# IS STATISTICAL INFERENCE WITHOUT SPARSITY POSSIBLE IN HIGH-DIMENSIONS?

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Consider a high dimensional linear regression setting,

$$\mathbf{Y} = \mathbf{X}\boldsymbol{\gamma}^* + \mathbf{Z}\boldsymbol{\beta}^* + \boldsymbol{\varepsilon},\tag{1}$$

where  $Z \in \mathbb{R}^n$  and  $X \in \mathbb{R}^{n \times p}$  are the design matrices,  $p \gg n$ ,  $\varepsilon \in \mathbb{R}^n$  is the error term independent of the design with  $\mathbb{E}(\varepsilon) = 0$  and  $\mathbb{E}(\varepsilon \varepsilon^\top) = \sigma_{\varepsilon}^2 \mathbb{I}_n$ , and  $\gamma^*$  and  $\beta^*$  are unknown model parameters.

We focus on the problem of testing single entries of the model parameter, namely the following hypothesis:

$$H_0: \beta^* = \beta_0, \quad \text{versus} \quad H_1: \beta^* \neq \beta_0. \tag{2}$$

**Sparsity assumption**:  $\|\gamma^*\|_0 := s_\gamma \ll n$  and for inference procedures is such that  $s_\gamma \log p/\sqrt{n} \to 0$  as  $n \to \infty$ .

What happens if we apply sparsity-based methods when the underlying model parameter is not sparse? Can we obtain misleading and spurious results ?

# EXAMPLE 1

\* Assume:  $X = I_p$ ,  $\varepsilon_i$  are i.i.d. with  $\mathcal{N}(0, 1)$  and such that for  $a \in [-10, 10]$ 

$$\beta^* = 0$$
 and  $\gamma^* = ap^{-1/2}\mathbf{1}_p$ ,

- \* We consider the "de-biasing" approach as formulated in Van de Geer et.al (2014) Let π<sup>\*</sup> = (β<sup>\*</sup>, γ<sup>\*<sup>T</sup></sup>)<sup>T</sup> ∈ ℝ<sup>p+1</sup> and W = (Z, X) ∈ ℝ<sup>n×(p+1)</sup>. The debiased estimator is then defined π̃ = π̂ + I<sub>p+1</sub>W<sup>T</sup>(Y Wπ̂)/n
- \* Wald test rejects the hypothesis whenever  $|\tilde{\pi}_1| > \Phi^{-1}(1 \alpha/2)/\sqrt{n}$ .

## Theorem

In the above setup, we have  $\lim_{n\to\infty} P\left(|\tilde{\pi}_1| > \Phi^{-1}(1-\alpha/2)/\sqrt{n}\right) = F(\alpha, a)$ , where  $F(\alpha, a) = 2 - 2\Phi\left[\Phi^{-1}\left(1-\frac{\alpha}{2}\right)/\sqrt{1+a^2}\right]$ . Figure: Plot of the asymptotic Type I error of Wald test



The horizontal axis denotes a and the vertical axis denotes  $F(\alpha, a)$ .

- \* To develop sparsity-robust tests for the hypothesis (10)
   We say that a test is sparsity-robust if the Type I error is asymptotically bounded by the nominal level, regardless of whether or not γ\* is sparse.
- Moreover, whenever the sparsity condition holds, our method is shown to be optimal and matches existing sparsity-based methods in terms of Type II errors.
- \* We show minimax optimal power in certain dense models as well.
- \* Our methodology is based on the idea of exploiting the implication of the null hypothesis.
  - \* Instead of directly estimating the parameter under testing, we test a moment condition that is equivalent to the null hypothesis.

# Introduction

CorrT Methodology Moment Condition Adaptive Estimation Test Statistic

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Jelena Bradic 2018 BIRS @ Banff We observe that a pseudo-response  $V := Y - Z\beta_0$  satisfies a linear model

$$V = X\gamma^* + e, \qquad e = Z(\beta^* - \beta_0) + \varepsilon.$$

- $\star$  under H<sub>0</sub>, X is uncorrelated with the error e
- \* under H<sub>1</sub>, **e** might have correlation with **X** through **Z**.

We formally introduce a model to account for the dependence between **X** and **Z**:

$$\mathbf{Z} = \mathbf{X}\boldsymbol{\theta}^* + \mathbf{u}, \qquad \mathbf{i} = 1, \dots, \mathbf{n}. \tag{3}$$

where  $\theta^* \in \mathbb{R}^p$  is sparse and  $\mathbf{u} \in \mathbb{R}^n$  is independent of **X** with mean zero and variance  $\mathbb{E}(\mathbf{u}\mathbf{u}^{\top}) = \sigma_u^2 \mathbb{I}_n$ .

We notice that

$$\mathbb{E}\left[(\mathbf{V}-\mathbf{X}\boldsymbol{\gamma}^*)^{\top}(\mathbf{Z}-\mathbf{X}\boldsymbol{\theta}^*)\right]/n = \sigma_{u}^{2}(\beta^*-\beta_0).$$

Hence, solving the inference problem (10) is equivalent to testing

$$H_0: \mathbb{E}\left[ (\mathbf{V} - \mathbf{X} \boldsymbol{\gamma}^*)^\top (\mathbf{Z} - \mathbf{X} \boldsymbol{\theta}^*) \right] = 0, \tag{4}$$

versus

$$H_1: \mathbb{E}\left[ (\mathbf{V} - \mathbf{X} \boldsymbol{\gamma}^*)^\top (\mathbf{Z} - \mathbf{X} \boldsymbol{\theta}^*) \right] \neq 0.$$
 (5)

# $\star$ We define the following estimator

$$\widetilde{\gamma}(\sigma) := \underset{\substack{\gamma \in \mathbb{R}^{p} \\ \text{s.t.}}}{\arg \min \|\gamma\|_{1}}$$

$$\text{s.t.} \quad \frac{\|n^{-1}X^{\top}(V - X\gamma)\|_{\infty} \leq \eta_{0}\sigma}{\|V - X\gamma\|_{\infty} \leq \|V\|_{2}/\log^{2}n}$$

$$n^{-1}V^{\top}(V - X\gamma) \geq \rho_{n}n^{-1}\|V\|_{2}^{2}.$$
(6)

for 
$$\eta_0 = n^{-1/2} (1.1) \Phi^{-1} (1 - p^{-1} n^{-1}) \sqrt{\max_{1 \le j \le p} n^{-1} \sum_{i=1}^{n} x_{i,j}^2} \rho_n = 0.01 / \sqrt{\log n}.$$

 $\star \ \widehat{\sigma}_{\gamma} = \arg \max\{\sigma : \sigma \in S_{\gamma}\}$  and the set  $S_{\gamma}$  is defined as

$$\mathcal{S}_{\gamma} = \left\{ \sigma \ge \sqrt{\rho_{n}} \| \mathbf{V} \|_{2} / \sqrt{n} : \quad 1.5\sigma \ge n^{-1/2} \| \mathbf{V} - \mathbf{X} \widetilde{\gamma}(\sigma) \|_{2} \ge 0.5\sigma \right\}.$$
(7)

- $\rightarrow$  When the estimation target fails to be sparse, the estimator is stable;
- ightarrow when the estimation target is sparse, the estimator automatically achieves consistency
- $\rightarrow$  does not require knowledge of the noise level.

We propose to consider the following correlation test (CorrT) statistic

$$T_{n}(\beta_{0}) = \frac{n^{-1/2} (V - X \widehat{\gamma})^{\top} (Z - X \widehat{\theta})}{\widehat{\sigma}_{\varepsilon} \widehat{\sigma}_{u}}, \qquad (8)$$

where

$$\widehat{\sigma}_{\varepsilon} = \|\mathbf{V} - \mathbf{X}\widehat{\gamma}\|_2 / \sqrt{n}$$
 and  
 $\widehat{\sigma}_{u} = \|\mathbf{Z} - \mathbf{X}\widehat{\boldsymbol{\theta}}\|_2 / \sqrt{n}.$ 

## Why does this work?

We can show, without assuming sparsity of  $\gamma^*$ , that

$$n^{-1/2} (\mathbf{V} - \mathbf{X} \widehat{\boldsymbol{\gamma}})^{\top} (\mathbf{Z} - \mathbf{X} \widehat{\boldsymbol{\theta}}) = n^{-1/2} (\mathbf{V} - \mathbf{X} \widehat{\boldsymbol{\gamma}})^{\top} \mathbf{u} + O_{\mathsf{P}} (\sqrt{\log p} \| \widehat{\boldsymbol{\theta}} - \boldsymbol{\theta}^* \|_1),$$

where under the null hypothesis, the first term on the right hand side has zero expectation and the second term vanishes fast enough.

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What about linear tests ?

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## Consider a high dimensional linear regression setting,

$$\mathbf{Y} = \mathbf{X}\boldsymbol{\beta}^* + \boldsymbol{\varepsilon}. \tag{9}$$

We focus on the problem of testing linear combinations of the model parameter, namely the following hypothesis:

$$\mathsf{H}_0: \mathbf{a}^\top \boldsymbol{\beta}^* = \mathsf{g}_0, \quad \text{versus} \quad \mathsf{H}_1: \mathbf{a}^\top \boldsymbol{\beta}^* \neq \mathsf{g}_0. \tag{10}$$

Sparsity assumption:  $\|\mathbf{a}\|_0 := ??$  and  $\|\boldsymbol{\beta}^*\|_0 := ??$ 

Let  $\Omega_X = \Sigma_X^{-1}$ .

For each of the features  $\textbf{x}_i \in \mathbb{R}^p$  consider the following decomposition:

 $\mathbf{x}_i = \mathbf{a}\mathbf{z}_i + \mathbf{w}_i$ 

with

$$z_i = \left(\frac{\mathbf{\Omega}_X \mathbf{a}}{\mathbf{a}^\top \mathbf{\Omega}_X \mathbf{a}}\right)^\top \mathbf{x}_i$$

and

$$\mathbf{w}_{i} = \left[\mathbb{I}_{p} - \frac{\mathbf{a}\mathbf{a}^{\top}\mathbf{\Omega}_{X}}{\mathbf{a}^{\top}\mathbf{\Omega}_{X}\mathbf{a}}
ight]\mathbf{x}_{i}$$

Notice that  $\mathbf{a}_{z_i}$  can be viewed as the projection of  $\mathbf{x}_i$  onto the vector  $\mathbf{a}$  – taking into account  $\mathbf{\Omega}_{x_i}$  hence extracting information in  $\mathbf{x}_i$  regarding the null hypothesis.

Now, we see that the original model can be reparametrized as

 $y_i = z_i(\mathbf{a}^\top \boldsymbol{\beta}^*) + \mathbf{w}_i^\top \boldsymbol{\beta}^* + \varepsilon_i,$ 

which we refer to as restructured regression.

We observe that

$$\mathbb{E}[z_i(y_i - z_ig_0)] = \mathbb{E}[z_i^2(\mathbf{a}^\top \boldsymbol{\beta}^* - g_0)]$$

Hence, the original null is equivalent to the new null of the following kind

 $\mathbb{E}[z_i(y_i-z_ig_0)]=0.$ 

The test statistic then takes a simple form

$$\frac{n^{-1/2}\sum_{i=1}^{n} z_i(y_i - z_ig_0)}{\sqrt{n^{-1}\sum_{i=1}^{n} z_i^2(y_i - z_ig_0)^2}}$$

#### Remark

The novel methodology consists of two-stages. At the first stage, our procedure establishes a data-driven feature decomposition based on the structure of the null hypothesis directly. At the second stage, only "a moment condition" of the restructured regression is tested.

First, we pretend that  $\Sigma_{\text{X}} = \mathbb{I}_{\text{p}}$  and consider

$$z_i = \left(\frac{a}{a^{\top}a}\right)^{\top} x_i, \qquad w_i = \left(\mathbb{I}_p - \frac{aa^{\top}}{a^{\top}a}\right) x_i$$

Although the decomposition  $\mathbf{x}_i = \mathbf{a}zi + \mathbf{w}_i$  still holds, features  $z_i$  and  $\mathbf{w}_i$  might be highly correlated.

However, by introducing a orthogonal matrix  $U_a$  such that

$$\mathbb{I}_p - \frac{\mathbf{a}\mathbf{a}^\top}{\mathbf{a}^\top \mathbf{a}} = \mathbf{U}_a \mathbf{U}_a^\top$$

we can construct

$$\widetilde{W}=WU_{\text{a}}$$

and observe that

$$y_i = z_i(\mathbf{a}^{\top}\boldsymbol{\beta}^*) + \widetilde{\mathbf{W}}_i^{\top}\boldsymbol{\pi}_* + \epsilon_i,$$

for

$$\boldsymbol{\pi}_* = \boldsymbol{\mathsf{U}}_{\boldsymbol{\mathsf{Z}}}^\top \boldsymbol{\beta}^*.$$

Introduce a feature model

$$\mathbf{z}_{i} = \widetilde{\mathbf{W}}_{i}^{\top} \boldsymbol{\gamma}^{*} + \mathbf{u}_{i}$$

where  $\boldsymbol{\gamma}^*$  is the unknown parameter and  $u_i$  are independent of  $\widetilde{w}_i.$  Then, consider the moment

$$H_0: \mathbb{E}\left[ (\boldsymbol{z}_i - \widetilde{\boldsymbol{w}}_i^\top \boldsymbol{\gamma}^*)^\top \left( \boldsymbol{y}_i - \boldsymbol{z}_i \boldsymbol{g}_0 - \widetilde{\boldsymbol{w}}_i^\top \boldsymbol{\pi}^* \right) \right] = 0.$$

and develop a test

$$T_{n} = \sqrt{n} \frac{(z - \widetilde{W}\widehat{\gamma}) \left(y - zg_{0} - \widetilde{W}\widehat{\pi}\right)}{\|z - \widetilde{W}\widehat{\gamma}\|_{2}\|y - zg_{0} - \widetilde{W}\widehat{\pi}\|_{2}}$$

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# Condition

Let  $\mathbf{W} = (\mathbf{Z}, \mathbf{X})$  and  $\mathbf{w}_i = (\mathbf{z}_i, \mathbf{x}_i^{\top})^{\top}$ . The matrix  $\mathbf{\Sigma}_W = \mathbb{E}[\mathbf{W}^{\top}\mathbf{W}]/n \in \mathbb{R}^{p \times p}$ satisfies that  $\kappa_1 \leq \sigma_{\min}(\mathbf{\Sigma}_W) \leq \sigma_{\max}(\mathbf{\Sigma}_W) \leq \kappa_2$ . The vectors  $\mathbf{\Sigma}_W^{-1/2}\mathbf{w}_1$  are centered with sub-Gaussian norms upper bounded by  $\kappa_3$  and  $\mathbb{E}|\varepsilon_1|^{2+\delta} \leq \kappa_4$ . Moreover,  $\log p = o\left(n^{\delta/(2+\delta)} \wedge n\right)$ .

 $\rightarrow\,$  For the designs, it is standard to impose well-behaved covariance matrices and sub-Gaussian properties.

# Condition

$$\| \boldsymbol{\gamma}^* \|_2 \leq \kappa_5$$
 and  $\mathsf{s}_{ heta} = \mathsf{o}\left( \sqrt{\mathsf{n}/\log \mathsf{n}} / \log \mathsf{p} 
ight)$ , where  $\mathsf{s}_{ heta} = \| \boldsymbol{\theta}^* \|_0$ .

→ The assumption on  $s_{\theta}$  imposes sparsity in the first row of the precision matrix  $\Sigma_{w}$  and the rate for  $s_{\theta}$  is stronger than the conditions in BCH and NL imposing  $o(\sqrt{n}/\log p)$  and in VBRD imposing  $o(n/\log p)$ .

## Theorem

Let Conditions 1 and 2 hold. Then under  ${\rm H}_{\rm 0}$ 

$$\forall \alpha \in (0,1), \lim_{n \to \infty} \mathbb{P}\left( |\mathsf{T}_n(\beta_0)| > \Phi^{-1}(1-\alpha/2) \right) = \alpha.$$

 $\rightarrow$  Theorem 2 formally establishes that the new CorrT test is asymptotically exact in testing  $\beta^* = \beta_0$ . In particular, CorrT is robust to dense  $\gamma^*$  in the sense that even under dense  $\gamma^*$ , our procedure does not generate false positive results.

We say that a procedure for testing the hypothesis (10) is sparsity-adaptive if

(i) this procedure does not require knowledge of  $s_{\gamma}$ ,

(ii) provides valid inference under any  $s_{\gamma}$  and

(iii) achieves efficiency with sparse  $oldsymbol{\gamma}^*$ .

We now show the third property, efficiency under sparse  $\gamma^*$ . To formally discuss our results, we consider testing  $H_0: \beta^* = \beta_0$  versus

$$H_{1,h}: \ \beta^* = \beta_0 + h/\sqrt{n}.$$
(11)

where  $h \in \mathbb{R}$  is a fixed constant.

#### Theorem

Let Conditions 1 and 2 hold. Suppose that  $s_{\gamma} = o (n/log(p \lor n))$  and  $\sigma_u/\sigma_{\varepsilon} \to \kappa_0$  for some constant  $\kappa_0 > 0$ . Then, under  $H_{1,h}$  in (11),

$$\mathsf{P}\left(|\mathsf{T}_{\mathsf{n}}(\beta_0)| > \Phi^{-1}(1-\alpha/2)\right) \to \Psi(\alpha,\kappa_0,\mathsf{h}),$$

where  $\Psi(h, \kappa_0, \alpha) = 2 - \Phi \left( \Phi^{-1}(1 - \alpha/2) + h\kappa_0 \right) - \Phi \left( \Phi^{-1}(1 - \alpha/2) - h\kappa_0 \right).$ 

 $\rightarrow\,$  Theorem 3 establishes the local power of CorrT. It turns out that this local power matches that of existing sparsity-based methods, such as VBRD, NL and BCH, that are shown to be efficient.

## Theorem

Let Conditions 1 and 2 hold together with log p=o(n). Let  $\boldsymbol{\Sigma}_X=E[\boldsymbol{x}_i\boldsymbol{x}_i^\top]\in\mathbb{R}^{(p-1)\times(p-1)}.$  Suppose that

$$\|\mathbf{\Sigma}_{\mathbf{X}} \boldsymbol{\gamma}^*\|_{\infty} \sqrt{n \log p} = o(1),$$

and with  $n \to \infty$  and some  $\kappa > 0$ ,  $(\gamma^* {}^{\top} \Sigma_X \gamma^* + \sigma_{\varepsilon}^2) \sigma_u^{-2} \to \kappa$ . Then, under  $H_{1,h}$  in (11),

$$\lim_{\mathsf{n},\mathsf{p}\to\infty}\mathsf{P}_{\beta^*}\left(|\mathsf{T}_\mathsf{n}|>\Phi^{-1}(1-\alpha)\right)=\Psi(\mathsf{h},\kappa,\alpha),$$

where  $\Psi(h, \kappa, \alpha)$  is defined in Theorem 3.

- \* For n, p  $\rightarrow \infty$ ,  $\sqrt{\log p}/n = o(1)$  (i.e.  $n/p \rightarrow 0$ ), the Type II error of the proposed CorrT test, against alternatives that are larger than  $O(n^{-1/2})$ , converges to zero.
- \* If  $\Sigma_X = \mathbb{I}_p$ , the condition  $\|\Sigma_X \gamma^*\|_{\infty} \sqrt{n \log p} = o(1)$  is satisfied for all  $\gamma^*$  for which

$$\|\boldsymbol{\gamma}^*\|_{\infty} = O(1/\sqrt{n\log p}), \|\boldsymbol{\gamma}^*\|_2 = O(\sqrt{n}/\log p);$$

\* If  $\max_{1 \le j \le p} \|\Sigma_{X,j}\|_1 = o(\sqrt{p/(n \log p)})$ , we can consider all

$$oldsymbol{\gamma}^* = {\mathsf{c}}/{\sqrt{\mathsf{p}}}$$

with  $\|c\|_{\infty} = O(1)$ .

 Minimax testing of one coordinate (not the whole parameter) in dense high-dimensional testing is possible!

### Theorem

Let Conditions 1 and 2 hold together with log p=o(n). Let  $\mathbf{\Sigma}_X=E[\mathbf{x}_i\mathbf{x}_i^\top]\in\mathbb{R}^{(p-1)\times(p-1)}.$  Suppose that

$$oldsymbol{\gamma}^* = oldsymbol{\pi}^* + oldsymbol{\mu}^*$$

for  $\pi^*$  and  $\mu^*$  satisfying  $\|\pi^*\|_0 = o(\sqrt{n}/\log p)$ ,  $(\mu^{*\top}\Sigma_X\mu^* + \sigma_{\varepsilon}^2)\sigma_u^{-2} \to \kappa$  and  $\|\Sigma_X\mu^*\|_{\infty}\sqrt{n\log p} = o(1)$  for some  $\kappa > 0$  as  $n \to \infty$ . Then, under  $H_{1,h}$  in (11),

$$\lim_{h,p\to\infty}\mathsf{P}_{\beta^*}\left(|\mathsf{T}_{\mathsf{n}}|>\Phi^{-1}(1-\alpha)\right)=\Psi(\mathsf{h},\kappa,\alpha),$$

where  $\Psi(h, \kappa, \alpha)$  is defined in Theorem 3.

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# Setting

LTD Light-tailed design: N(0,  $\Sigma_{(\rho)}$ ) with the (i, j) entry of  $\Sigma_{(\rho)}$  being  $\rho^{|i-j|}$ .

HTD Heavy-tailed design: each row of W is generated as  $\Sigma_{(\rho)}^{1/2}$ U, where  $U \in \mathbb{R}^n$  contains i.i.d random variables of Student's t-distribution with 3 degrees of freedom normalized to have variance one. (the third moment does not exist.)

The error term  $\varepsilon \in \mathbb{R}^n$  contains i.i.d random variables from either N(0, 1) (light-tailed error, or LTE) or Student's t-distribution with 6 degrees of freedom normalized to have variance one (heavy-tailed error, or HTE).

We set

$$\pi_j^* = \begin{cases} 2/\sqrt{n} & 2 \le j \le 4\\ 0 & j > \max\{s, 4\}\\ U(0, 4)/\sqrt{n} & \text{otherwise.} \end{cases}$$

We test the hypothesis

$$H_0: \pi_3^* = 2/\sqrt{n} + h.$$

# Table: Size properties (h = 0)

	LTD + LTE, $ ho = 0$			LTD + LTE, $\rho = -\frac{1}{2}$			HTD + HTE, $ ho = 0$		
	CorrT	Debias	Score	CorrT	Debias	Score	CorrT	Debias	Score
s = 1	0.03	0.05	0.04	0.05	0.04	0.05	0.06	0.04	0.02
s = 3	0.06	0.05	0.05	0.06	0.06	0.05	0.05	0.11	0.03
s = 5	0.09	0.09	0.09	0.07	0.11	0.10	0.07	0.04	0.04
s = 10	0.01	0.03	0.03	0.03	0.05	0.03	0.06	0.05	0.03
s = 20	0.08	0.12	0.11	0.03	0.06	0.06	0.03	0.12	0.04
s = 50	0.07	0.16	0.17	0.04	0.10	0.12	0.02	0.09	0.09
s = 100	0.05	0.29	0.28	0.01	0.15	0.14	0.05	0.20	0.21
s = n	0.04	0.35	0.33	0.04	0.27	0.27	0.04	0.38	0.38
s = p	0.07	0.54	0.52	0.04	0.39	0.40	0.05	0.57	0.53
	LTD + HTE, $ ho=0$		LTD + HTE, $ ho = -rac{1}{2}$			HTD + LTE, $ ho=0$			
	CorrT	Debias	Score	CorrT	Debias	Score	CorrT	Debias	Score
s = 1	0.03	0.05	0.04	0.04	0.04	0.02	0.06	0.05	0.05
s = 3	0.06	0.05	0.05	0.11	0.06	0.06	0.03	0.07	0.04
s = 5	0.09	0.09	0.09	0.05	0.06	0.05	0.06	0.11	0.07
s = 10	0.01	0.03	0.03	0.03	0.04	0.03	0.09	0.11	0.10
s = 20	0.08	0.12	0.11	0.06	0.11	0.10	0.05	0.13	0.06
s = 50	0.07	0.16	0.17	0.07	0.16	0.15	0.06	0.19	0.14
s = 100	0.05	0.29	0.28	0.05	0.33	0.26	0.05	0.24	0.22
s = n	0.04	0.35	0.33	0.05	0.43	0.41	0.05	0.40	0.31
s — n	0.07	0.54	0.52	0.06	0.51	0.50	0.06	0.53	0.51

## Power curves

# Figure: Light-tailed errors





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- \* Genome-wide gene expression profiling was performed using micro RNA from biopsies from 114 pre-treated patients with HER2+ breast cancer.
- \* The complete data contains gene expression values of about 20000 genes located on different chromosomes.
- BRCA1 is a human tumor suppressor gene that is normally expressed in the cells of breast and other tissue, where they help repair damaged DNA.
- \* Research suggests that the BRCA1 proteins regulate the activity of other genes including tumor suppressors and regulators of the cell division cycle.
- \* Moreover, it is believed that BRCA1 may regulate pathways that remove the damages in DNA introduced by the certain drugs.
- Thus, understanding associations between BRCA1 and other genes provides a potentially important tool for tailoring chemotherapy in cancer treatment.

Gene	Biological association	Test Statistic				
		CorrT	Debias	Score		
IGF2R <sup>1</sup>	breast cancer tumor suppressor	-4.692	-4.285	-4.445		
Nmi <sup>2</sup>	endogenously associated with BRCA1	-4.239	-2.956	-2.669		
RBBP4 <sup>3</sup>	breast cancer	-4.186	-3.314	-2.806		
NPM1 <sup>4</sup>	breast cancer	-3.027	-2.112	-1.601		
NARS2 <sup>5</sup>	breast cancer	-4.163	-5.000	-4.983		
B3GALNT1	lung cancer	1.151	2.082	2.065		
C3orf62	lung cancer	-1.274	-2.143	-2.139		
LTB	lung cancer	-0.131	-2.107	-2.143		
TNFAIP1	lung cancer	1.231	2.181	2.118		
CCPG1	prostate cancer	-1.597	-2.154	-2.251		
LRRIQ3	colorectal cancer	-1.025	-2.480	-2.240		
LOC100507537	bladder cancer	-0.137	-1.966	-1.135		
ELOVL4	ataxia	-1.354	-2.152	-2.136		

<sup>1</sup>sensitivity marker for radiation, chemotherapy, and endocrine therapy

<sup>2</sup>interactive binding protein

<sup>3</sup>retinoblastoma binding protein, a chromatin modeling factor

<sup>4</sup>blocks breast cancer cells

<sup>5</sup>partial or complete loss of

- \* Study the equity risk premia during different states from 1980-2014. of the economy
- The response is the excess return of the U.S stock market observed at time t, covariates are a large number of macroeconomic variables observed at time t – 1 (McCracken, M. W. and Ng, S. (2015)) and st denotes the NBER recession indicator; st = 1 means that the economy is in recession at time t.
- \* Are risk premia in recessions higher than in expansions with the magnitude of difference that is economically meaningful?



Thank you for your attention!