^2, \dots \hat{\beta}_j^B)$
- $\text{Cindex}(X_j) = \min(C_j^1, C_j^2, \dots C_j^B)$

Criteria for feature selection

- Significance of X_j (quantile includes 0)
- $\text{Cindex}(X_j) > \text{cutoff value}$

Simulation Study Design



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1) Observed time T

$$T = \min(\tilde{T}, C)$$

$\tilde{T}$: The latent time had everyone's survival time observed

C: The censoring time

2) Observed status Y

$$Y = \begin{cases} \text{event}, & T = \tilde{T} \\ \text{censored}, & T = C \end{cases}$$

Simulation Study Design

Step 1) Latent event time $\tilde{T}$

- Survival function

$$S(\tilde{T}) = 1 - F(\tilde{T}) \sim \text{Unif}\,(0,1)$$

- Cox model

$$S(\tilde{T}|x) = \exp[-H_0(\tilde{T})\exp(Z)]$$

H_0: cumulative baseline hazard

Z: linear predictor

- Inverse of survival function

$$\boldsymbol{\tilde{T}} = \boldsymbol{H_0}^{-1}(-\boldsymbol{log}(\boldsymbol{S})\exp(-\boldsymbol{Z}))$$

Step 2) Censoring time C

$$C \sim \text{Unif}\,(0, b)$$

Step 3) Compare $\tilde{T}$ and C

$$T = \min(\tilde{T}, C)$$

$$Y = \begin{cases} \text{event}, & T = \tilde{T} \\ \text{censored}, & T = C \end{cases}$$

Simulation Study Design

True model

$$\lambda(t|\boldsymbol{x}) = \lambda_0(t)\exp(Z)$$

$$= \lambda_0(t)\exp(X_1 + X_2 + 0.75X_3 - 0.75X_4 + 0.75X_5 + X_1X_2 - X_3X_4)$$

$X_1, X_2, \ldots X_5$: continuous, generated from multinormal

Samples

1000 for training; 500 for testing (Event rate: ~ 40%)

Features

True

- 5 marginal + 2 interactive

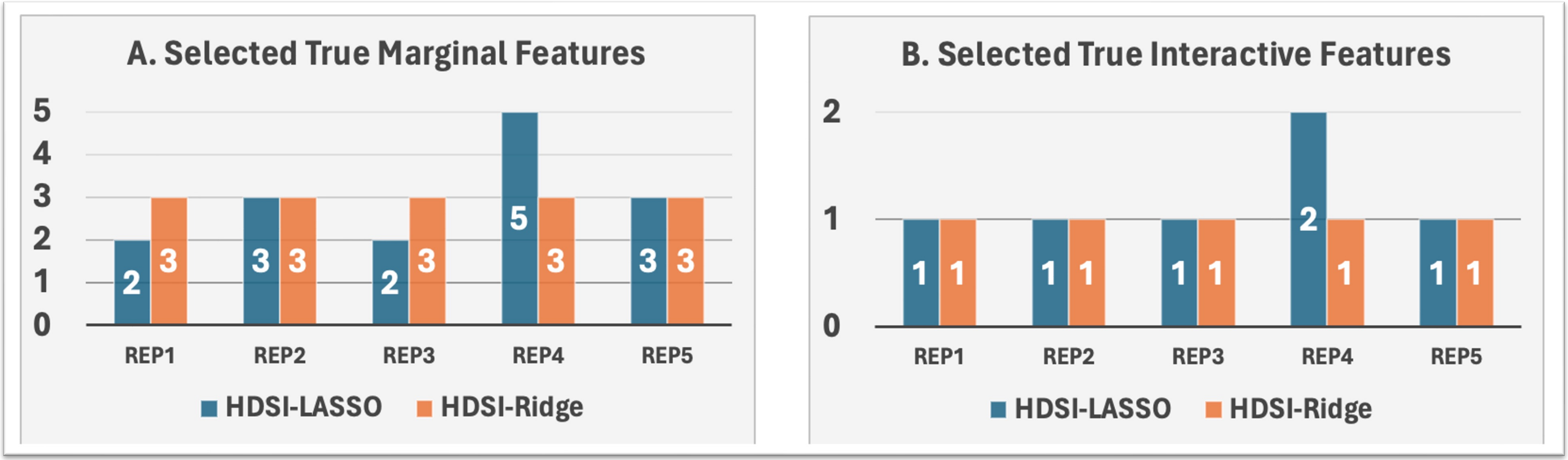
Noisy

- 20 marginal + 298 interactive

Simulation Study Results

True model: 5 true marginal, 2 true interactive features

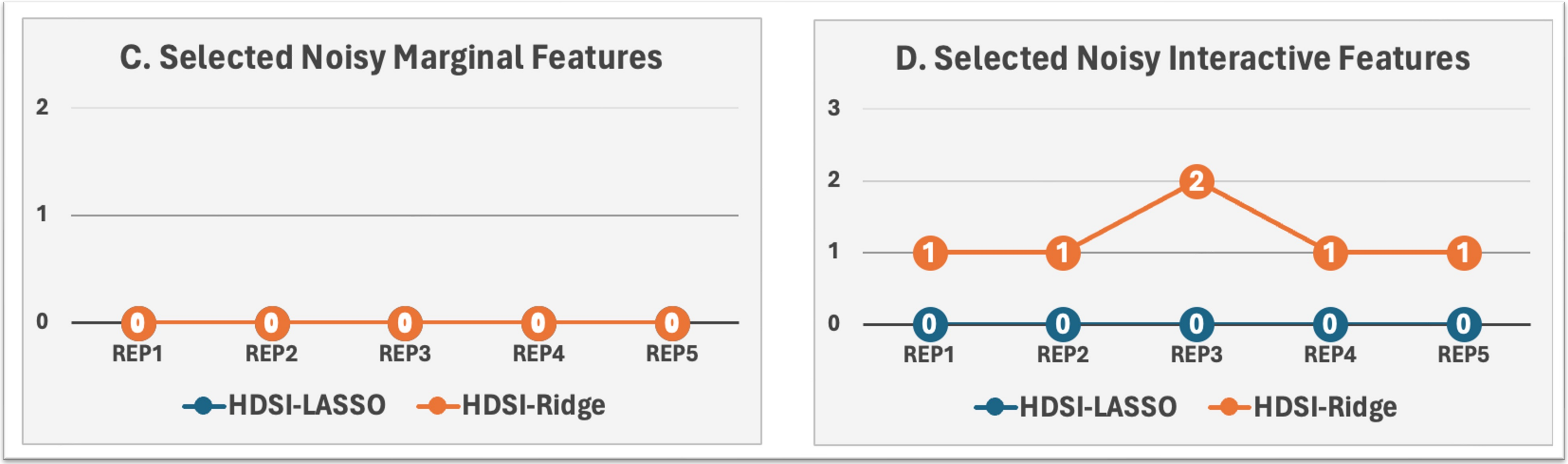
Are all true effective features selected?



Simulation Study Results

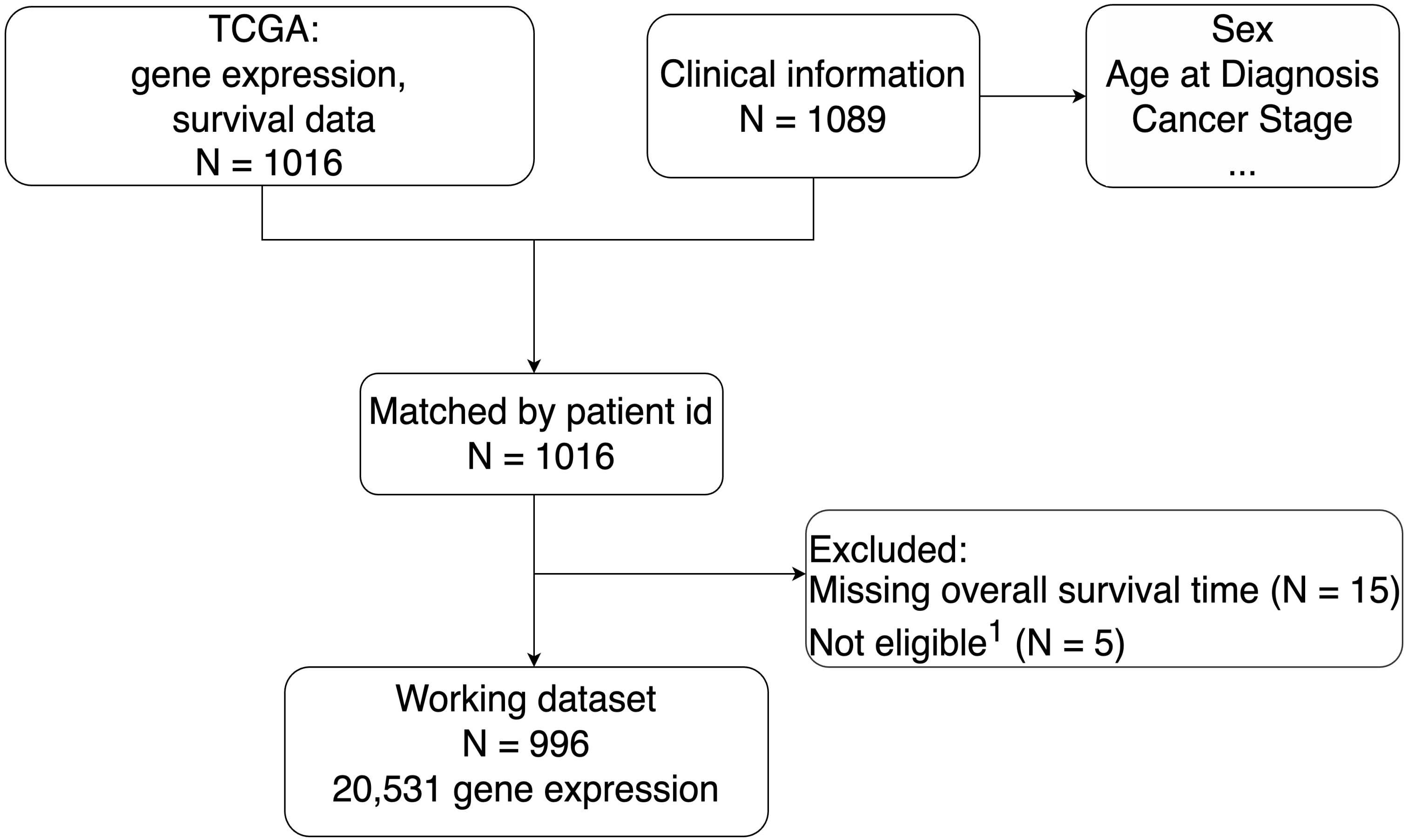
Noisy: 20 noisy marginal, 298 noisy interactive features

Are any noisy features selected?



Real-World Study

Setting: relationship between gene expression profile & overall survival in lung cancer patients?



Summary statistics:

Event rate: 40%

Median survival time: ~2 yrs

Univariate analysis:

- Age at diagnosis
- cancer stage
- Top 50 and 100 significant genes

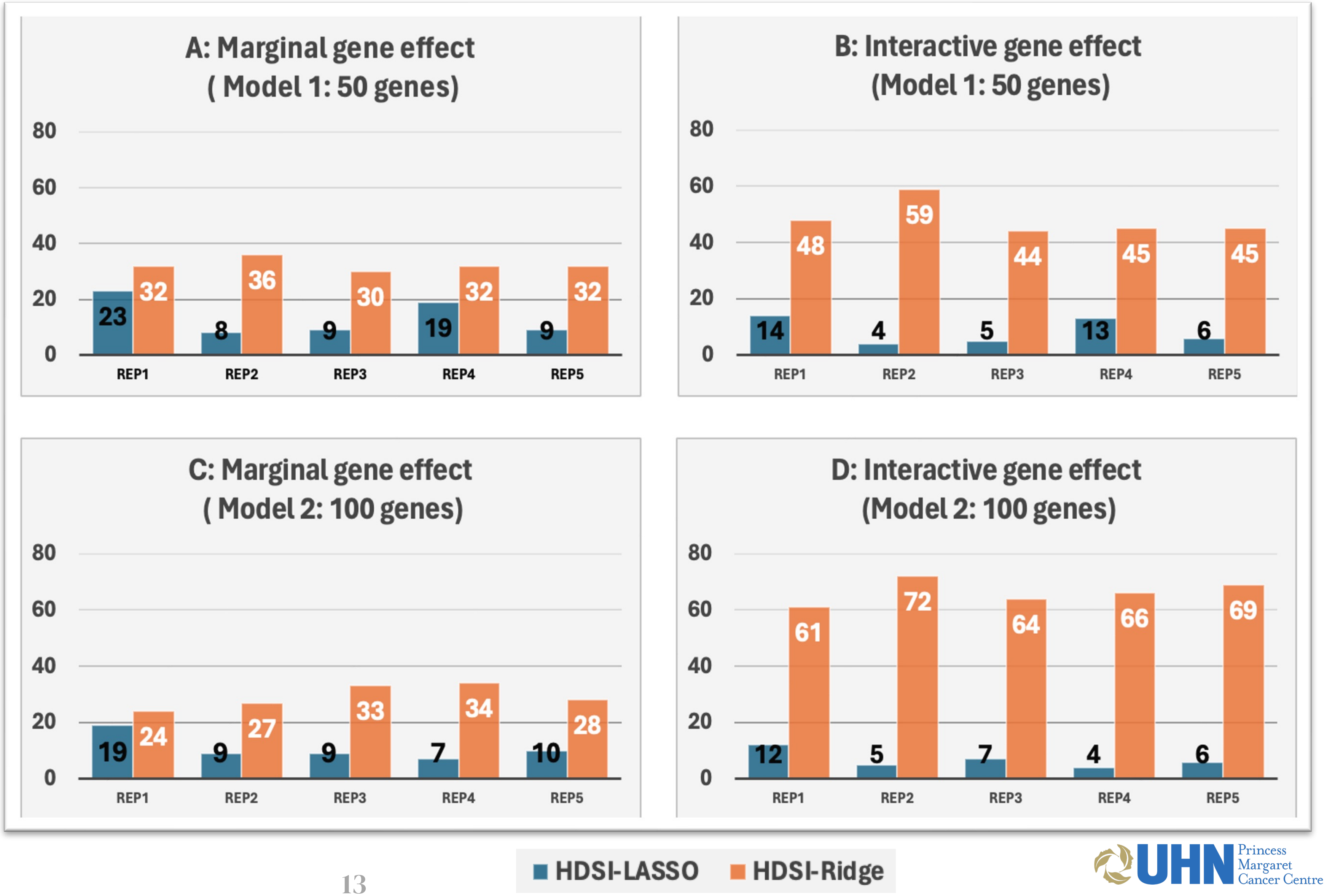
1: subjects who died or censored at the enrollment

Real-World Study Results

Model 1 : 50 marginal + 1225 interactive; **Model 2**: 100 marginal + 4950 interactive

Summary:

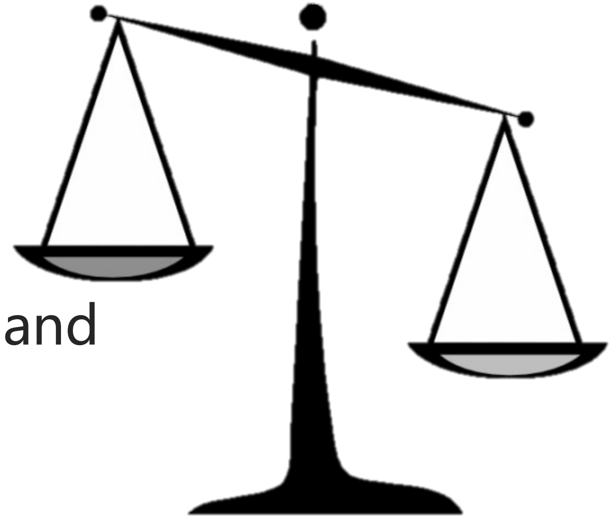
- HDSI-Ridge selected more genes
- Marginal features: Both robust
- Interactive features: only HDSI-LASSO robust
- C-index: HDSI-Ridge> HDSI-LASSO



Discussion

HDSI-LASSO:

- Selected **less** features
- **Robust** to the increase in the number of features(marginal and interactive)
- Slightly lower C-index



HDSI-Ridge:

- Selected more features
- Only robust to the increase in the number of marginal features; **Selected more noisy features**

Limitations and future work:

- Corporate other algorithms into the HDSI framework
- Consider other simulation settings (e.g., different effect sizes)

References

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5. Zhuang, Z., Xu, W., & Jain, R. (n.d.). *High Dimensional Selection with Interactions Algorithm on Feature Selection for Binary Outcome*.

Thank you ☺