Scalable Design with Posterior-Based Operating Characteristics

Luke Hagar

lmhagar@uwaterloo.ca

2024 Joint Research Conference
June 20, 2024

UNIVERSITY OF WATERLOO

Associated Work

Hagar, L. and Stevens, N. T. (2024+)

Scalable design with posterior-based operating characteristics.

Revision invited at the *Journal of the American Statistical Association*

arxiv.org/abs/2312.10814

Semaglutide Effectiveness [2]

- Patients in groups 1 and 2 are respectively given a semaglutide and placebo for 68 weeks.

Illustrative Example

Semaglutide Effectiveness [2]

- Patients in groups 1 and 2 are respectively given a semaglutide and placebo for 68 weeks.
- We model weight loss in kg via Bayesian linear regression: $y_i = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \varepsilon_i$.

Illustrative Example

Semaglutide Effectiveness [2]

- Patients in groups 1 and 2 are respectively given a semaglutide and placebo for 68 weeks.
- We model weight loss in kg via Bayesian linear regression: $y_i = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \varepsilon_i$.
  - $x_1 = \mathbb{I}(Group = 1)$, x_2 is baseline waist circumference in cm, and $\varepsilon \sim \mathcal{N}(0, \sigma_\varepsilon^2)$.

Illustrative Example

Semaglutide Effectiveness [2]

- Patients in groups 1 and 2 are respectively given a semaglutide and placebo for 68 weeks.
- We model weight loss in kg via Bayesian linear regression: $y_i = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \varepsilon_i$.
  - $x_1 = \mathbb{I}(Group = 1)$, x_2 is baseline waist circumference in cm, and $\varepsilon \sim \mathcal{N}(0, \sigma_\varepsilon^2)$.
- We assess the hypotheses $H_0 : \beta_1 \leq 5$ vs. $H_1 : \beta_1 > 5$.

Illustrative Example

Semaglutide Effectiveness [2]

- Patients in groups 1 and 2 are respectively given a semaglutide and placebo for 68 weeks.
- We model weight loss in kg via Bayesian linear regression: $y_i = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \varepsilon_i$.
  - $x_1 = \mathbb{I}(Group = 1)$, x_2 is baseline waist circumference in cm, and $\varepsilon \sim \mathcal{N}(0, \sigma_\varepsilon^2)$.
- We assess the hypotheses $H_0 : \beta_1 \leq 5$ vs. $H_1 : \beta_1 > 5$.

Hypothesis Testing

- We conclude H_1 is true if $Pr(H_1 | data) > \gamma$ for a critical value $\gamma \in [0.5, 1)$.

Illustrative Example

Semaglutide Effectiveness [2]

- Patients in groups 1 and 2 are respectively given a semaglutide and placebo for 68 weeks.
- We model weight loss in kg via Bayesian linear regression: $y_i = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \varepsilon_i$.
  - $x_1 = \mathbb{I}(Group = 1)$, x_2 is baseline waist circumference in cm, and $\varepsilon \sim \mathcal{N}(0, \sigma_\varepsilon^2)$.
- We assess the hypotheses $H_0 : \beta_1 \leq 5$ vs. $H_1 : \beta_1 > 5$.

Hypothesis Testing

- We conclude H_1 is true if $Pr(H_1 | data) > \gamma$ for a critical value $\gamma \in [0.5, 1)$.
  - We choose γ and sample sizes $n_1 = 2n$ and $n_2 = n$ a priori.

Semaglutide Effectiveness [2]

- Patients in groups 1 and 2 are respectively given a semaglutide and placebo for 68 weeks.
- We model weight loss in kg via Bayesian linear regression: $y_i = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \varepsilon_i$.
  - $x_1 = \mathbb{I}(Group = 1)$, x_2 is baseline waist circumference in cm, and $\varepsilon \sim \mathcal{N}(0, \sigma^2_\varepsilon)$.
- We assess the hypotheses $H_0 : \beta_1 \leq 5$ vs. $H_1 : \beta_1 > 5$.

Hypothesis Testing

- We conclude H_1 is true if $Pr(H_1 | data) > \gamma$ for a critical value $\gamma \in [0.5, 1)$.
  - We choose γ and sample sizes $n_1 = 2n$ and $n_2 = n$ a priori.
  - We use an uninformative normal-inverse-gamma prior for $(\beta_0, \beta_1, \beta_2, \sigma^2_\varepsilon)$.

Operating Characteristics for Posterior Analyses

Data Generation Process

- $\Psi_0(\cdot)$: $(\beta_0, \beta_1, \beta_2) = (-25.75, 5, 0.25)$, $x_2 \sim \mathcal{N}(115, 14.5^2)$, and $\varepsilon \sim \mathcal{N}(0, 10.07^2)$.

Operating Characteristics for Posterior Analyses

Data Generation Process

- $\Psi_0(\cdot)$: $(\beta_0, \beta_1, \beta_2) = (-25.75, 5, 0.25)$, $x_2 \sim \mathcal{N}(115, 14.5^2)$, and $\varepsilon \sim \mathcal{N}(0, 10.07^2)$.
- $\Psi_1(\cdot)$: the same as $\Psi_0(\cdot)$ except $\beta_1 = \{9, 12\}$ with probability 0.5 each.

Operating Characteristics for Posterior Analyses

Data Generation Process

- $\Psi_0(\cdot)$: $(\beta_0, \beta_1, \beta_2) = (-25.75, 5, 0.25)$, $x_2 \sim \mathcal{N}(115, 14.5^2)$, and $\varepsilon \sim \mathcal{N}(0, 10.07^2)$.
- $\Psi_1(\cdot)$: the same as $\Psi_0(\cdot)$ except $\beta_1 = \{9, 12\}$ with probability 0.5 each.

Two Operating Characteristics

- *Power* is the probability that $Pr(H_1 | data) > \gamma$ according to $\Psi_1(\cdot)$.

Operating Characteristics for Posterior Analyses

Data Generation Process

- $\Psi_0(\cdot)$: $(\beta_0, \beta_1, \beta_2) = (-25.75, 5, 0.25)$, $x_2 \sim \mathcal{N}(115, 14.5^2)$, and $\varepsilon \sim \mathcal{N}(0, 10.07^2)$.
- $\Psi_1(\cdot)$: the same as $\Psi_0(\cdot)$ except $\beta_1 = \{9, 12\}$ with probability 0.5 each.

Two Operating Characteristics

- *Power* is the probability that $Pr(H_1 | data) > \gamma$ according to $\Psi_1(\cdot)$.
  - We want power $\geq 1 - \beta = 0.8$.

Operating Characteristics for Posterior Analyses

Data Generation Process

- $\Psi_0(\cdot)$: $(\beta_0, \beta_1, \beta_2) = (-25.75, 5, 0.25)$, $x_2 \sim \mathcal{N}(115, 14.5^2)$, and $\varepsilon \sim \mathcal{N}(0, 10.07^2)$.
- $\Psi_1(\cdot)$: the same as $\Psi_0(\cdot)$ except $\beta_1 = \{9, 12\}$ with probability 0.5 each.

Two Operating Characteristics

- *Power* is the probability that $Pr(H_1|data) > \gamma$ according to $\Psi_1(\cdot)$.
  - We want power $\geq 1 - \beta = 0.8$.
- The *type I error rate* is the probability that $Pr(H_1|data) > \gamma$ according to $\Psi_0(\cdot)$.

Operating Characteristics for Posterior Analyses

Data Generation Process

- $\Psi_0(\cdot)$: $(\beta_0, \beta_1, \beta_2) = (-25.75, 5, 0.25)$, $x_2 \sim \mathcal{N}(115, 14.5^2)$, and $\varepsilon \sim \mathcal{N}(0, 10.07^2)$.
- $\Psi_1(\cdot)$: the same as $\Psi_0(\cdot)$ except $\beta_1 = \{9, 12\}$ with probability 0.5 each.

Two Operating Characteristics

- *Power* is the probability that $Pr(H_1|data) > \gamma$ according to $\Psi_1(\cdot)$.
  - We want power $\geq 1 - \beta = 0.8$.
- The *type I error rate* is the probability that $Pr(H_1|data) > \gamma$ according to $\Psi_0(\cdot)$.
  - We want the type I error rate $\leq \alpha = 0.05$.

Estimating Sampling Distributions

1. Generate $\{y_i, x_{1i}, x_{2i}\}_{i=1}^{3n}$ according to $\Psi_1(\cdot)$ or $\Psi_0(\cdot)$.

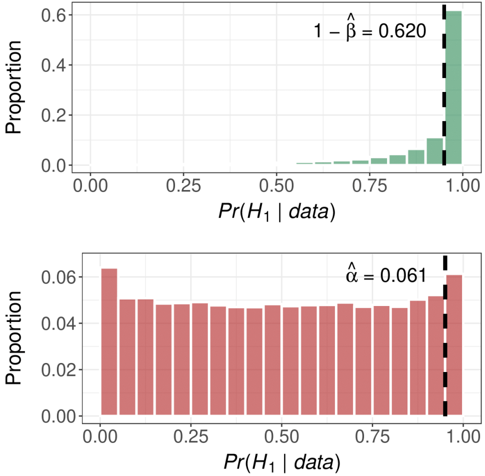


Figure 1: Sampling Distributions of $Pr(H_1|data)$ for $n = 20$ and $\gamma = 0.95$

Sampling Distributions of Posterior Probabilities

Estimating Sampling Distributions

1. Generate $\{y_i, x_{1i}, x_{2i}\}_{i=1}^{3n}$ according to $\Psi_1(\cdot)$ or $\Psi_0(\cdot)$.
2. Estimate $Pr(H_1 | data)$.

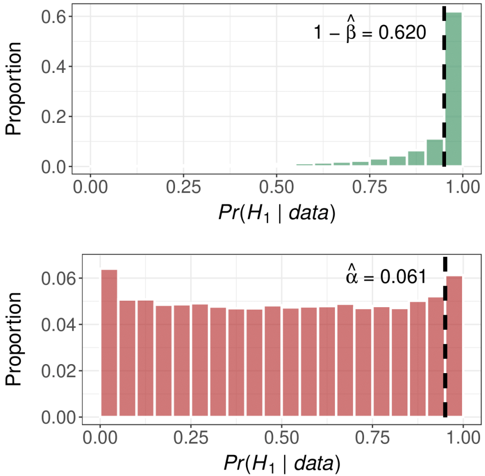


Figure 1: Sampling Distributions of $Pr(H_1 | data)$ for $n = 20$ and $\gamma = 0.95$

Estimating Sampling Distributions

1. Generate $\{y_i, x_{1i}, x_{2i}\}_{i=1}^{3n}$ according to $\Psi_1(\cdot)$ or $\Psi_0(\cdot)$.
2. Estimate $Pr(H_1 | data)$.
3. Repeat m times.

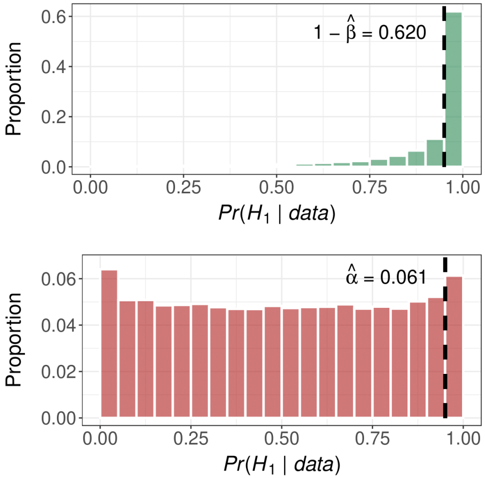


Figure 1: Sampling Distributions of $Pr(H_1 | data)$ for $n = 20$ and $\gamma = 0.95$

Sampling Distributions of Posterior Probabilities

Estimating Sampling Distributions

1. Generate $\{y_i, x_{1i}, x_{2i}\}_{i=1}^{3n}$ according to $\Psi_1(\cdot)$ or $\Psi_0(\cdot)$.
2. Estimate $Pr(H_1 | data)$.
3. Repeat m times.

Sampling Distribution Segments

- We choose (n, γ) to satisfy criteria for both operating characteristics.

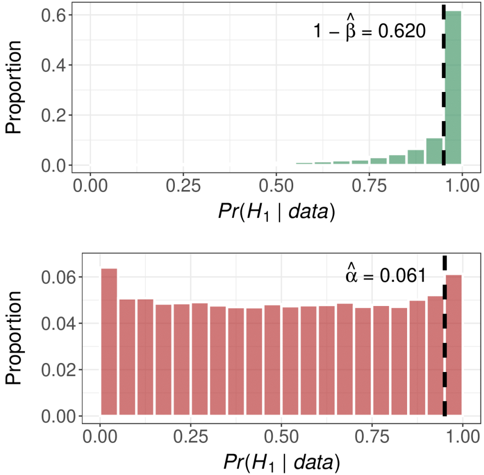


Figure 1: Sampling Distributions of $Pr(H_1 | data)$ for $n = 20$ and $\gamma = 0.95$

Sampling Distributions of Posterior Probabilities

Estimating Sampling Distributions

1. Generate $\{y_i, x_{1i}, x_{2i}\}_{i=1}^{3n}$ according to $\Psi_1(\cdot)$ or $\Psi_0(\cdot)$.
2. Estimate $Pr(H_1 | data)$.
3. Repeat m times.

Sampling Distribution Segments

- We choose (n, γ) to satisfy criteria for both operating characteristics.
- Can we use only sampling distribution segments near the β-quantile under H_1 and the $(1-\alpha)$-quantile under H_0?

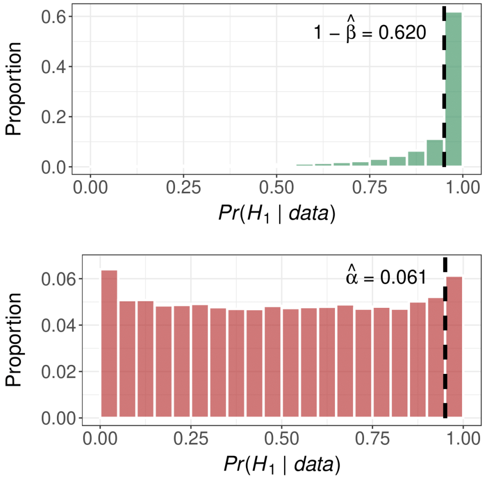


Figure 1: Sampling Distributions of $Pr(H_1 | data)$ for $n = 20$ and $\gamma = 0.95$

Pseudorandom vs. Sobol' Sequences

- In d dimensions, we often generate points $\{\boldsymbol{u}_r\}_{r=1}^{m} \overset{i.i.d}{\sim} U([0,1]^d)$.

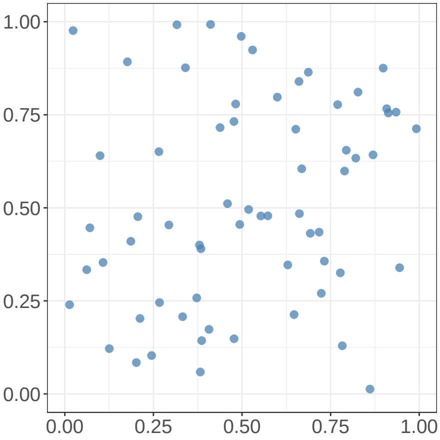


Figure 2: 2D Pseudorandom Sequence with $m = 64$ Points

Pseudorandom vs. Sobol' Sequences

- In d dimensions, we often generate points $\{\boldsymbol{u}_r\}_{r=1}^{m} \overset{i.i.d}{\sim} U([0,1]^d)$.
- Low-discrepancy Sobol' sequences [3] arise from integer expansion in base 2.

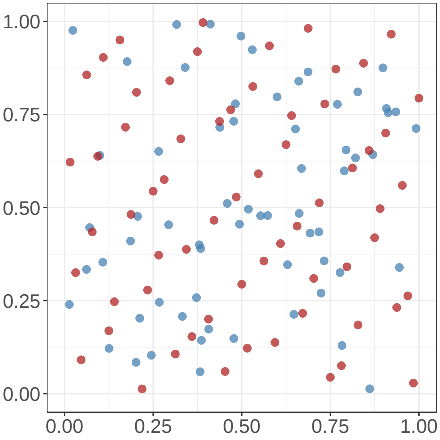


Figure 3: 2D Pseudorandom (Blue) vs. Sobol' (Red) Sequences with $m = 64$ Points

Pseudorandom vs. Sobol' Sequences

- In d dimensions, we often generate points $\{\boldsymbol{u}_r\}_{r=1}^{m} \overset{i.i.d}{\sim} U([0,1]^d)$.
- Low-discrepancy Sobol' sequences [3] arise from integer expansion in base 2.
- If we randomize these sequences [4], each point $\boldsymbol{u}_r \sim U([0,1]^d)$.

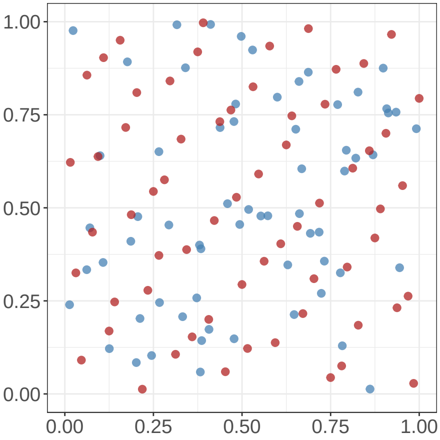


Figure 3: 2D Pseudorandom (Blue) vs. Sobol' (Red) Sequences with $m = 64$ Points

Simulation-Based Design

Pseudorandom vs. Sobol' Sequences

- In d dimensions, we often generate points $\{\boldsymbol{u}_r\}_{r=1}^m \overset{i.i.d}{\sim} U([0,1]^d)$.
- Low-discrepancy Sobol' sequences [3] arise from integer expansion in base 2.
- If we randomize these sequences [4], each point $\boldsymbol{u}_r \sim U([0,1]^d)$.
- These dependent points $\{\boldsymbol{u}_r\}_{r=1}^m$ can prompt consistent, precise estimators of power and the type I error rate.

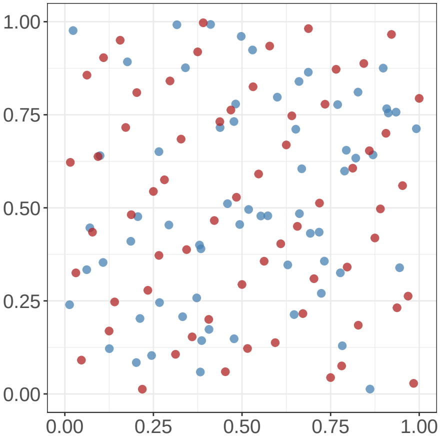


Figure 3: 2D Pseudorandom (Blue) vs. Sobol' (Red) Sequences with $m = 64$ Points

The Unit Hypercube

- The illustrative example uses Sobol' sequences $\{\boldsymbol{u}_r\}_{r=1}^{m}$ from $[0, 1]^7$.

The Unit Hypercube

- The illustrative example uses Sobol' sequences $\{\boldsymbol{u}_r\}_{r=1}^{m}$ from $[0, 1]^7$.

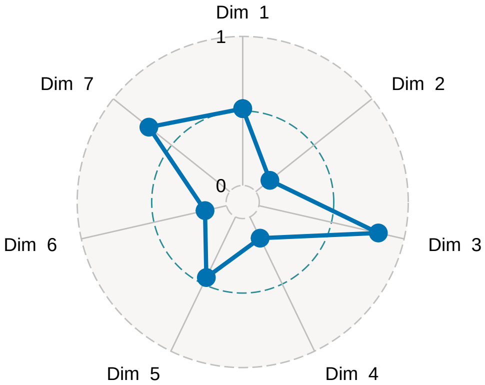


Figure 4: Points from $[0, 1]^7$

The Unit Hypercube

- The illustrative example uses Sobol' sequences $\{\boldsymbol{u}_r\}_{r=1}^{m}$ from $[0, 1]^7$.

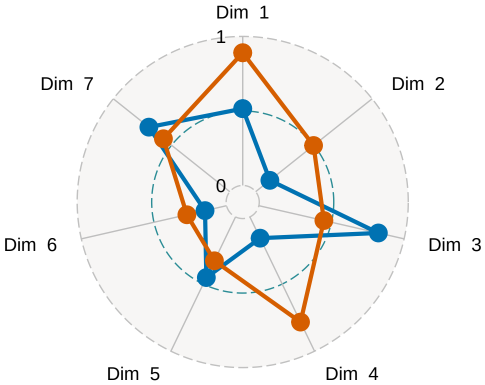


Figure 4: Points from $[0, 1]^7$

The Unit Hypercube

- The illustrative example uses Sobol' sequences $\{\boldsymbol{u}_r\}_{r=1}^{m}$ from $[0,1]^7$.

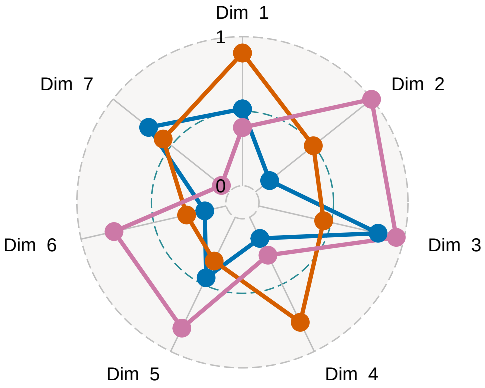


Figure 4: Points from $[0,1]^7$

Simulation in Higher Dimensions

The Unit Hypercube

- The illustrative example uses Sobol' sequences $\{\boldsymbol{u}_r\}_{r=1}^m$ from $[0, 1]^7$.
- These sums over all patients i are low-dimensional conduits for the data: x_{2i}, $x_{1i}x_{2i}$, ε_i, $x_{1i}\varepsilon_i$, x_{2i}^2, ε_i^2, $x_{2i}\varepsilon_i$.

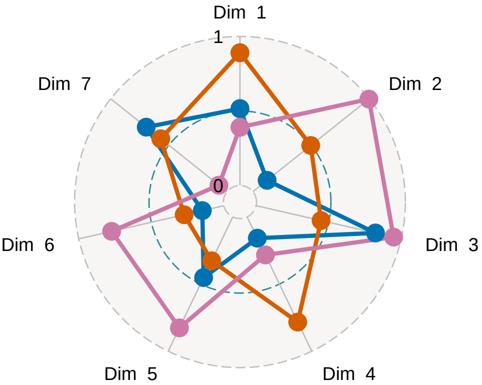


Figure 4: Points from $[0, 1]^7$

Mapping $[0, 1]^7$ to Posterior Probabilities

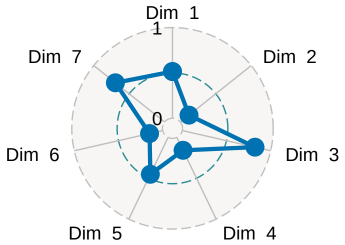
Low-Dimensional Conduits for the Data

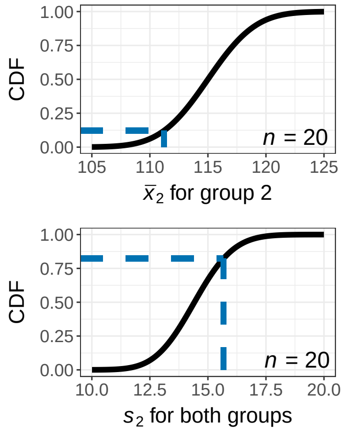
- The sufficient statistics are based on normal and chi-squared distributions.

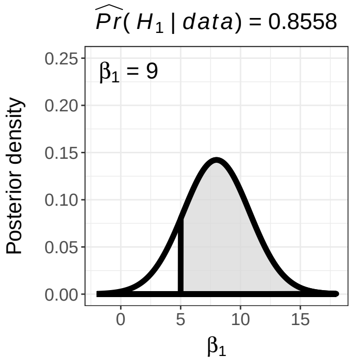
Mapping $[0, 1]^7$ to Posterior Probabilities

Low-Dimensional Conduits for the Data

- The sufficient statistics are based on normal and chi-squared distributions.



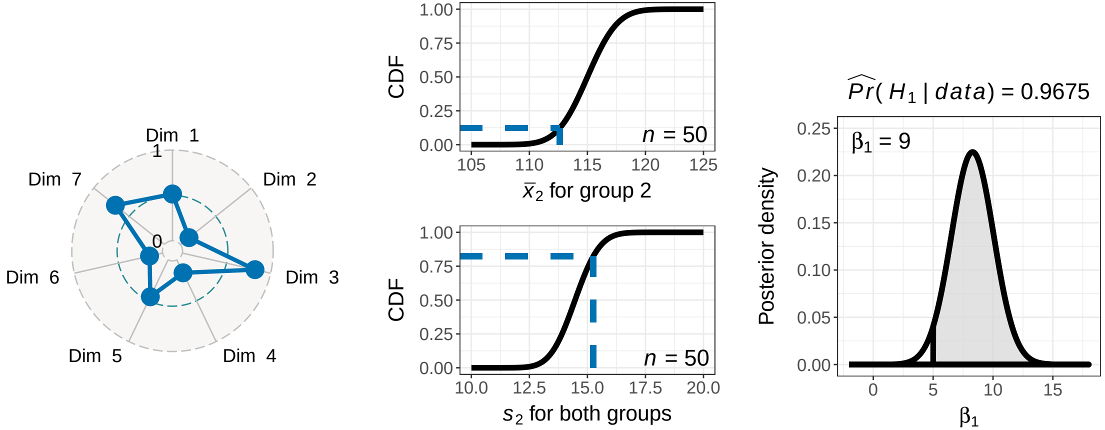




Mapping $[0, 1]^7$ to Posterior Probabilities

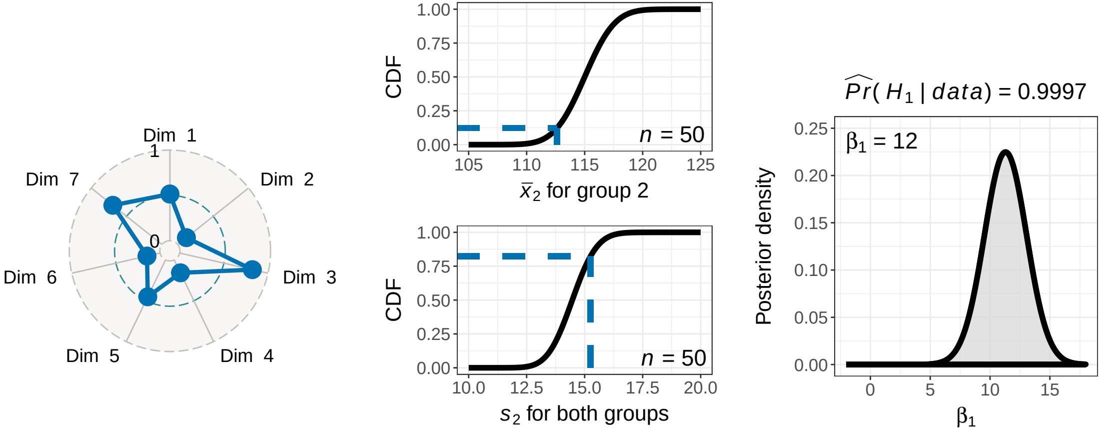
Low-Dimensional Conduits for the Data

- The sufficient statistics are based on normal and chi-squared distributions.



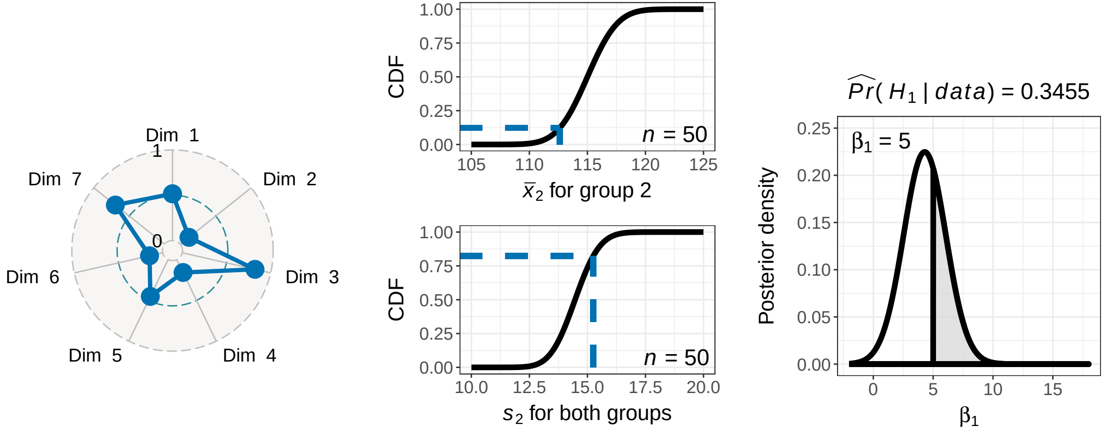
Low-Dimensional Conduits for the Data

- The sufficient statistics are based on normal and chi-squared distributions.



Low-Dimensional Conduits for the Data

- The sufficient statistics are based on normal and chi-squared distributions.



Selecting Sampling Distribution Segments

Algorithm

1. Generate $\{\boldsymbol{u}_r\}_{r=1}^{m} \in [0, 1]^7$ for H_0 and H_1.

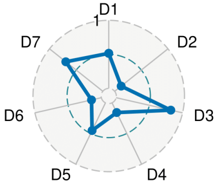


Figure 6: Posterior Probabilities with Data Conduits

Algorithm

1. Generate $\{\boldsymbol{u}_r\}_{r=1}^m \in [0, 1]^7$ for H_0 and H_1.

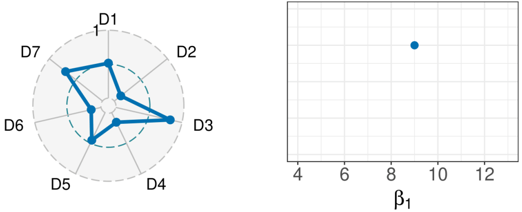


Figure 6: Posterior Probabilities with Data Conduits

Selecting Sampling Distribution Segments

Algorithm

1. Generate $\{\boldsymbol{u}_r\}_{r=1}^{m} \in [0, 1]^7$ for H_0 and H_1.
2. For fixed $\boldsymbol{u}_r$, consider $Pr(H_1 \,|\, data(\boldsymbol{u}_r, n))$ as a function of n prompted by the data conduits.

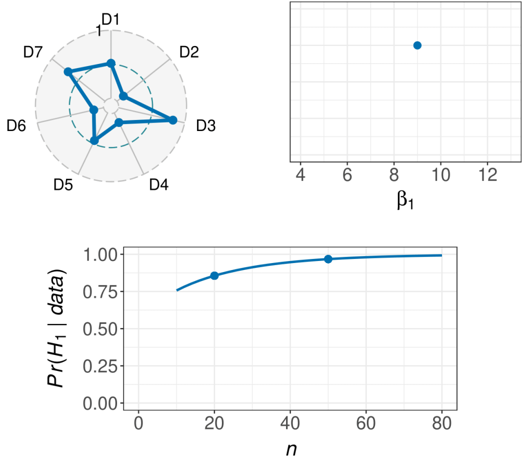


Figure 6: Posterior Probabilities with Data Conduits

Selecting Sampling Distribution Segments

Algorithm

1. Generate $\{\boldsymbol{u}_r\}_{r=1}^{m} \in [0,1]^7$ for H_0 and H_1.
2. For fixed $\boldsymbol{u}_r$, consider $Pr(H_1 \,|\, data(\boldsymbol{u}_r, n))$ as a function of n prompted by the data conduits.
3. $Pr(H_1 \,|\, data(\boldsymbol{u}_r, n))$ generally $\uparrow$ or remains constant with n when β_1 > or = 5.

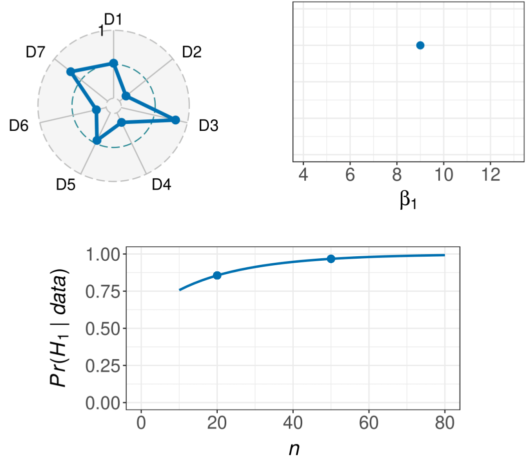


Figure 6: Posterior Probabilities with Data Conduits

Selecting Sampling Distribution Segments

Algorithm

1. Generate $\{\boldsymbol{u}_r\}_{r=1}^{m} \in [0, 1]^7$ for H_0 and H_1.
2. For fixed $\boldsymbol{u}_r$, consider $Pr(H_1 | data(\boldsymbol{u}_r, n))$ as a function of n prompted by the data conduits.
3. $Pr(H_1 | data(\boldsymbol{u}_r, n))$ generally $\uparrow$ or remains constant with n when β_1 > or = 5.

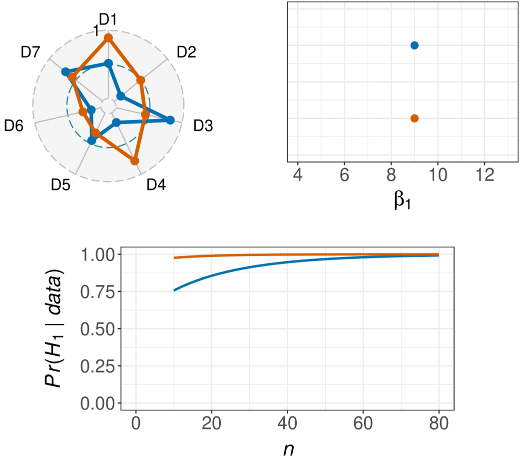


Figure 6: Posterior Probabilities with Data Conduits

Selecting Sampling Distribution Segments

Algorithm

1. Generate $\{\boldsymbol{u}_r\}_{r=1}^{m} \in [0, 1]^7$ for H_0 and H_1.
2. For fixed $\boldsymbol{u}_r$, consider $Pr(H_1 \,|\, data(\boldsymbol{u}_r, n))$ as a function of n prompted by the data conduits.
3. $Pr(H_1 \,|\, data(\boldsymbol{u}_r, n))$ generally $\uparrow$ or remains constant with n when β_1 > or = 5.

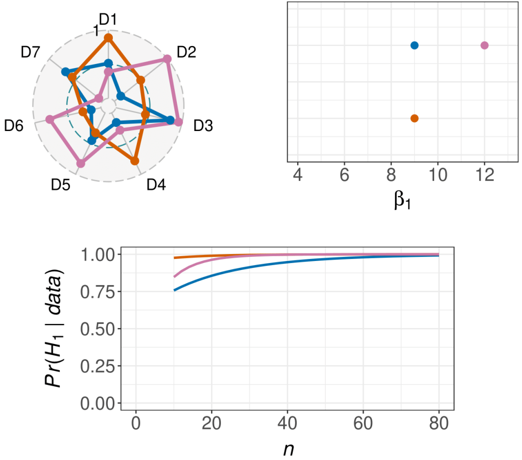


Figure 6: Posterior Probabilities with Data Conduits

Algorithm

1. Generate $\{\boldsymbol{u}_r\}_{r=1}^{m} \in [0, 1]^7$ for H_0 and H_1.
2. For fixed $\boldsymbol{u}_r$, consider $Pr(H_1 | data(\boldsymbol{u}_r, n))$ as a function of n prompted by the data conduits.
3. $Pr(H_1 | data(\boldsymbol{u}_r, n))$ generally $\uparrow$ or remains constant with n when β_1 > or = 5.

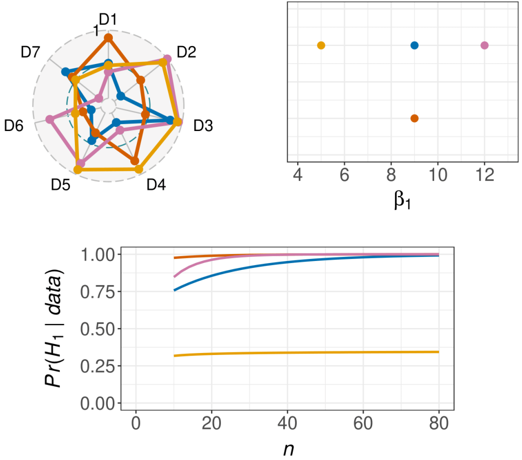


Figure 6: Posterior Probabilities with Data Conduits

Algorithm

1. Generate $\{\boldsymbol{u}_r\}_{r=1}^{m} \in [0,1]^7$ for H_0 and H_1.
2. For fixed $\boldsymbol{u}_r$, consider $Pr(H_1 | data(\boldsymbol{u}_r, n))$ as a function of n prompted by the data conduits.
3. $Pr(H_1 | data(\boldsymbol{u}_r, n))$ generally $\uparrow$ or remains constant with n when β_1 > or = 5.

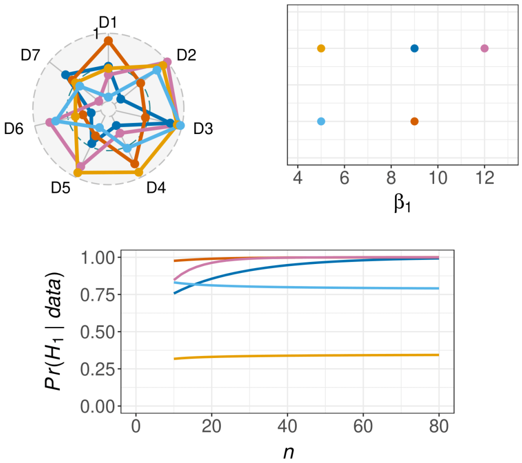


Figure 6: Posterior Probabilities with Data Conduits

Selecting Sampling Distribution Segments

Algorithm

1. Generate $\{\boldsymbol{u}_r\}_{r=1}^{m} \in [0, 1]^7$ for H_0 and H_1.
2. For fixed $\boldsymbol{u}_r$, consider $Pr(H_1 | data(\boldsymbol{u}_r, n))$ as a function of n prompted by the data conduits.
3. $Pr(H_1 | data(\boldsymbol{u}_r, n))$ generally $\uparrow$ or remains constant with n when β_1 > or = 5.
4. The logit of this function is approximately linear!

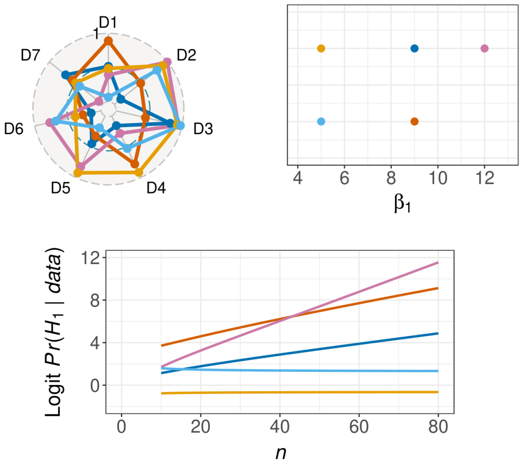


Figure 6: Posterior Probabilities with Data Conduits

Algorithm

1. Generate $\{\boldsymbol{u}_r\}_{r=1}^{m} \in [0, 1]^7$ for H_0 and H_1.
2. For fixed $\boldsymbol{u}_r$, consider $Pr(H_1 | data(\boldsymbol{u}_r, n))$ as a function of n prompted by the data conduits.
3. $Pr(H_1 | data(\boldsymbol{u}_r, n))$ generally $\uparrow$ or remains constant with n when $\beta_1 >$ or $= 5$.
4. The logit of this function is approximately linear!
5. We use these linear approximations to select segments.

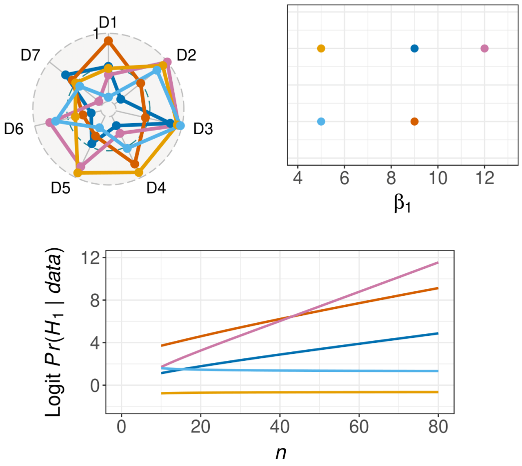


Figure 6: Posterior Probabilities with Data Conduits

Finding (n, γ) that minimizes n

Obtaining Linear Approximations

- Let $n^{(0)}$ be an initial sample size.

Finding (n, γ) that minimizes n

Obtaining Linear Approximations

- Let $n^{(0)}$ be an initial sample size.
- Use $\{\boldsymbol{u}_r\}_{r=1}^{m}$ to explore the sampling distributions of $Pr(H_1 | data)$ under H_1 and H_0.

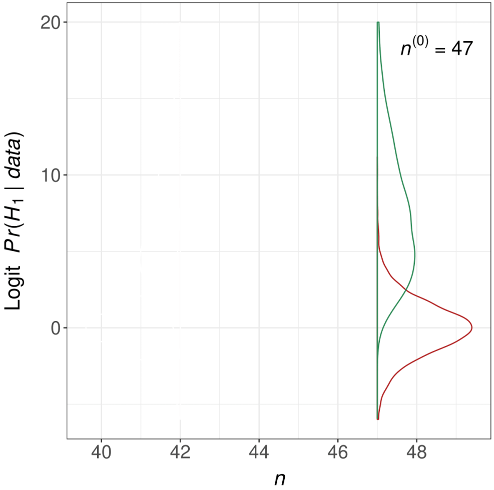


Figure 7: Full Sampling Distribution Exploration

Obtaining Linear Approximations

- Let $n^{(0)}$ be an initial sample size.
- Use $\{\boldsymbol{u}_r\}_{r=1}^{m}$ to explore the sampling distributions of $Pr(H_1 | data)$ under H_1 and H_0.
  - If $(1-\alpha)$-quantile under H_0 > β-quantile under H_1, $n^{(1)} > n^{(0)}$.

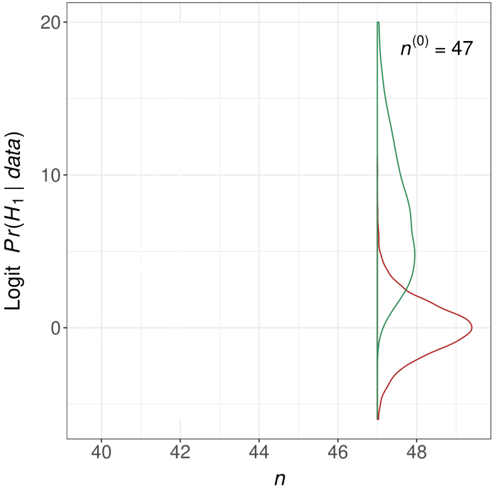


Figure 7: Full Sampling Distribution Exploration

Finding (n, γ) that minimizes n

Obtaining Linear Approximations

- Let $n^{(0)}$ be an initial sample size.
- Use $\{\boldsymbol{u}_r\}_{r=1}^{m}$ to explore the sampling distributions of $Pr(H_1 | data)$ under H_1 and H_0.
  - If $(1-\alpha)$-quantile under H_0 > β-quantile under H_1, $n^{(1)} > n^{(0)}$.
  - Otherwise, let $n^{(1)} < n^{(0)}$.

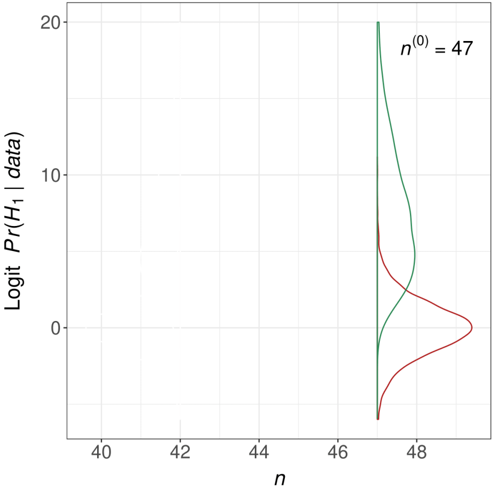


Figure 7: Full Sampling Distribution Exploration

Finding (n, γ) that minimizes n

Obtaining Linear Approximations

- Let $n^{(0)}$ be an initial sample size.
- Use $\{\boldsymbol{u}_r\}_{r=1}^{m}$ to explore the sampling distributions of $Pr(H_1 | data)$ under H_1 and H_0.
  - If $(1-\alpha)$-quantile under H_0 > β-quantile under H_1, $n^{(1)} > n^{(0)}$.
  - Otherwise, let $n^{(1)} < n^{(0)}$.
- Use the *same* points to explore the sampling distributions of $Pr(H_1 | data)$ under H_1 and H_0 for $n^{(1)}$.

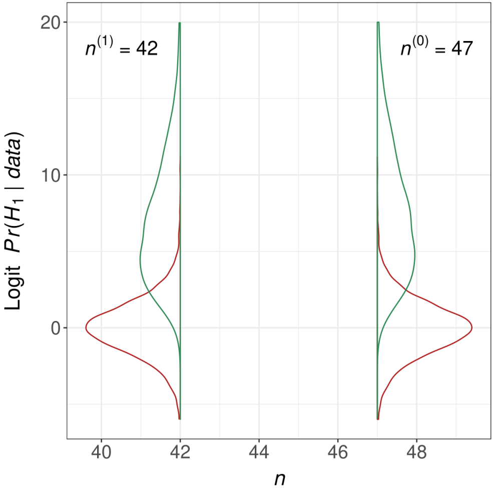


Figure 7: Full Sampling Distribution Exploration

Finding (n, γ) that minimizes n

Obtaining Linear Approximations

- Let $n^{(0)}$ be an initial sample size.
- Use $\{\boldsymbol{u}_r\}_{r=1}^{m}$ to explore the sampling distributions of $Pr(H_1 | data)$ under H_1 and H_0.
  - If $(1-\alpha)$-quantile under H_0 > β-quantile under H_1, $n^{(1)} > n^{(0)}$.
  - Otherwise, let $n^{(1)} < n^{(0)}$.
- Use the *same* points to explore the sampling distributions of $Pr(H_1 | data)$ under H_1 and H_0 for $n^{(1)}$.

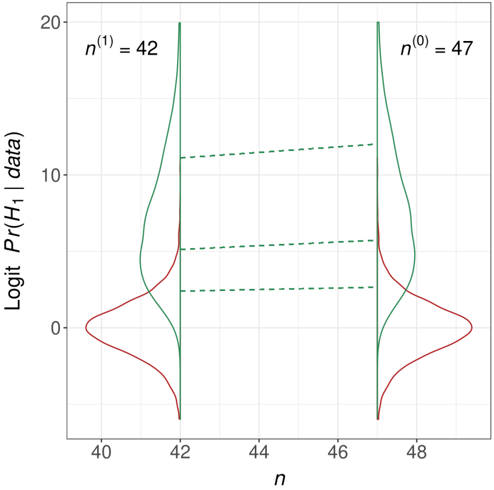


Figure 7: Full Sampling Distribution Exploration

Finding (n, γ) that minimizes n

Obtaining Linear Approximations

- Let $n^{(0)}$ be an initial sample size.
- Use $\{\boldsymbol{u}_r\}_{r=1}^{m}$ to explore the sampling distributions of $Pr(H_1 | data)$ under H_1 and H_0.
    - If $(1-\alpha)$-quantile under H_0 > β-quantile under H_1, $n^{(1)} > n^{(0)}$.
    - Otherwise, let $n^{(1)} < n^{(0)}$.
- Use the *same* points to explore the sampling distributions of $Pr(H_1 | data)$ under H_1 and H_0 for $n^{(1)}$.

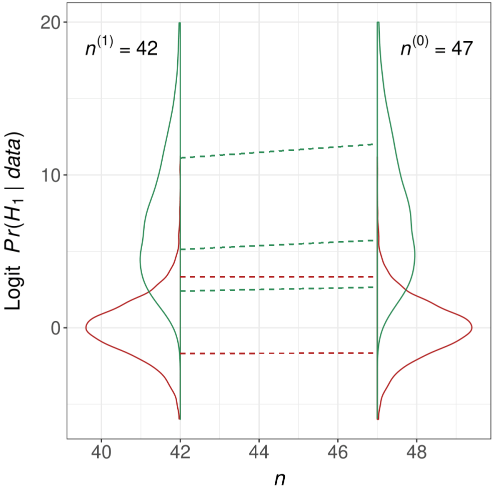


Figure 7: Full Sampling Distribution Exploration

Finding (n, γ) that minimizes n

Quantile Estimation with Segments

- Explore n-space with the $m_0 << m$ points whose linear approximations are closest to the relevant quantiles.

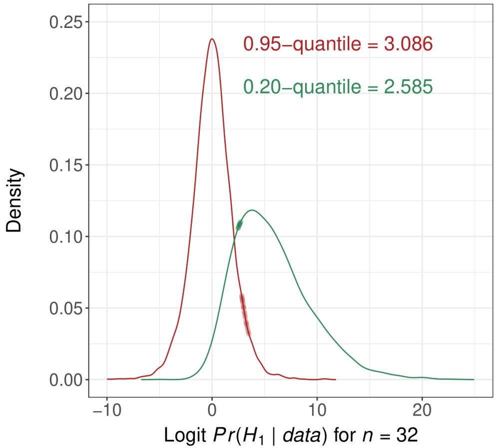


Figure 8: Sampling Distribution Segments

Quantile Estimation with Segments

- Explore n-space with the $m_0 << m$ points whose linear approximations are closest to the relevant quantiles.
  - Let $n^{(2)}$ be the smallest n such that the $(1-\alpha)$-quantile under $H_0 \leq \beta$-quantile under H_1.

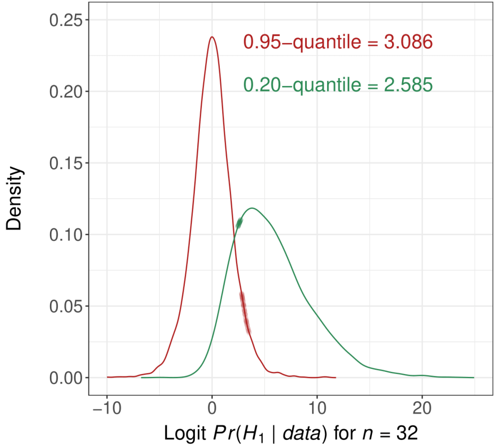


Figure 8: Sampling Distribution Segments

Finding (n, γ) that minimizes n

Quantile Estimation with Segments

- Explore n-space with the $m_0 << m$ points whose linear approximations are closest to the relevant quantiles.
  - Let $n^{(2)}$ be the smallest n such that the $(1 - \alpha)$-quantile under $H_0 \leq \beta$-quantile under H_1.

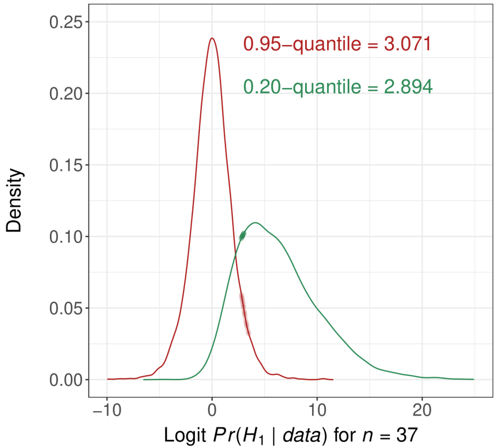


Figure 8: Sampling Distribution Segments

Finding (n, γ) that minimizes n

Quantile Estimation with Segments

- Explore n-space with the $m_0 << m$ points whose linear approximations are closest to the relevant quantiles.
  - Let $n^{(2)}$ be the smallest n such that the $(1-\alpha)$-quantile under $H_0 \leq \beta$-quantile under H_1.

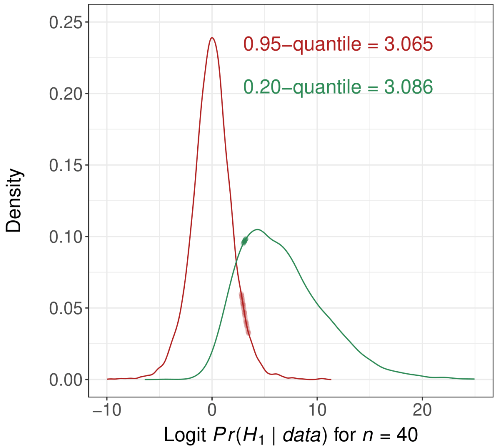


Figure 8: Sampling Distribution Segments

Finding (n, γ) that minimizes n

Quantile Estimation with Segments

- Explore n-space with the $m_0 << m$ points whose linear approximations are closest to the relevant quantiles.
  - Let $n^{(2)}$ be the smallest n such that the $(1-\alpha)$-quantile under $H_0 \leq \beta$-quantile under H_1.

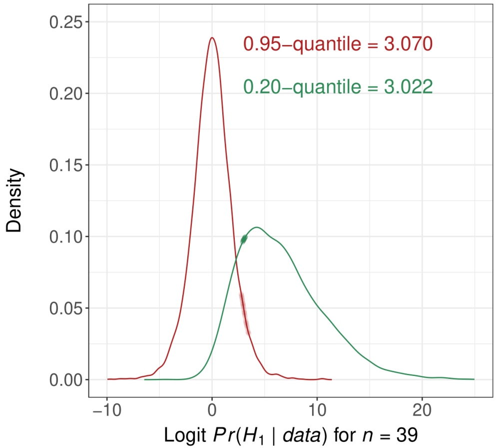


Figure 8: Sampling Distribution Segments

Finding (n, γ) that minimizes n

Quantile Estimation with Segments

- Explore n-space with the $m_0 << m$ points whose linear approximations are closest to the relevant quantiles.
  - Let $n^{(2)}$ be the smallest n such that the $(1 - \alpha)$-quantile under $H_0 \leq \beta$-quantile under H_1.
  - Explore entire sampling distributions for $n^{(2)}$.

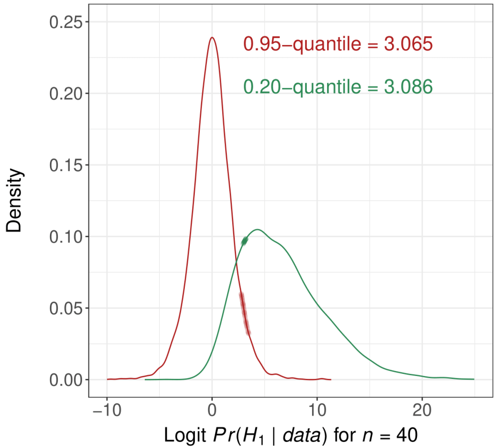


Figure 8: Sampling Distribution Segments

Finding (n, γ) that minimizes n

Quantile Estimation with Segments

- Explore n-space with the $m_0 << m$ points whose linear approximations are closest to the relevant quantiles.
  - Let $n^{(2)}$ be the smallest n such that the $(1-\alpha)$-quantile under $H_0 \leq \beta$-quantile under H_1.
  - Explore entire sampling distributions for $n^{(2)}$.
  - Choose $n = n^{(2)}$ and γ as the $(1-\alpha)$-quantile under H_0 for $n^{(2)}$.

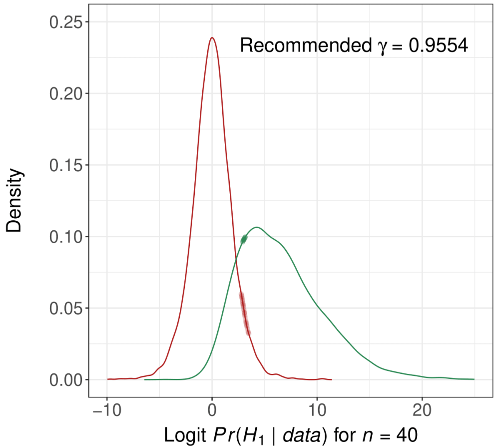


Figure 8: Sampling Distribution Segments

Finding (n, γ) that minimizes n

Quantile Estimation with Segments

- Explore n-space with the $m_0 << m$ points whose linear approximations are closest to the relevant quantiles.
  - Let $n^{(2)}$ be the smallest n such that the $(1-\alpha)$-quantile under $H_0 \leq \beta$-quantile under H_1.
  - Explore entire sampling distributions for $n^{(2)}$.
  - Choose $n = n^{(2)}$ and γ as the $(1-\alpha)$-quantile under H_0 for $n^{(2)}$.
- Sample size recommendations align with (slower) unbiased calculations.

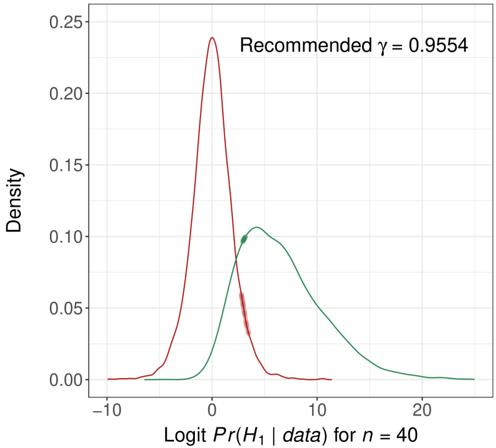


Figure 8: Sampling Distribution Segments

Computational Savings

Runtime Considerations

- Using sampling distribution segments is most beneficial when the recommended n is large.

Computational Savings

Runtime Considerations

- Using sampling distribution segments is most beneficial when the recommended n is large.
- The savings from using Sobol' sequences depends on the statistical model and simulation dimension d.

Runtime Considerations

- Using sampling distribution segments is most beneficial when the recommended n is large.
- The savings from using Sobol' sequences depends on the statistical model and simulation dimension d.

Table 1: Runtime for illustrative example with various exploration methods and sequence types.

Exploration	Sequence	Seconds	Savings
Segments	Sobol'	4	—
Full	Sobol'	14	250%
Segments	Pseudorandom	31	675%
Full	Pseudorandom	118	2850%

Contour Plots to Consider Various (n, γ)

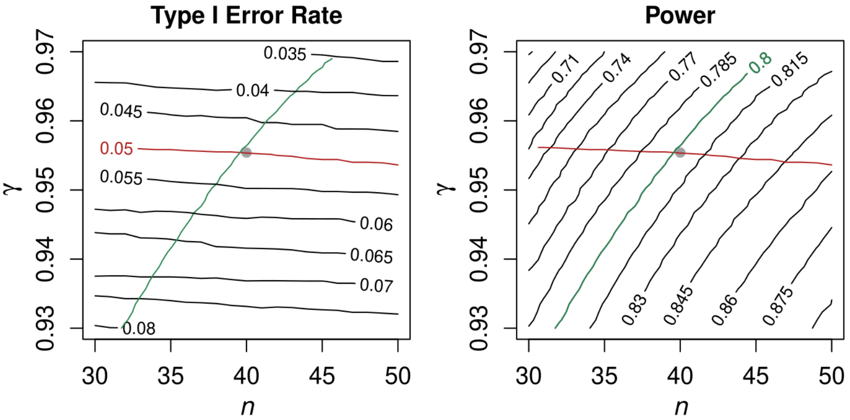


Figure 9: Plots with Repurposed Sampling Distributions and Optimal Design (Grey)

Approximate Normality of the Posterior

- This is required for the logit of $Pr(H_1 | data(\boldsymbol{u}_r, n))$ to be linear for large enough n.

General Theoretical Considerations

Approximate Normality of the Posterior

- This is required for the logit of $Pr(H_1 | data(\boldsymbol{u}_r, n))$ to be linear for large enough n.
- This normality holds under the conditions for the Bernstien-von Mises theorem [5].

General Theoretical Considerations

Approximate Normality of the Posterior

- This is required for the logit of $Pr(H_1 | data(\boldsymbol{u}_r, n))$ to be linear for large enough n.
- This normality holds under the conditions for the Bernstien-von Mises theorem [5].
- Monotonic transformations of the parameters can improve the normal approximation, especially when using the Laplace approximation [6] .

General Theoretical Considerations

Approximate Normality of the Posterior

- This is required for the logit of $Pr(H_1 | data(\boldsymbol{u}_r, n))$ to be linear for large enough n.
- This normality holds under the conditions for the Bernstien-von Mises theorem [5].
- Monotonic transformations of the parameters can improve the normal approximation, especially when using the Laplace approximation [6] .

Conduits for the Data

- The data must be summarized by conduits that are approximately normally distributed for large enough n.

Conclusion

Computational Efficiency

- Our method only thoroughly explores sampling distributions of posterior probabilities at 3 values of n.

Conclusion

Computational Efficiency

- Our method only thoroughly explores sampling distributions of posterior probabilities at 3 values of n.

Extensions

- We could extend these methods to settings where low-dimensional sufficient statistics do not exist [7].

Conclusion

Computational Efficiency

- Our method only thoroughly explores sampling distributions of posterior probabilities at 3 values of n.

Extensions

- We could extend these methods to settings where low-dimensional sufficient statistics do not exist [7].
- These methods could promote scalable design for sequential Bayesian hypothesis tests.

References

[1] Hagar, L. and N. T. Stevens. (2024+). Scalable design with posterior-based operating characteristics. Revision at the *Journal of the American Statistical Association*. https://arxiv.org/abs/2312.10814

[2] Wilding, J. P., R. L. Batterham, S. Calanna, M. Davies, L. F. Van Gaal, I. Lingvay, B. M. McGowan, J. Rosenstock, M.T. Tran, T.A. Wadden, and S. Wharton. (2021). Once-weekly semaglutide in adults with overweight or obesity. *The New England Journal of Medicine 384*(11): 989-1002.

[3] Sobol', I. M. (1967). "On the distribution of points in a cube and the approximate evaluation of integrals." *Zhurnal Vychislitel'noi Matematiki i Matematicheskoi Fiziki 7*(4): 784–802.

[4] Lemieux, C. (2009). "Using quasi–Monte Carlo in practice." In *Monte Carlo and Quasi-Monte Carlo Sampling*, 1–46. Springer.

[5] van der Vaart, A. W. (1998). *Asymptotic Statistics*. Cambridge Series in Statistical and Probabilistic Mathematics. Cambridge University Press.

[6] Gelman, A., J. B. Carlin, H. S. Stern, D. B. Dunson, A. Vehtari, D. B. and Rubin. (2020). *Bayesian Data Analysis*. CRC Press.

[7] Hagar, L. and N. T. Stevens. (2024+). Fast power curve approximation for posterior analyses. Revision at *Bayesian Analysis*. https://arxiv.org/abs/2310.12427