Second-Generation *p*-values: Statistical Properties

Jeffrey D. Blume, PhD

Departments of Biostatistics,

Biomedical Informatics

VANDERBILT UNIVERSITY

Outline

- Review
  - Second-generation *p*-value definition
  - Evidential Metrics
- Frequentist Properties
- False Discovery Rates
  - Prostate Cancer SNP data (~247,000)
- FDR example: False Discovery / Confirmation Rates
  - Leukemia Data
  - α=0.05 vs α=0.05/7128 vs SG *p*-value

Definition

Second-generation *p*-value (SGPV)

$$p_\delta = \frac{|I \cap H_0|}{|I|} \times \max\left\{\frac{|I|}{2|H_0|}, 1\right\}$$

Proportion of data-supported hypotheses that are also null hypotheses

Small-sample correction factor

shrinks proportion to ½ when $|I|$ wide

when $|I| > 2|H_0|$

Evidential metrics

1. Measure of the strength evidence
   - → Axiomatic and intuitive justification
   - → Summary statistic, yardstick
2. Propensity to collect data that will yield a misleading #1
   - → Error rates
   - → Properties of the study design (!)
3. Probability that an observed #1 is misleading
   - → False Discovery rate, False Confirmation rate
   - → Chance that an observed result is mistaken
   - → Properties of the observed data (!)

Likelihood

Law of Likelihood: The hypothesis that does a better job at predicting the observed events is better supported by the data.

Evidential Metric	What it measures	Likelihood
1	strength of the evidence	Likelihood Ratio (LR)
2	propensity for study to yield misleading evidence	$P(LR > k \mid H_0)$ $P(LR < 1/k \mid H_1)$
3	propensity for observed results to be misleading	$P(H_0 \mid LR = k)$ $P(H_1 \mid LR = 1/k)$

Testing

Evidential Metric	What it measures	Hypothesis Testing	Significance Testing
1	strength of the evidence	Absent	**Tail-area probability** (p-value)
2	propensity for study to yield misleading evidence	**Tail-area probability** (error rates)	Absent
3	propensity for observed results to be misleading	misinterpret #2	misinterpret #1

- The *tail-area probability* is used to measure *three* distinct metrics

Second-generation p-value

- StatisticalEvidence.com
- Statistical properties in TAS & PLOS One
- Retains strict error control

Evidential Metric	What it measures	SPGV
1	Summary measure	SGPV (p_δ)
2	Operating characteristics	$P(p_\delta = 0 \mid H_0)$ $P(p_\delta = 1 \mid H_1)$ $P(0 < p_\delta < 1 \mid H)$
3	False discovery rates	$P(H_0 \mid p_\delta = 0)$ $P(H_1 \mid p_\delta = 1)$

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Statistical Properties

Suppose interval I has coverage probability 1-α, then

Three 'Error' Rates

1. $P(p_\delta = 0|H_0) \leq \alpha$ and $\rightarrow 0$ as $n \rightarrow \infty$
2. $P(p_\delta = 1|H_1) \leq \alpha$ and $\rightarrow 0$ as $n \rightarrow \infty$
3. $P(0 < p_\delta < 1|H)$ controlled through sample size

Will examine these first

Two False Discovery Rates

1. $P(H_0 \mid p_\delta = 0)$
2. $P(H_1 \mid p_\delta = 1)$

Will graph to illustrate

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Statistical Properties

- Three Inferential Categories
  1. $p_\delta = 0 \Rightarrow$ data incompatible with null
  2. $p_\delta = 1 \Rightarrow$ data compatible with null
  3. $0 < p_\delta < 1 \Rightarrow$ data are inconclusive

- Three 'error' rates
  1. $P(p_\delta = 0|H)$ when H is null
  2. $P(p_\delta = 1|H)$ when H is not null
  3. $P(0 < p_\delta < 1|H)$ when H is either

- Assume H makes statements about a parameter θ
- Large sample setting

Statistical Properties

- How often are the data incompatible with null?

- Examine $P(p_\delta = 0|\theta)$ as θ varies
  - Power function

- This probability
  - converges to one for alternatives not near the edge of interval null
  - converges to zero for null hypotheses not near the edge of the null set
  - converges to alpha for hypotheses approaching or on the edge of the null set

‘Power’ Function

- θ_0: point null, σ: standard deviaiton
- δ: half-width of indifference zone

$$P(p_\delta = 0|\theta) = \Phi\left[\frac{\sqrt{n}(\theta_0 - \theta)}{\sigma} - \frac{\sqrt{n}\delta}{\sigma} - Z_{\alpha/2}\right] + \Phi\left[-\frac{\sqrt{n}(\theta_0 - \theta)}{\sigma} - \frac{\sqrt{n}\delta}{\sigma} - Z_{\alpha/2}\right]$$

$$P_{\theta_0}(p_\delta = 0|\theta_0) = 2\Phi\left[-\frac{\sqrt{n}\delta}{\sigma} - Z_{\alpha/2}\right]$$

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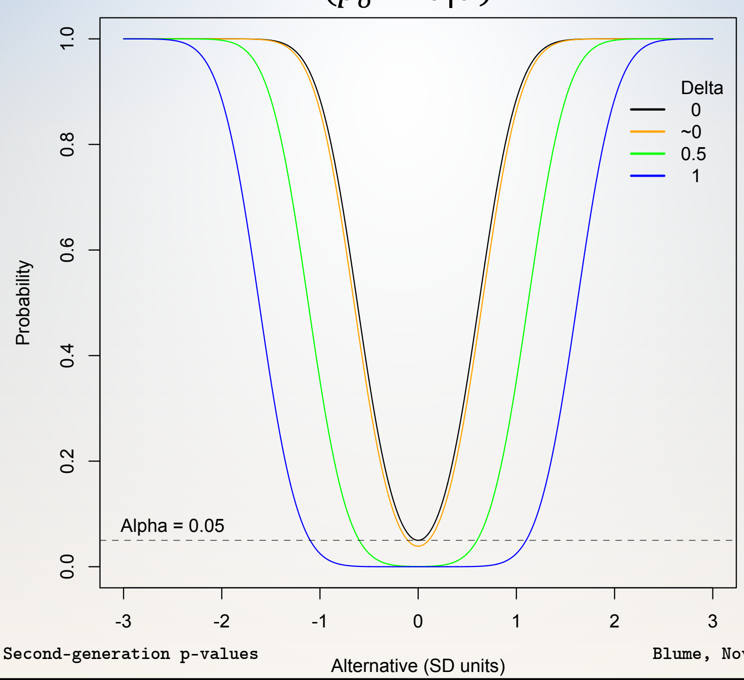
$P(p_\delta = 0|\theta)$



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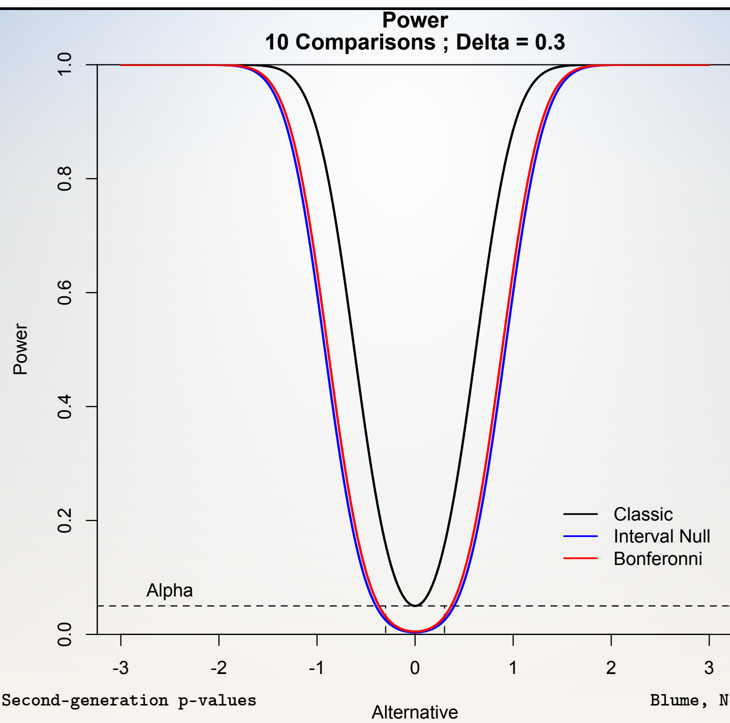
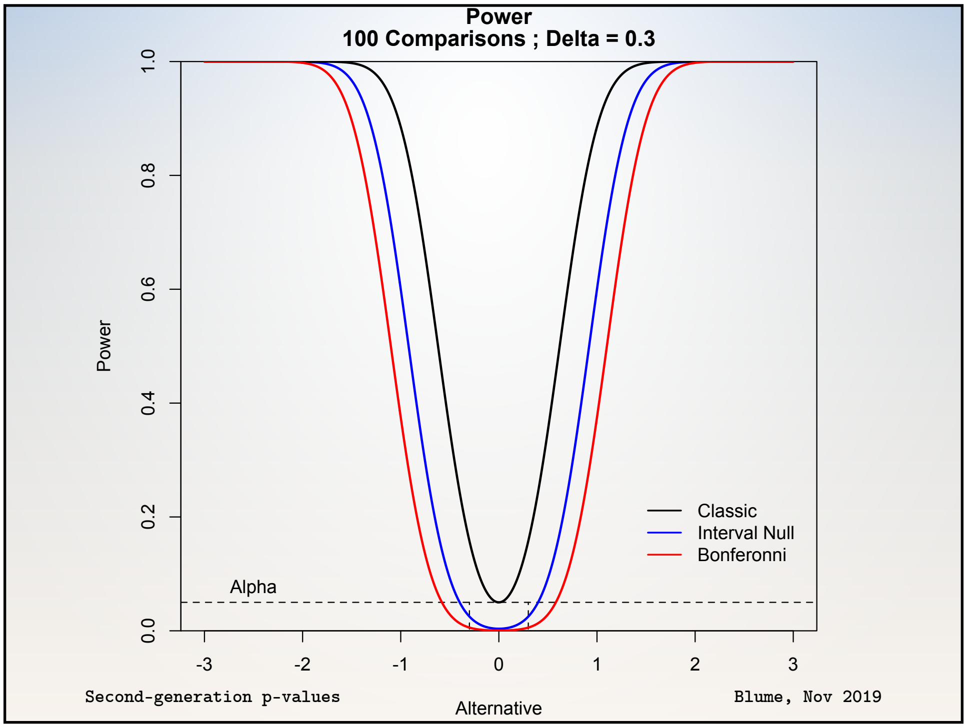
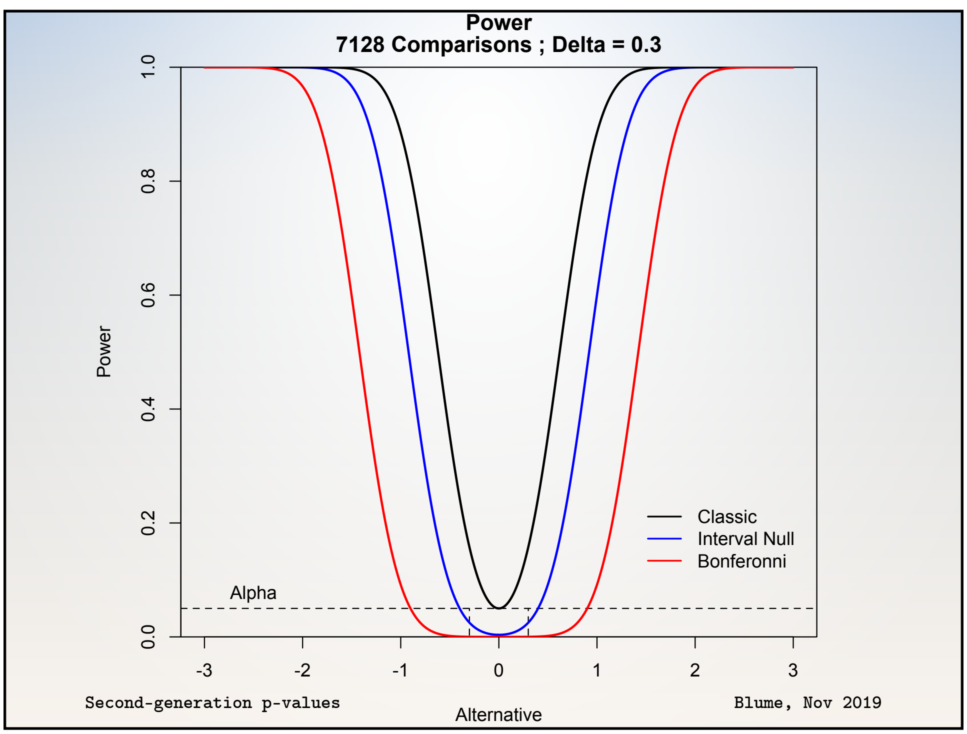
Compare with standard methods

- Second-generation p-value vs. Bonferroni correction
  - Adjusted for {10, 100, 7128} comparisons
  - Leukemia data example

- Remember SGPV are not adjusted for comparisons
- Discuss?




Power
100 Comparisons ; Delta = 0.3
Power
1.0
0.8
0.6
0.4
0.2
0.0
Alpha
Classic
Interval Null
Bonferonni
-3
-2
-1
0
1
2
3
Second-generation p-values
Alternative
Blume, Nov 2019


Power
7128 Comparisons ; Delta = 0.3
Power
1.0
0.8
0.6
0.4
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0.0
Alpha
Classic
Interval Null
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-3
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Compatible with Null

- How often are the data compatible with null?

- Examine $P(p_\delta = 1|\theta)$ when θ is null or practically null
  - Essentially opposite of power function

- Sample size must be large enough to allow the null interval to contain the interval estimate

- This probability
  - converges to zero or one quickly for alternatives not near the edge of interval null

'Null Power' Function

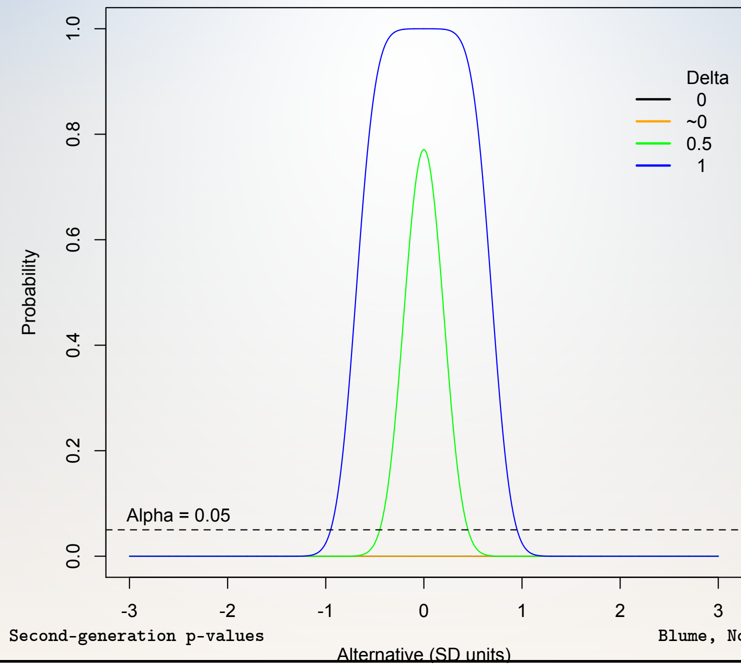
- **How often are the data compatible with null?**
- Sample size must be large enough to allow null interval to contain the interval estimate, so $(\delta > Z_{\alpha/2}/\sqrt{n})$ or $(\sqrt{n} > Z_{\alpha/2}/\delta)$

- This probability converges to 0 or 1 quickly

$$P(p_\delta = 1|\theta) = \Phi\left[\frac{\sqrt{n}(\theta_0+\delta)}{\sigma} - \frac{\sqrt{n}\theta}{\sigma} - Z_{\alpha/2}\right]$$
$$-\Phi\left[\frac{\sqrt{n}(\theta_0-\delta)}{\sigma} - \frac{\sqrt{n}\theta}{\sigma} + Z_{\alpha/2}\right]$$

when $\delta > Z_{\alpha/2}/\sqrt{n}$

$P(p_\delta = 1|\theta)$

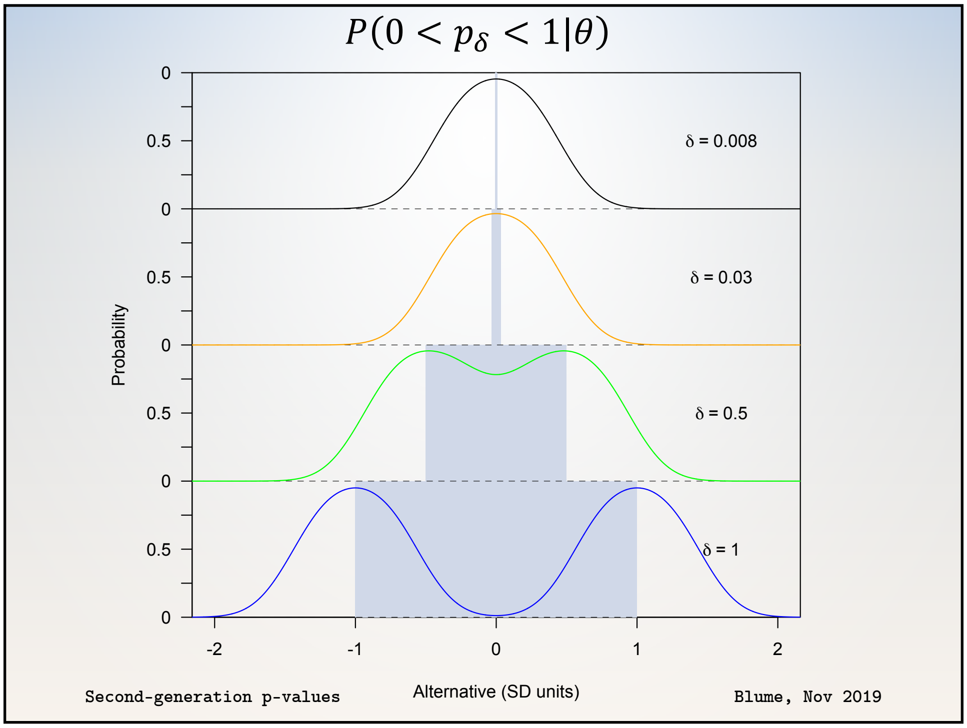


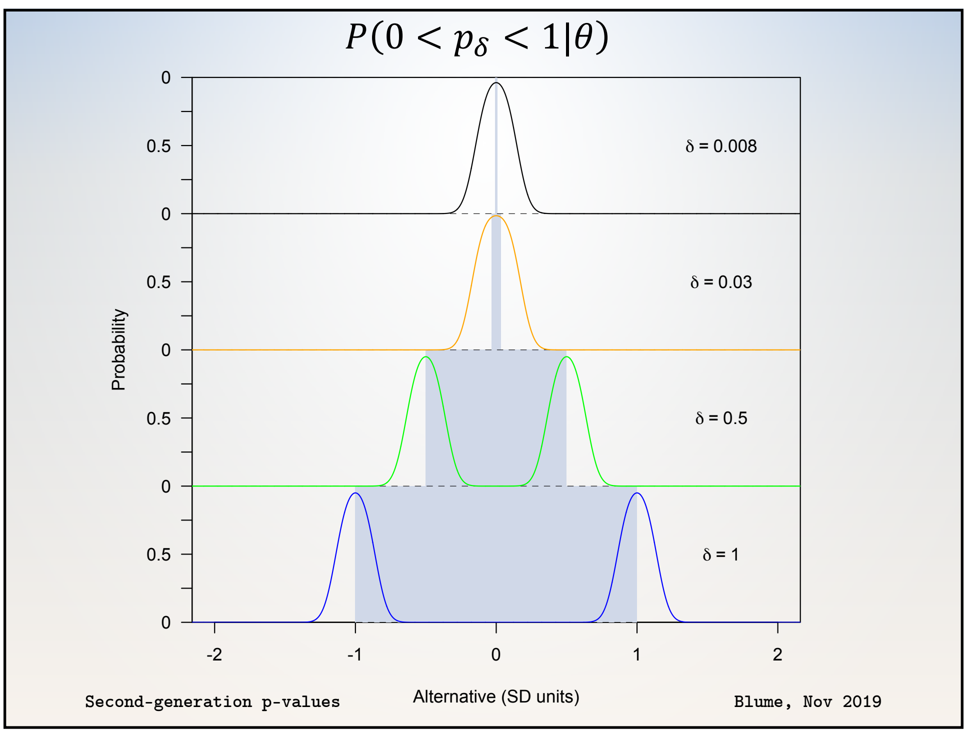
Second-generation p-values Blume, Nov 2019

Probability of Inconclusive Data

- How often are the data inconclusive?
- Examine $P(0 < p_\delta < 1|\theta)$ for various θ
- This probability
  - drives sample size projections
  - is maximized when H is near the interval null edge
  - decreases quickly as H moves away from edge of null
- $P(0 < p_\delta < 1|\theta) = 1 - P(p_\delta = 0|\theta) - P(p_\delta = 1|\theta)$

Second-generation p-values Blume, Nov 2019


$P(0 < p_\delta < 1|\theta)$
Probability
δ = 0.008
δ = 0.03
δ = 0.5
δ = 1
Alternative (SD units)
Second-generation p-values
Blume, Nov 2019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Two False Discovery Rates

1. $P(H_0 \mid p_\delta = 0)$
2. $P(H_1 \mid p_\delta = 1)$

False Discovery Rates

- FDR for 5 SGPV=0 findings; computed under various null and alternative configurations (w/ flat prior).

SNP ID	SGPV rank	p-value rank	OR	1/8 SI lower limit	1/8 SI upper limit	FDR_1	FDR_2	FDR_3
kgp4568244_C	1	133	0.10	0.03	0.37	2.9%	17.1%	3.3%
kgp8051290_G	13	2002	15.58	1.95	124.68	4.3%	30.3%	4.9%
kgp4497498_A	28	255	4.37	1.80	10.64	2.5%	8.6%	3.1%
rs3123636_G	423	1	1.39	1.26	1.55	0.01%	0.1%	0.4%
kgp7460928_G	1443	3310	1.78	1.11	2.87	2.4%	2.0%	3.0%

False discovery rates

- Impact of α=0.05 vs α=0.05/7128 (7128 comparisons)

Error rates

- False Discovery Rate (FDR)

$$P(H_0|p < \alpha) = \left[1 + \frac{(1-\beta)}{\alpha} r\right]^{-1}$$

- False Confirmation Rate (FCR)

$$P(H_1|p > \alpha) = \left[1 + \frac{(1-\alpha)}{\beta} \frac{1}{r}\right]^{-1}$$

$r = P(H_1)/P(H_0)$

Error rates

Second-generation p-values

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False discovery rates

- Second-generation p-values
- False Discovery Rate (FDR)

Error Rates

$$P(H_0|p_\delta = 0) = \left[1 + \frac{P(p_\delta = 0|H_1)}{P(p_\delta = 0|H_0)} r\right]^{-1}$$

- False Confirmation Rate (FCR)

$$P(H_1|p_\delta = 1) = \left[1 + \frac{P(p_\delta = 1|H_0)}{P(p_\delta = 1|H_1)} \frac{1}{r}\right]^{-1}$$

$r = P(H_1)/P(H_0)$

Error Rates

Second-generation p-values

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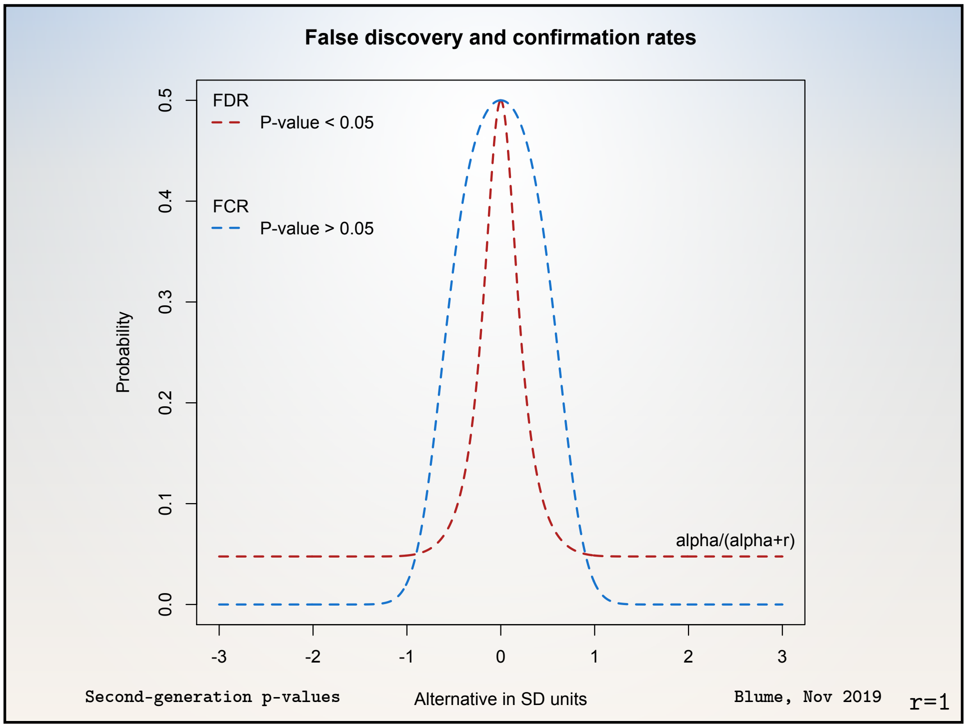
False discovery and confirmation rates
FDR
P-value < 0.05
FCR
P-value > 0.05
alpha/(alpha+r)
Probability
0.0
0.1
0.2
0.3
0.4
0.5
-3
-2
-1
0
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2
3
Second-generation p-values
Alternative in SD units
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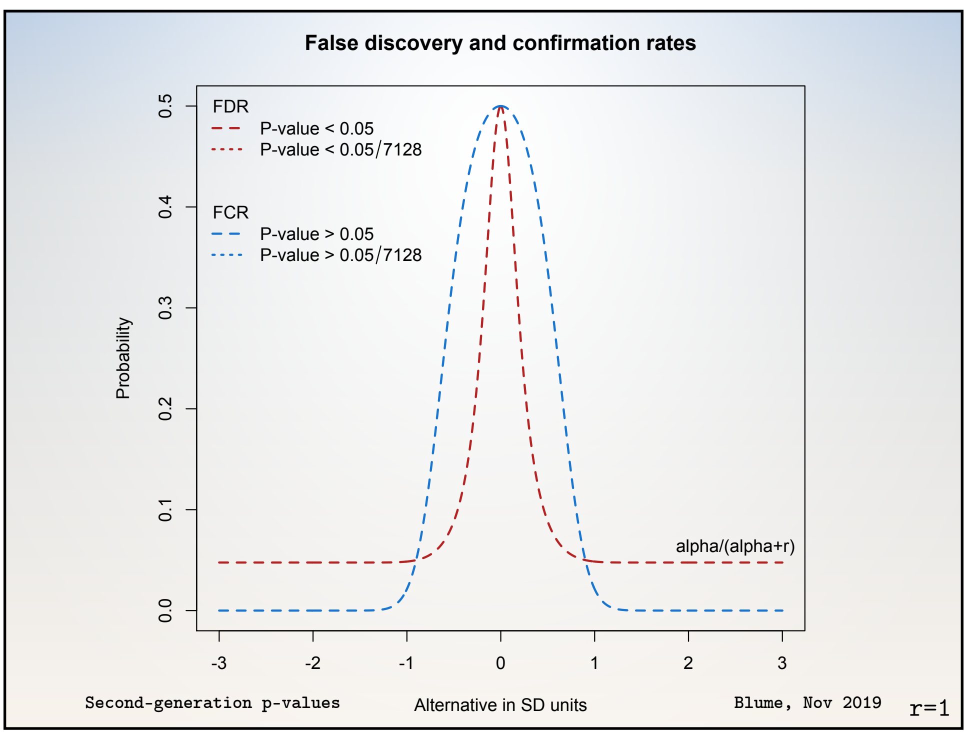
r=1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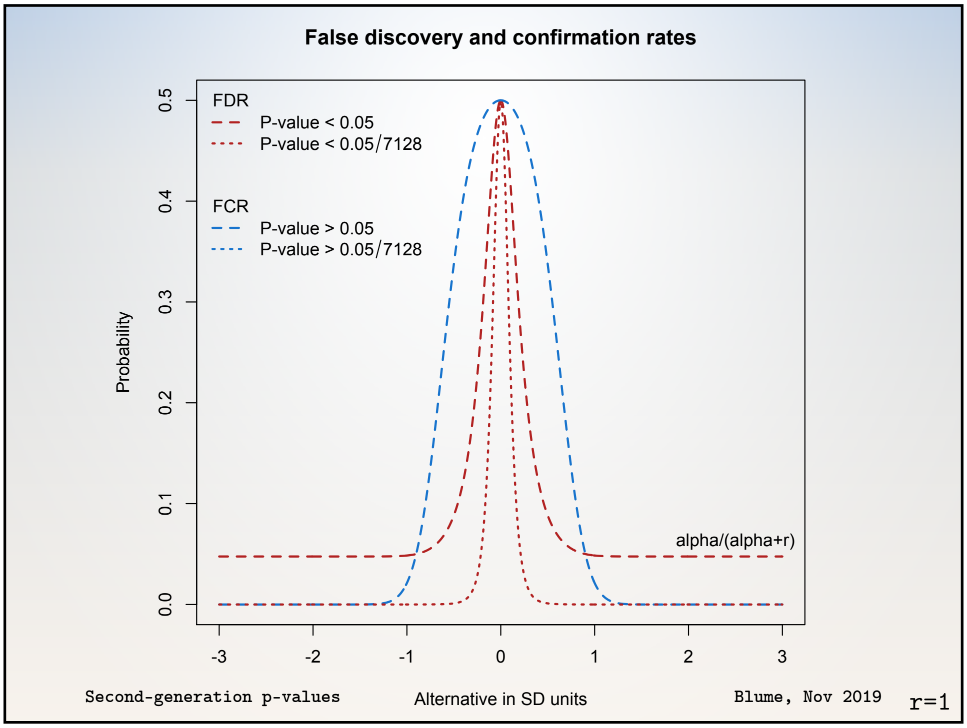
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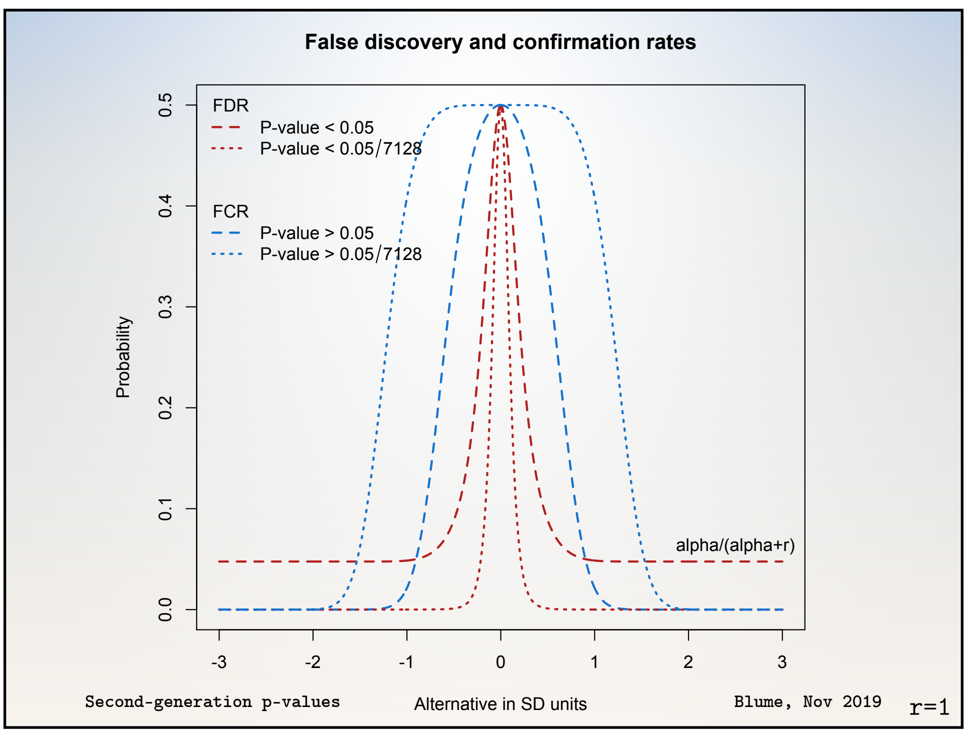
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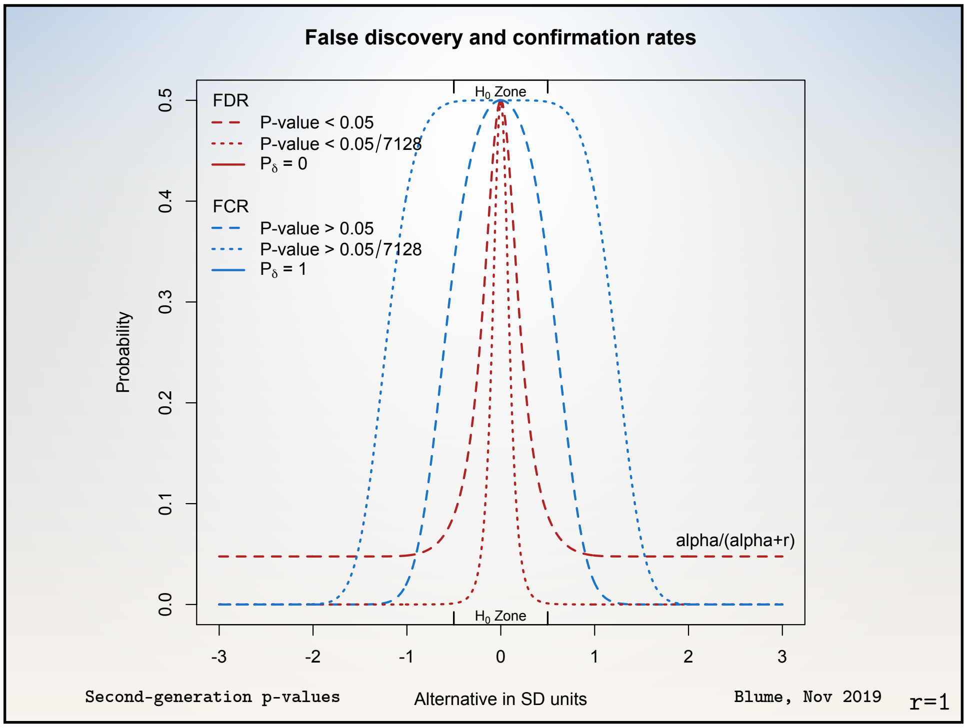
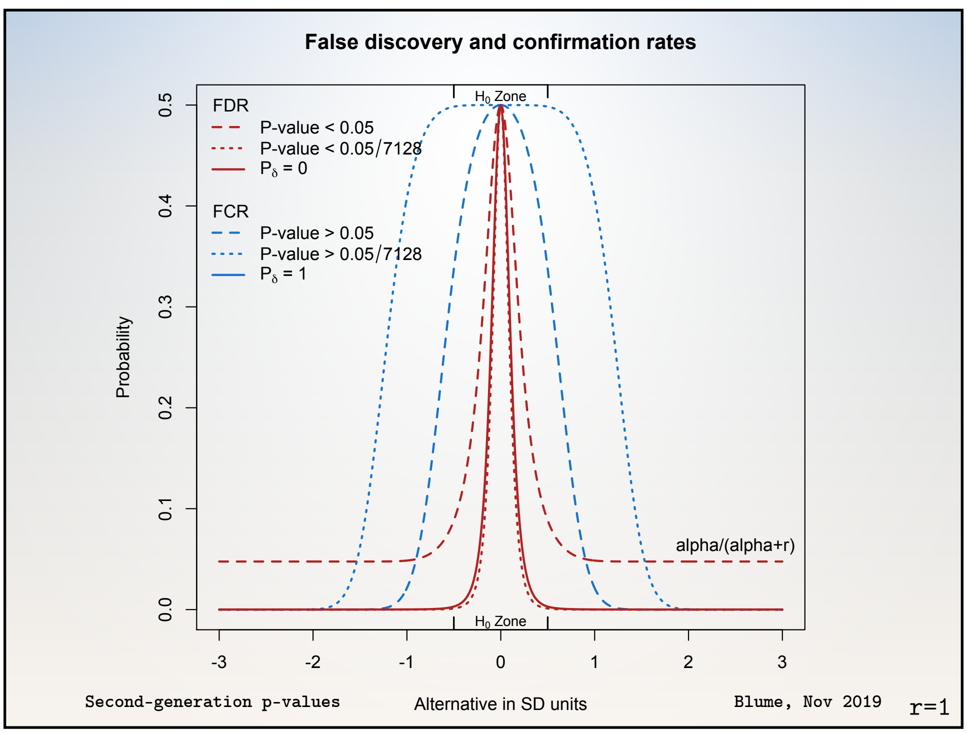
Alternative in SD units
Second-generation p-values
Blume, Nov 2019
r=1


False discovery and confirmation rates
FDR
P-value < 0.05
P-value < 0.05/7128
Pδ = 0
FCR
P-value > 0.05
P-value > 0.05/7128
Pδ = 1
H0 Zone
alpha/(alpha+r)
Probability
Alternative in SD units
Second-generation p-values
Blume, Nov 2019
r=1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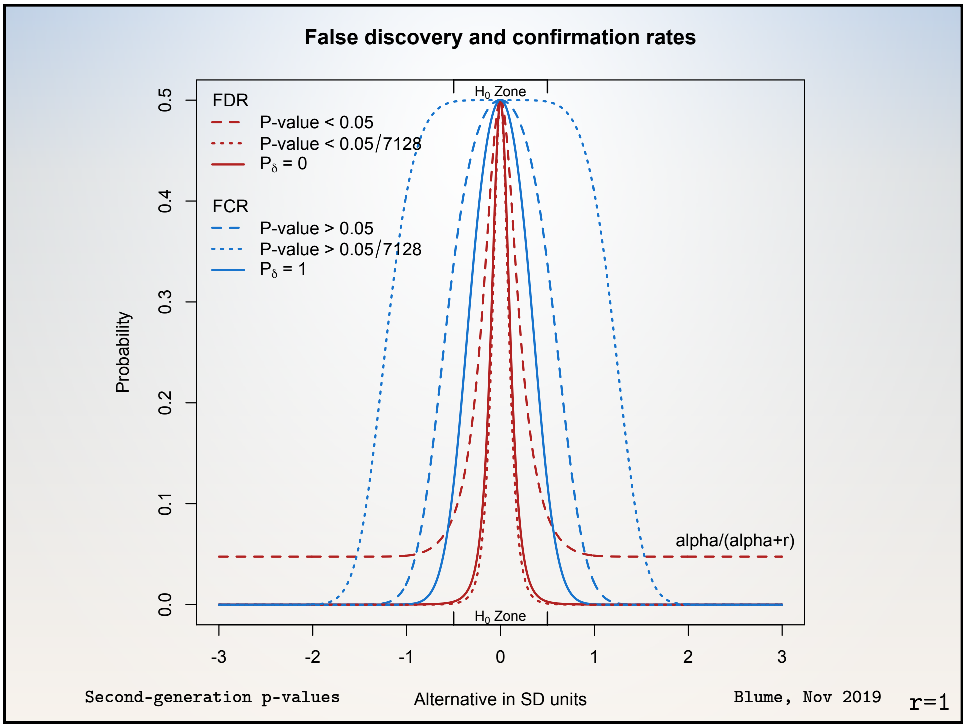

Remarks

- Second-generation *p*-values…
  - Has three "Error" rates
  - Allows Type I and II rate to converge to zero
  - Control changes of inconclusive results
  - Controls error rate using *science*
  - Reduces the false discovery rate
- Anchoring the scale of the effect size…
  - Eliminates most Type I Errors
  - Improves scientific translation of statistical model

Acknowledgements

- Collaborators
  - William D. Dupont
  - Robert A. Greevy
  - Lucy D'Agostino McGowan
  - Valerie Welty
  - Jeffrey R. Smith

- Website / Papers / Code
  - statisticalevidence.com
  - PLOS One ; TAS (In Press)
  - Google "Second-Generation *p*-value"
  - devtools::install_github("weltybiostat/sgpv")

Outrageous Claim (!?)

The SGPV achieves the inferential properties that many scientists hope, or believe, are attributes of the classic *p*-value.