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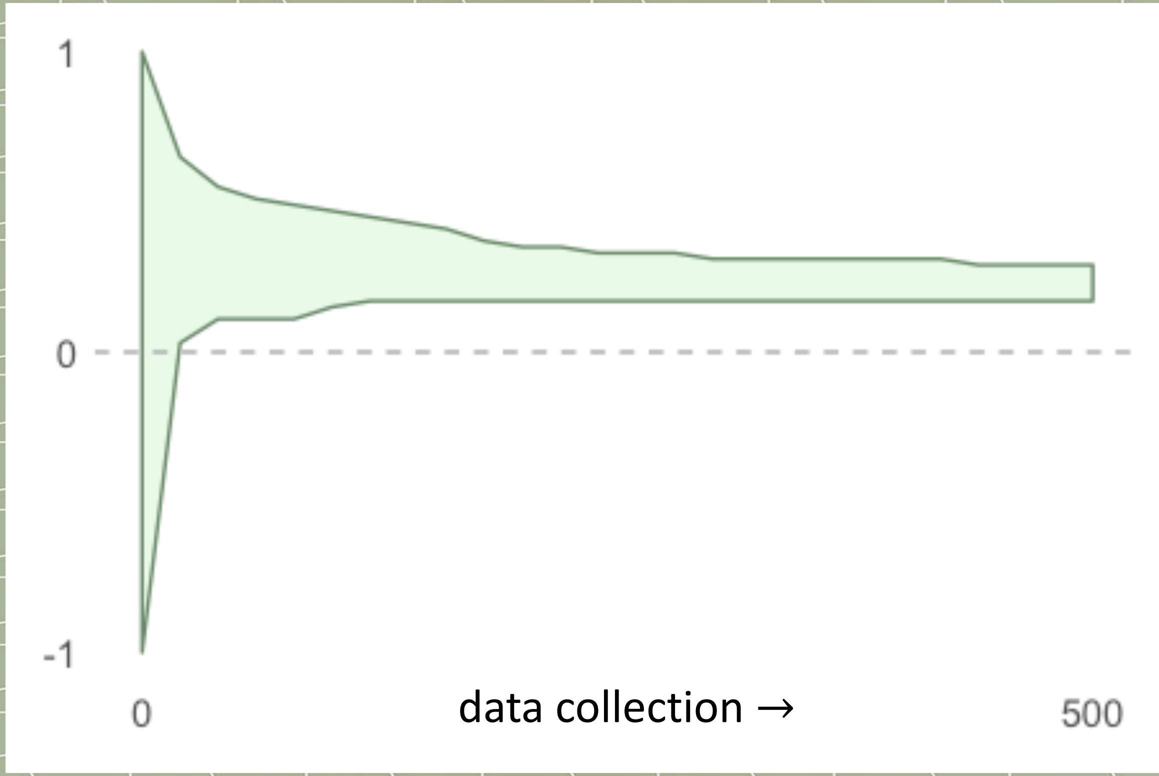
Anytime-valid testing and confidence intervals in contingency tables and beyond

Rosanne J. Turner and Peter Grünwald

A/B Testing Worksop 2022

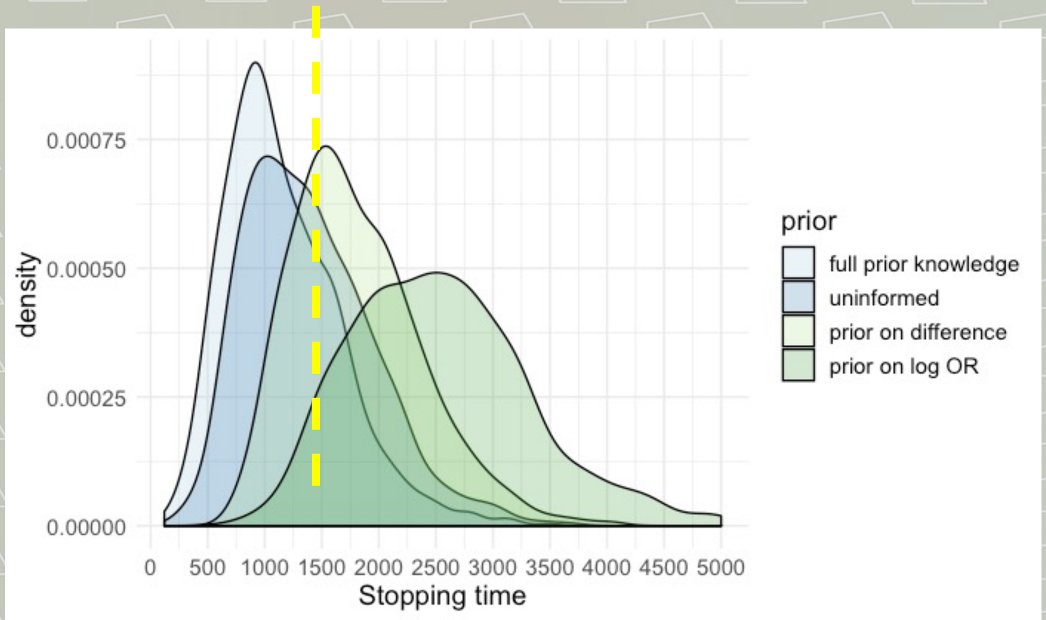
Goal: tests that can be used under optional stopping (sequential research), *with* a notion of effect size



Example: SWEPIS study on stillbirth

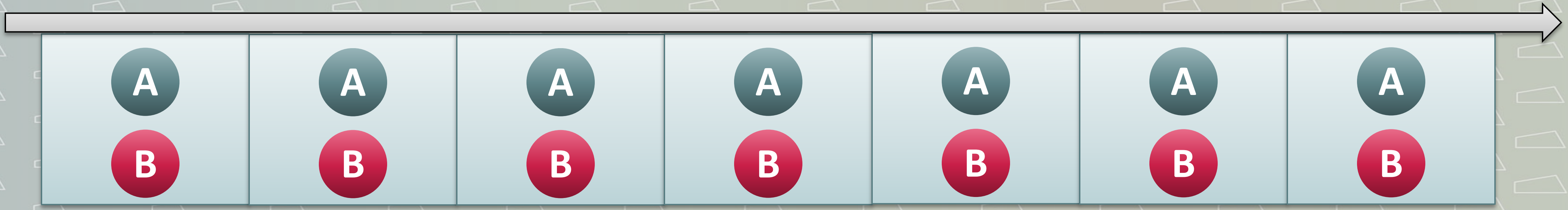
- Comparing perinatal death in labour induction at 41 or 42 weeks
- Stopped after ±1380 births in each group: 6 perinatal deaths in 42 weeks group
- ***Sequential test*** with balanced design: ***would often have stopped earlier***

Simulated stopping times with and without using knowledge from previous studies in sequential test*



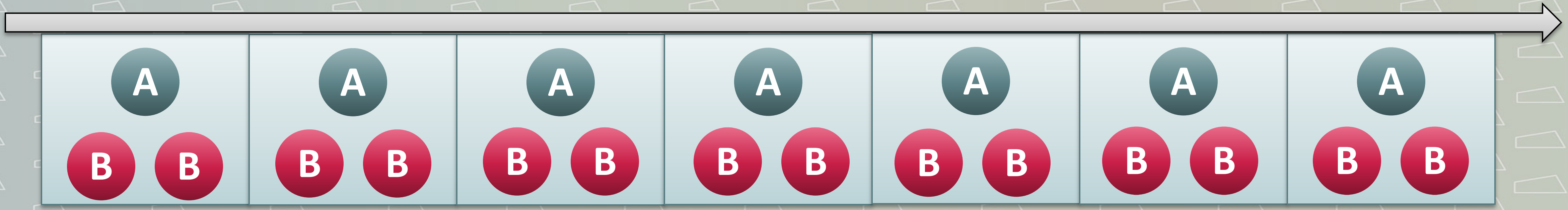
* SWEPIS study: Wennerholm et al. published in *bmj, 367, 2019.* Figure: adapted from Turner et al., 2021

Flexible, sequential setting



- data come in a stream of data blocks $j = 1, 2, \ldots$
- each block has $n = n_a + n_b$ observations
- observations seen up to and including block j:
  $y_a^{(j)} = \left(y_{1,a}, \ldots, y_{j\,n_a,a}\right)$ and $y_b^{(j)} = \left(y_{1,b}, \ldots, y_{j\,n_b,b}\right)$

Flexible, sequential setting



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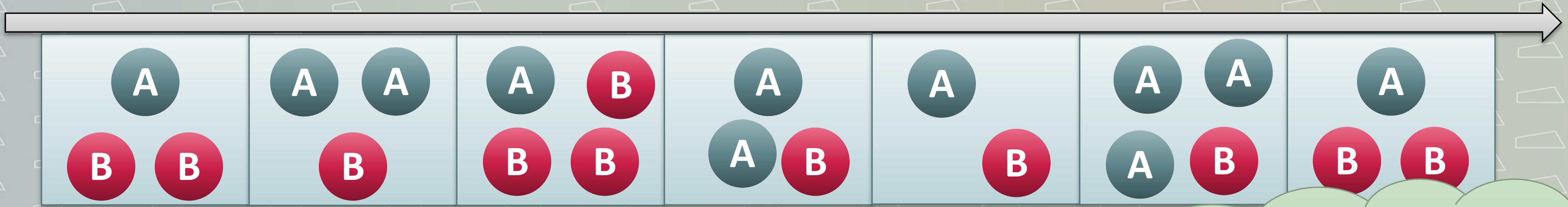


O.K. as long as we ”lock in” block composition before start of that block!

- data come in a stream of data blocks $j = 1, 2$
- each block has $n = n_a + n_b$ observations
- observations seen up to and including block j:

$$y_a^{(j)} = \left(y_{1,a}, \ldots, y_{j\, n_a, a}\right) \text{ and } y_b^{(j)} = \left(y_{1,b}, \ldots, y_{j\, n_b, b}\right)$$

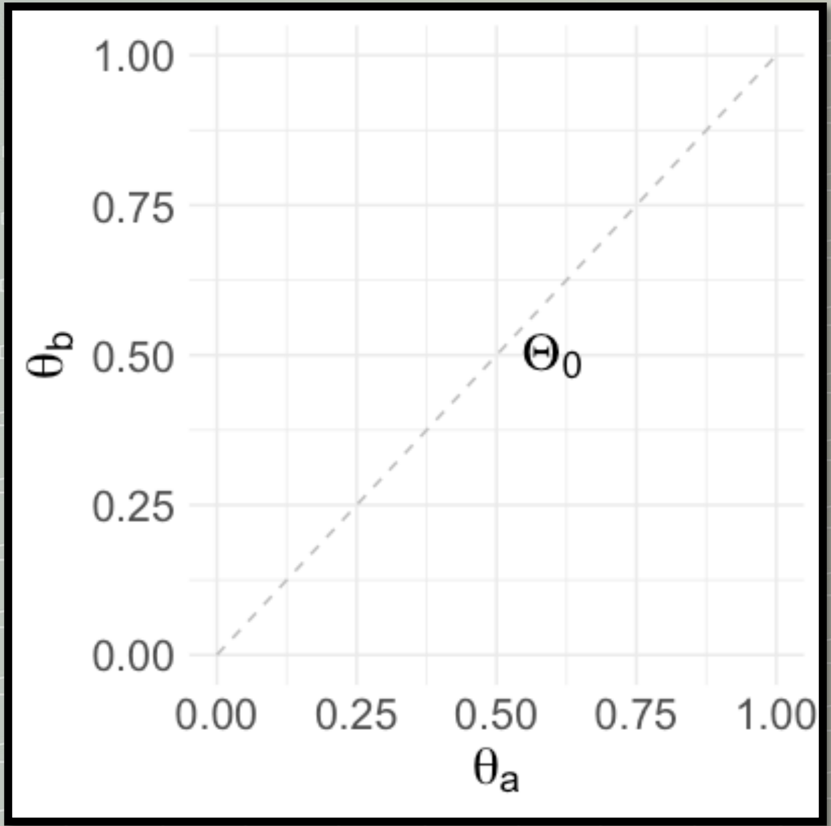
Running example: 2x2 contingency table setting

2x2 contingency table		Strategy A	Strategy B
Outcome	Success	S(A)	S(B)
Outcome	Failure	F(A)	F(B)

Do success probabilities differ between strategies?

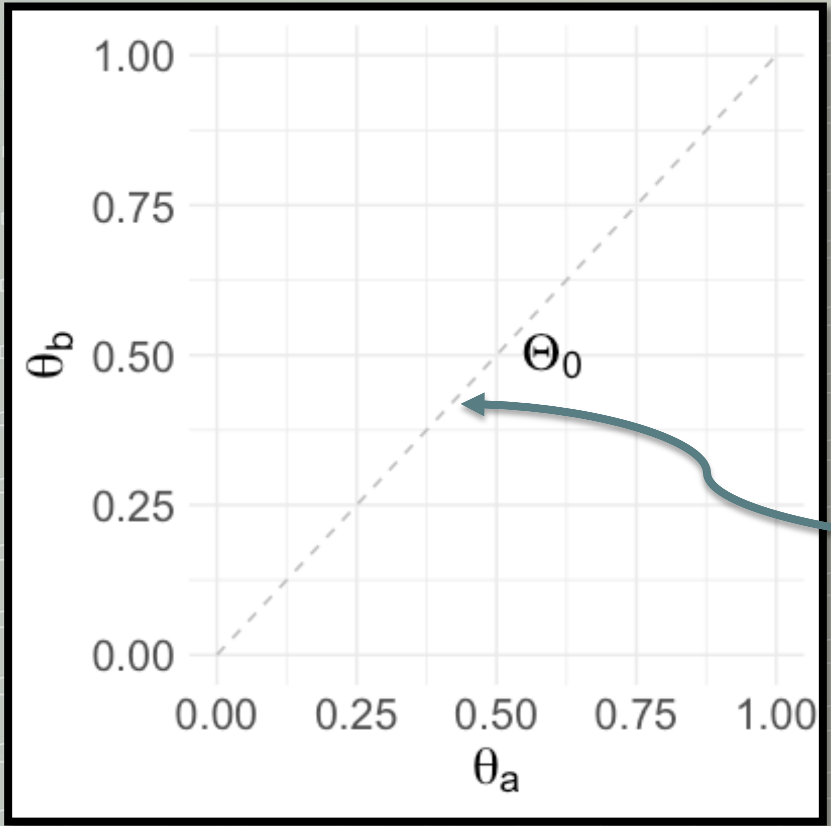
- $\mathcal{H}_0$: observations $Y \in \{0,1\}$ independent of strategy $X \in \{a, b\}$
- Equivalently, when $Y_x \overset{i.i.d.}{\sim}$ Bernoulli(θ_x): $\mathcal{H}_0 \colon \theta_a = \theta_b$.

2x2 contingency table setting



"True" success probabilities for each strategy somewhere in the unit square

2x2 contingency table setting



Testing: outside of the dashed line?

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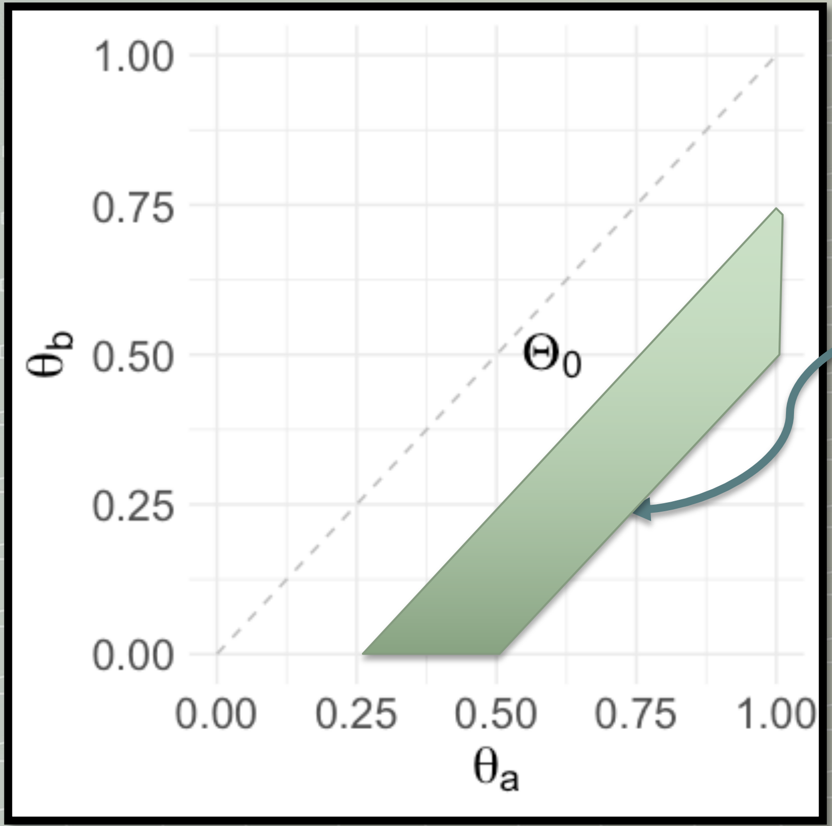
2x2 contingency table setting



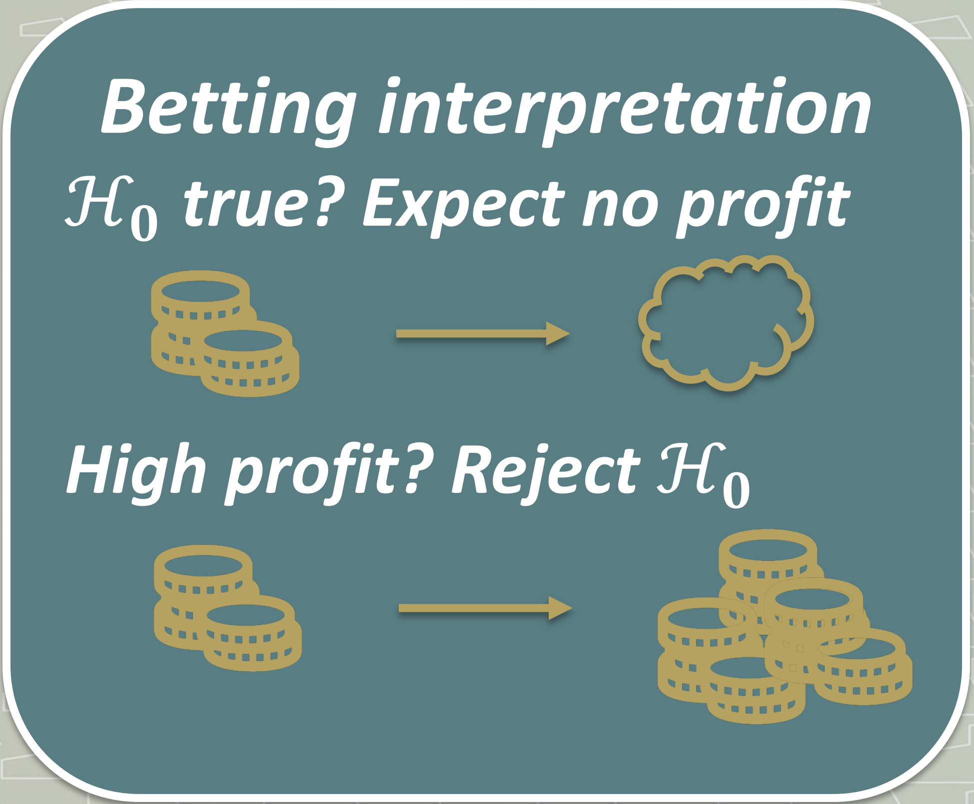
Estimating: somewhere in the shaded area?

Tool for analyzing sequential data: E-variables*

- Nonnegative RV S, where for all $P_0 \in \mathcal{H}_0$:

$$\mathbb{E}_{P_0}[S] \leq 1$$

- Straightforward implementation in test: reject $\mathcal{H}_0$ iff $S \geq \alpha^{-1}$
- Type-I error guarantee at α (e.g. $\alpha = 0.05$, reject if $S \geq 20$)



*Vovk and Wang (2021); Shafer (2021); Grünwald et al. (2019).

Point alternative 2 data streams: nice general expression!

Point $\mathcal{H}_1$ P_{θ_a,θ_b}(Turner, 2021):

$$S(Y^{(1)}) := \prod_{i=1}^{n_a} \frac{p_{\theta_a}(Y_{i,a})}{p_{\theta_0}(Y_{i,a})} \prod_{i=1}^{n_b} \frac{p_{\theta_b}(Y_{i,b})}{p_{\theta_0}(Y_{i,b})}$$

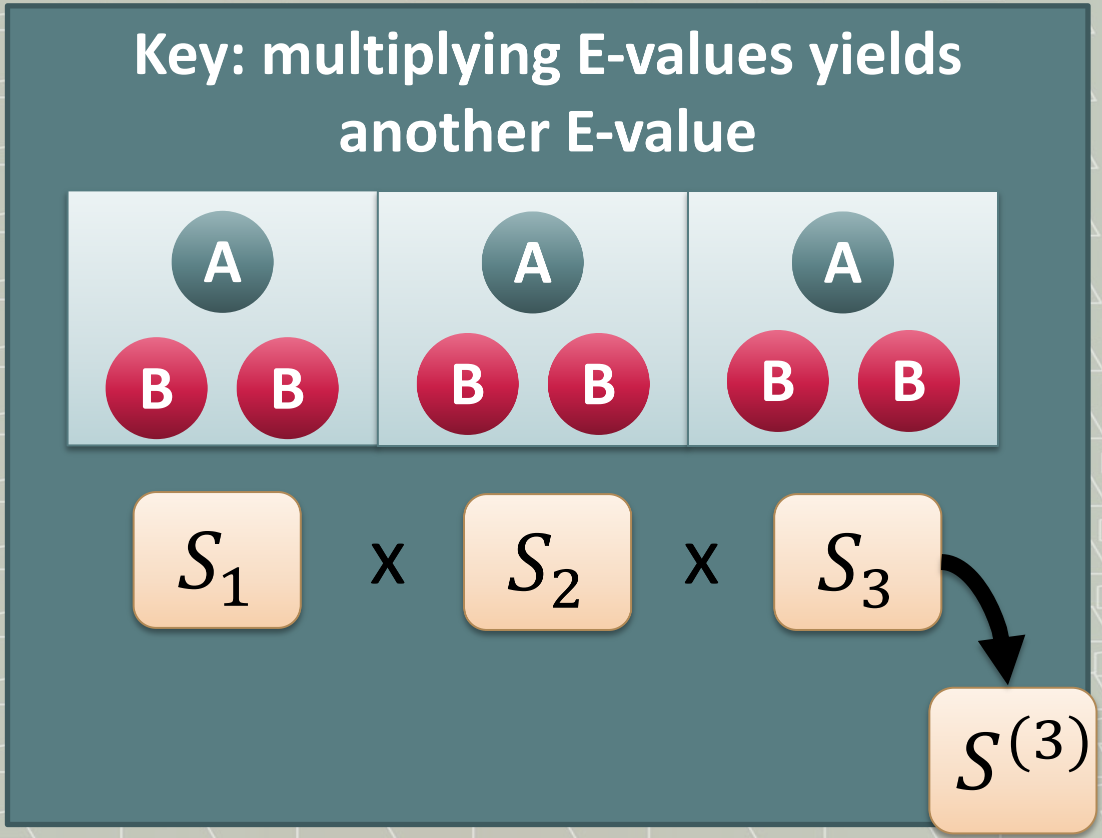
E-variable when we choose $\theta_0 = (n_a/n)\theta_a + (n_b/n)\theta_b$

E-process for two data streams

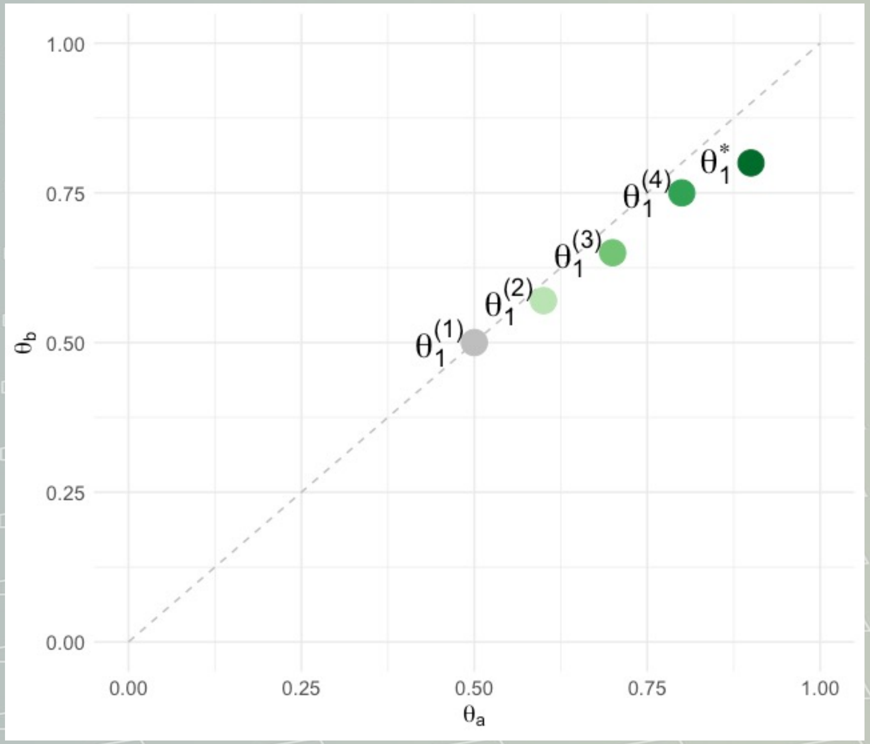
- Can make an **e-process**: multiply E-values for all data blocks

$$S^{(m)}(Y^{(m)}) := \prod_{j=1}^{m} S\,(Y_j)$$

- For **arbitrary stopping rule** (E-value ≥ 20, no money for further experiment, etc..):
  $P_0\left(\exists m: S^{(m)}\left(Y^{(m)}\right) \geq \alpha^{-1}\right) \leq \alpha$

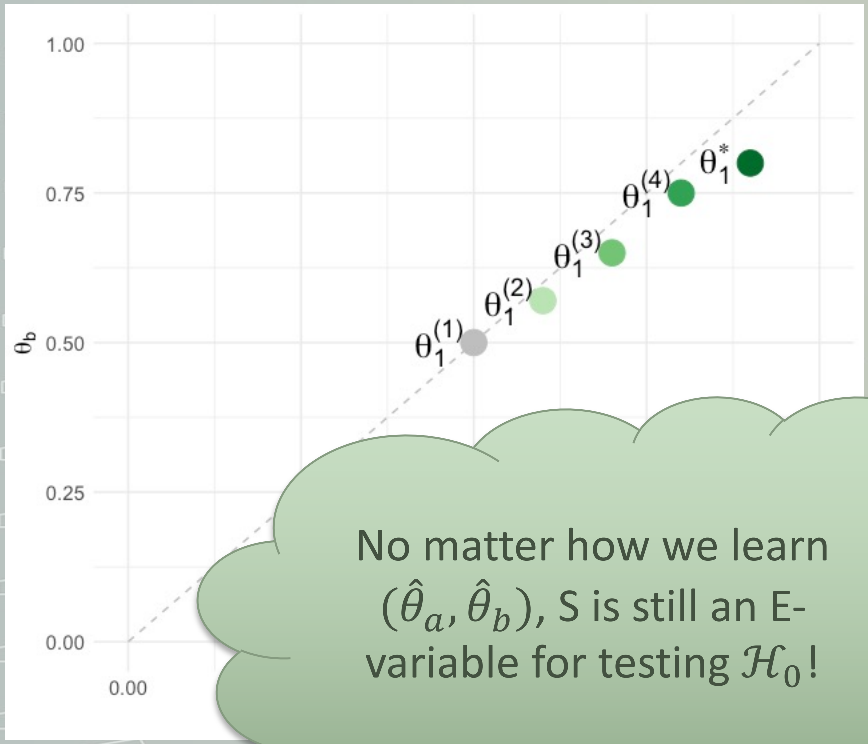


Learn parameter for $\mathcal{H}_1$



- Can learn estimate $(\hat{\theta}_a, \hat{\theta}_b)$ of true alternative before each new data block, based on past data
  - Maximum likelihood
  - MAP estimator
  - Posterior mean, …
- Restrict search space based on expert knowledge

Learn parameter for $\mathcal{H}_1$



No matter how we learn $(\hat{\theta}_a, \hat{\theta}_b)$, S is still an E-variable for testing $\mathcal{H}_0$!

- Can learn estimate $(\hat{\theta}_a, \hat{\theta}_b)$ of true alternative before each new data block, based on past data
  - Maximum likelihood
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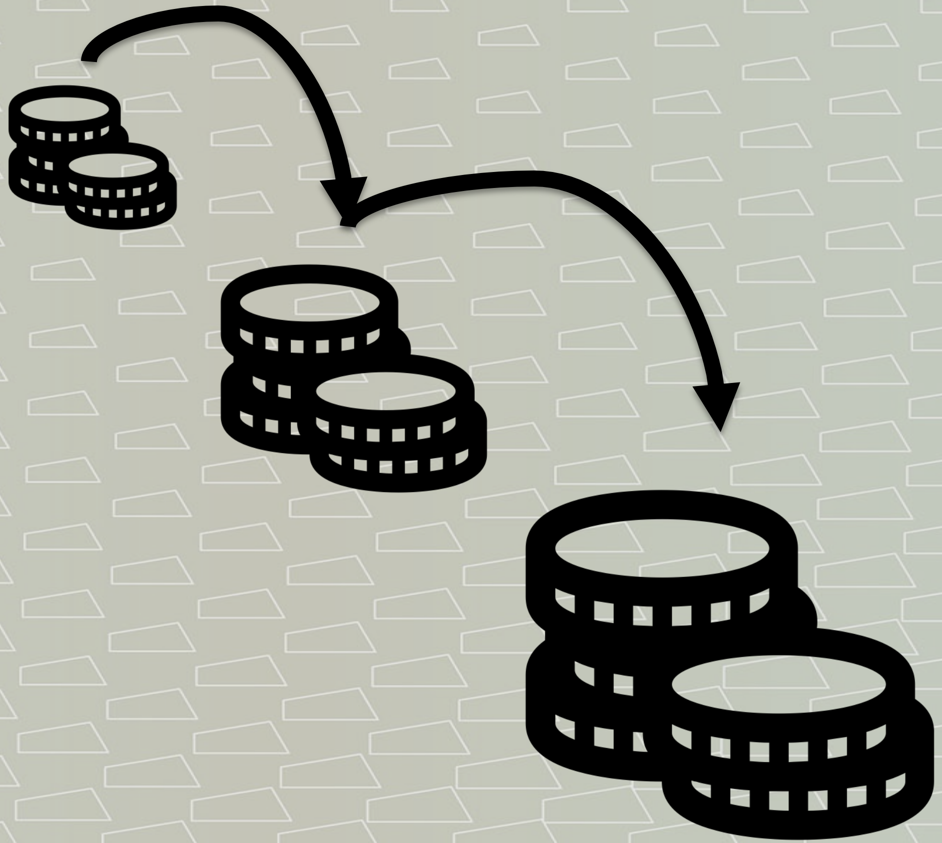
Evidence against $\mathcal{H}_1$ and Type-II error

- **GRO criterion:** in sequential experiments: optimize "growth rate" of E-variable, $\mathbb{E}_{P_1}[\log S]$ (Grünwald, 2019)
- Minimize notion of **regret**: loss of capital growth under alternative due to not knowing true P_1.
- Closely connected to optimizing power



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2x2 E-values vs classical counterpart

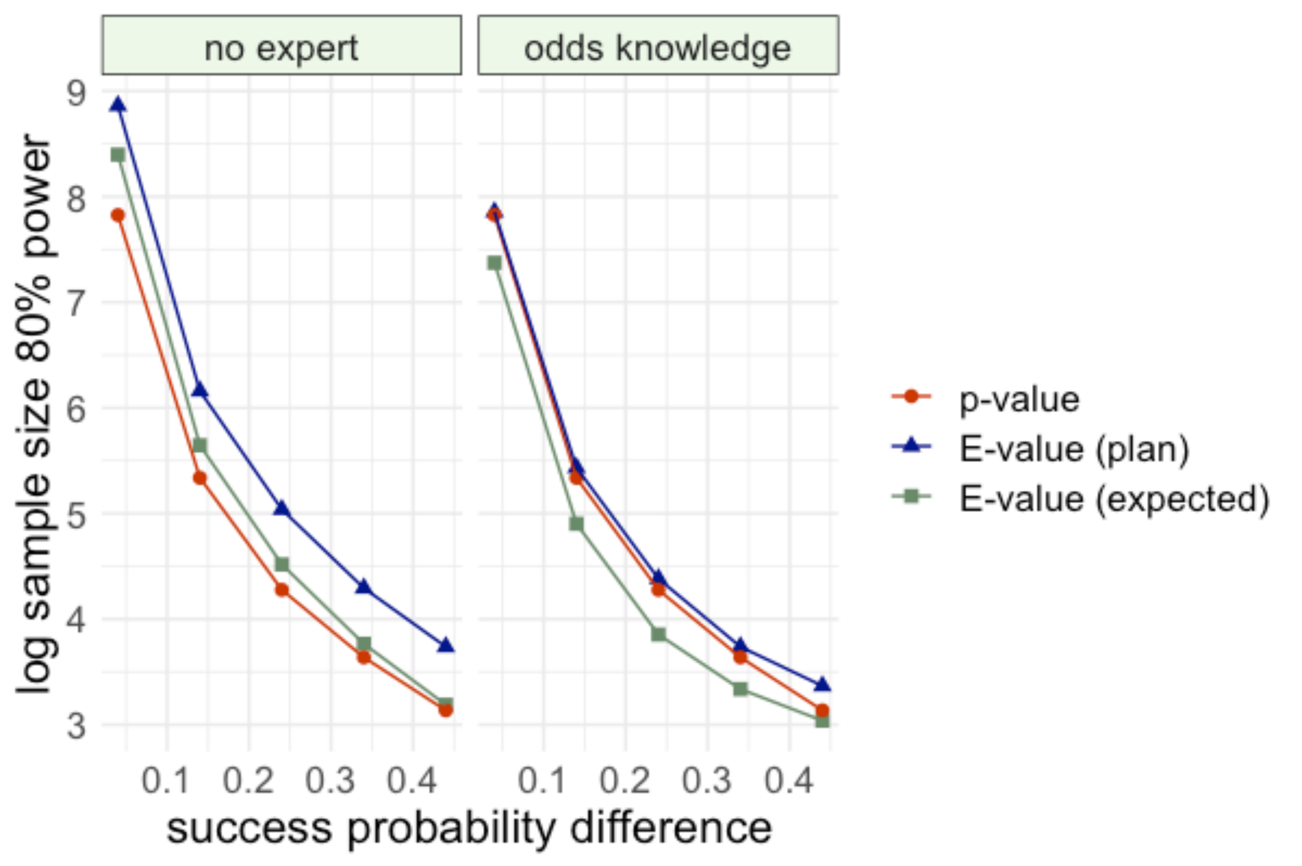

Figure adapted from Turner et al., 2021, figure 4

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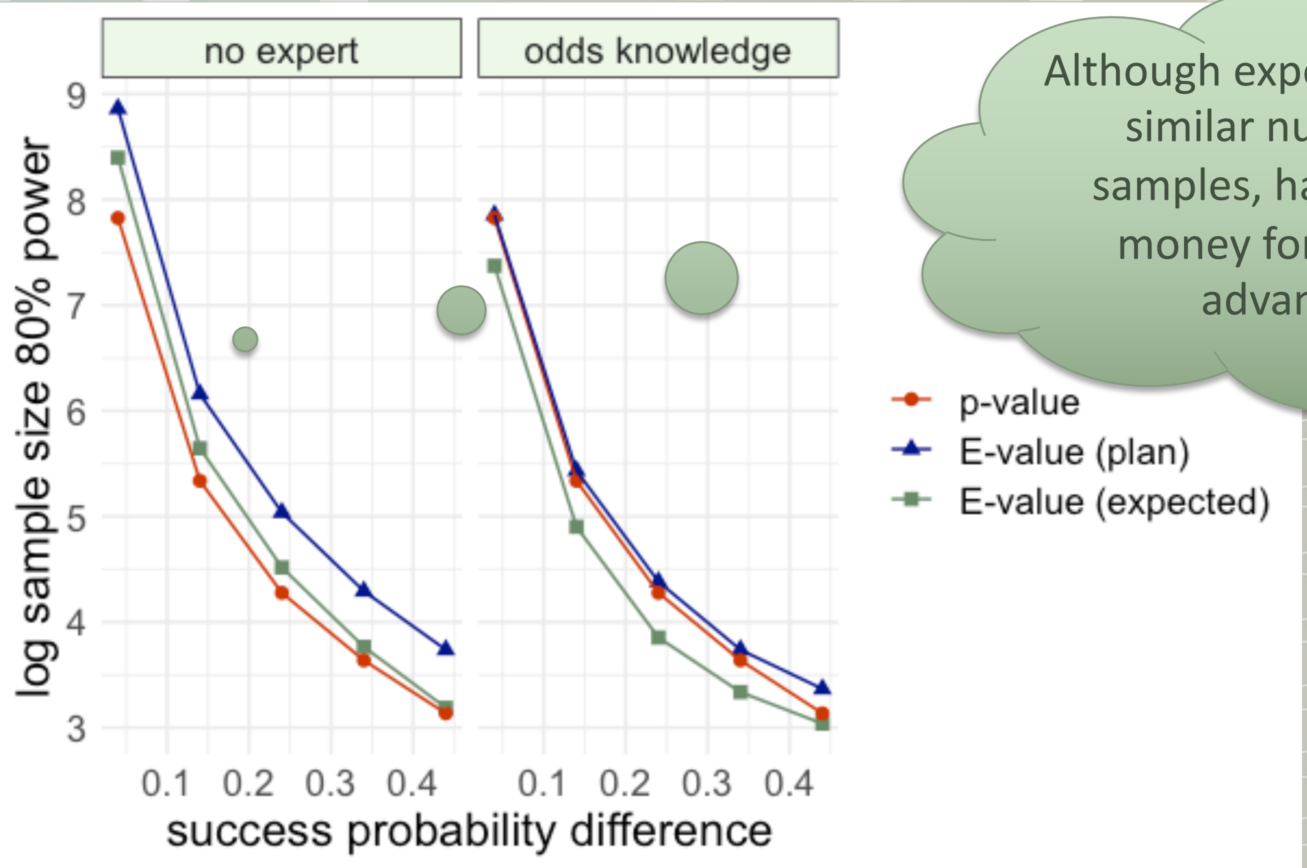
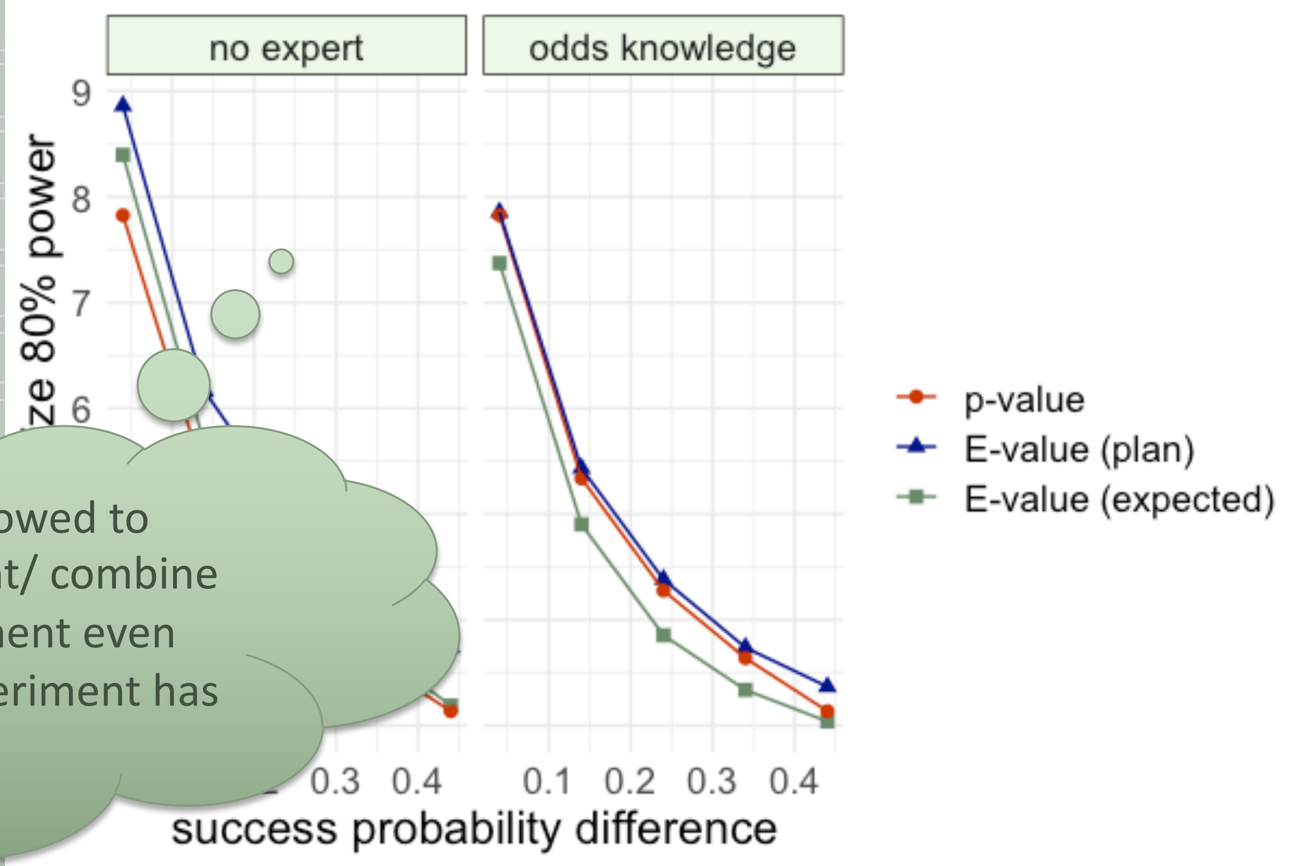


Although expect to collect similar number of samples, have to alot money for more in advance…

Figure adapted from Turner et al., 2021, figure 4

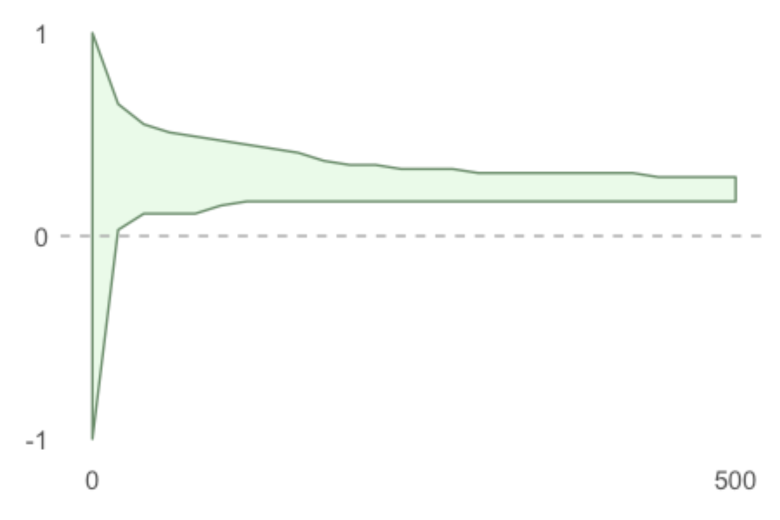
2x2 E-values vs classical counterpart



On plus side: allowed to continue experiment/ combine with new experiment even years after first experiment has ended!

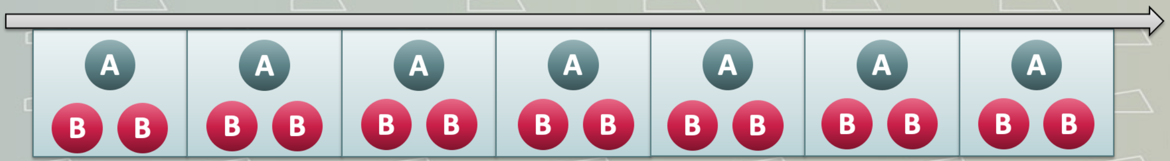
Figure adapted from Turner et al., 2021, figure 4

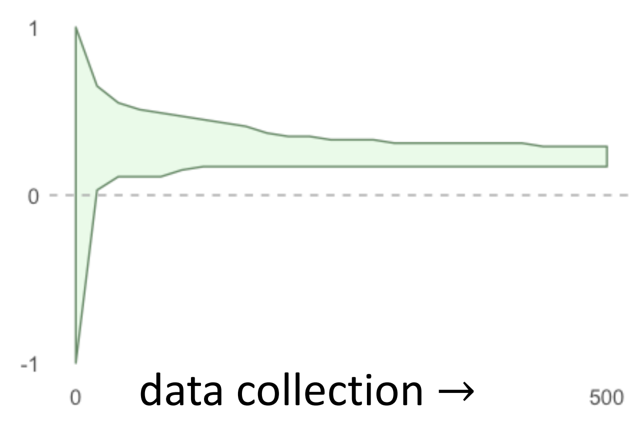
Extension to confidence intervals



Anytime-valid confidence sequences

Update effect size estimate each time a new batch of data has come in, **with coverage guarantee** (real value is in my estimate with some minimum probability)





Formally; confidence sequence CS with coverage at level $(1-\alpha)$:

- $P_{\theta_a,\theta_b}\Big(\text{for any } m = 1, 2, \ldots : \delta(\theta_a, \theta_b) \notin CS_{(m)}\Big) \leq \alpha$
- $\delta(\theta_a, \theta_b)$: measure of ***effect size***

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Key: use E-process to test effect size values

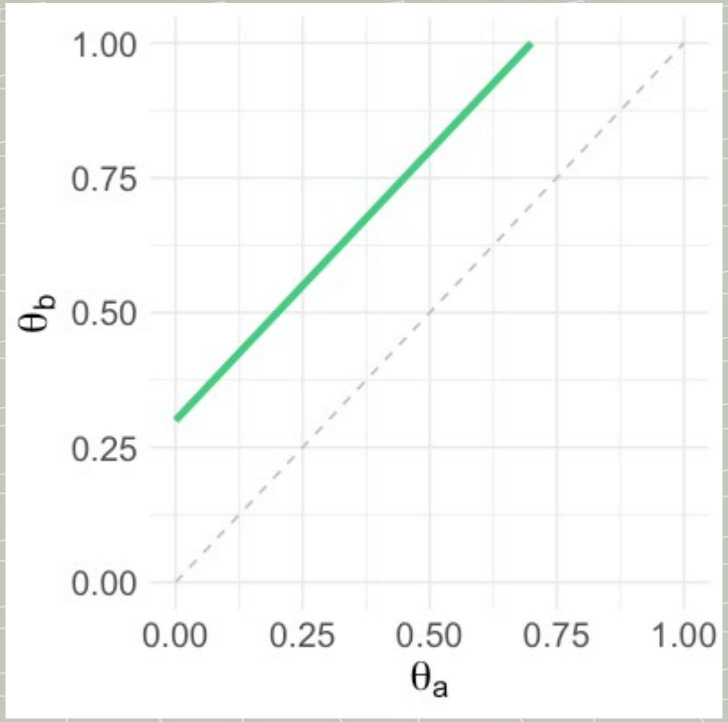
- Let $S^{(m)}_{\Theta_0(\delta)}$ be an E-process for testing: $\mathcal{H}_0 \coloneqq \{P_{\theta_0} : \theta_0 \in \Theta_0(\delta)\}$
- Probability of falsely rejecting $\mathcal{H}_0$ bounded by α (because it is an E-process)!
- Construct anytime-valid confidence sequence $CS_{\alpha,(m)} = \left\{\delta : S^{(m)}_{\Theta_0(\delta)} \leq \frac{1}{\alpha}\right\}$
- $\rightarrow$ gives us the desired coverage at level $(1 - \alpha)$.

Extension to $\mathcal{H}_0$ beyond $\theta_a = \theta_b$: examples

Effect size $\delta: (\theta_a, \theta_b) \to \gamma; \gamma \in \Gamma.$

- E.g. Risk Difference: $\delta(\theta_a, \theta_b) = \theta_b - \theta_a, \Gamma = [-1, 1]$
- E.g. Odds Ratio: $\delta(\theta_a, \theta_b) = \frac{\theta_b}{1-\theta_b}\frac{1-\theta_a}{\theta_a}, \Gamma = \mathbb{R}^+$

$\Theta_0(\delta) = \{(\theta_a, \theta_b): \theta_b - \theta_a = 0.3\}$



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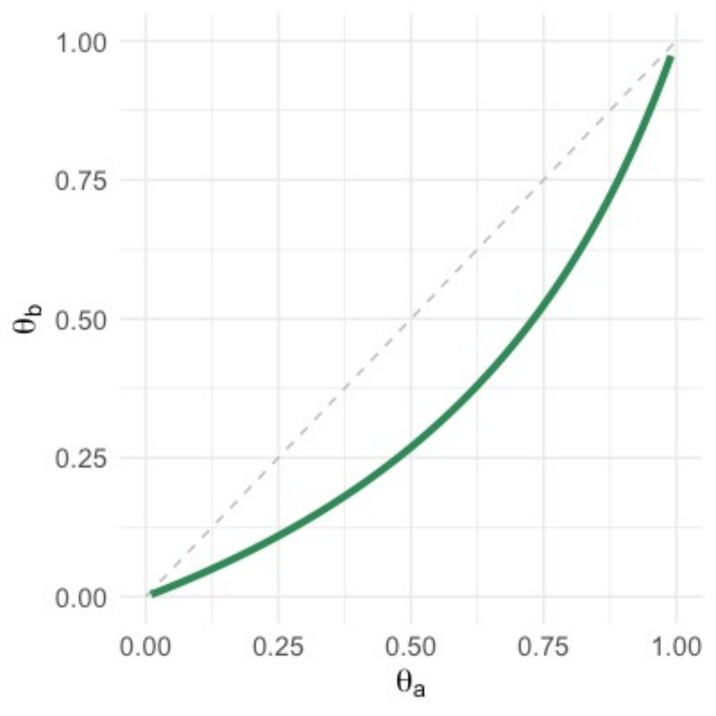
$\Theta_0(\delta) = \{(\theta_a, \theta_b): lOR(\theta_b, \theta_a) = -1\}$



Extension of E-variable for streams to general null hypothesis $\Theta_0(\delta)$ for 2x2 tables

$$S_{\Theta_0}(Y^{(1)}) := \prod_{i=1}^{n_a} \frac{p_{\hat{\theta}_a}(Y_{i,a})}{p_{\theta_a^\circ}(Y_{i,a})} \prod_{i=1}^{n_b} \frac{p_{\hat{\theta}_b}(Y_{i,b})}{p_{\theta_b^\circ}(Y_{i,b})},$$

where $(\theta_a^\circ, \theta_b^\circ)$ achieve

$$\min_{(\theta_a,\theta_b)\in\Theta_0(\delta)} D(P_{\hat{\theta}_a,\hat{\theta}_b}(Y_a^{n_a}, Y_b^{n_b}) | P_{\theta_a^\circ,\theta_b^\circ}(Y_a^{n_a}, Y_b^{n_b}))$$

and we estimate the point $(\hat{\theta}_a, \hat{\theta}_b)$ as before (Turner, 2022)

Tricky case: odds ratio and convexity of $\mathcal{H}_0$

- Need convexity of $\Theta_0(\delta)$ to construct E-variable
- $\delta > 0 \rightarrow$ can estimate lower bound (see figure)
- $\delta < 0 \rightarrow$ can estimate upper bound

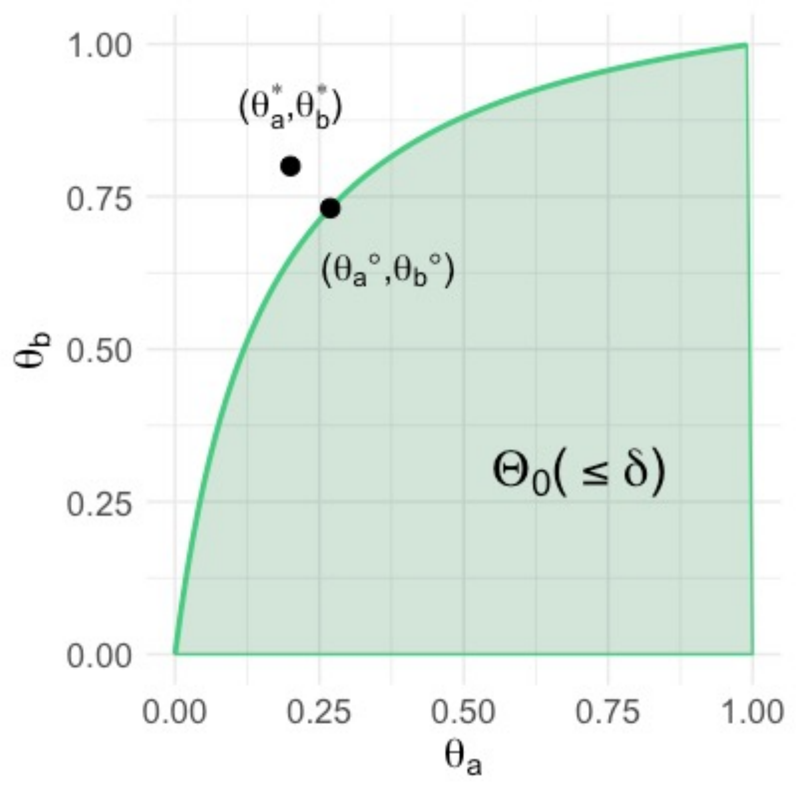


Figure adapted from Turner et al., 2022

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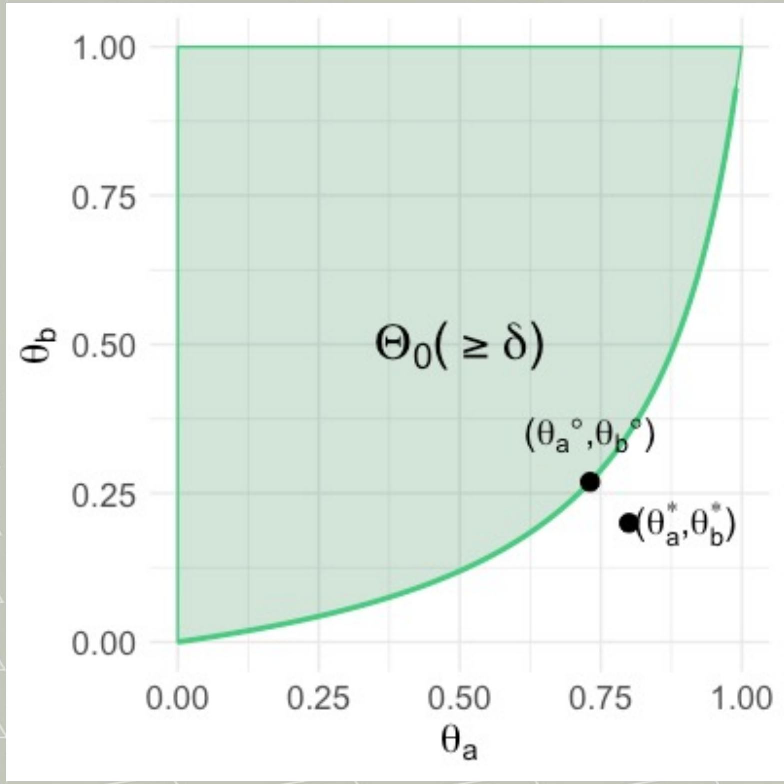

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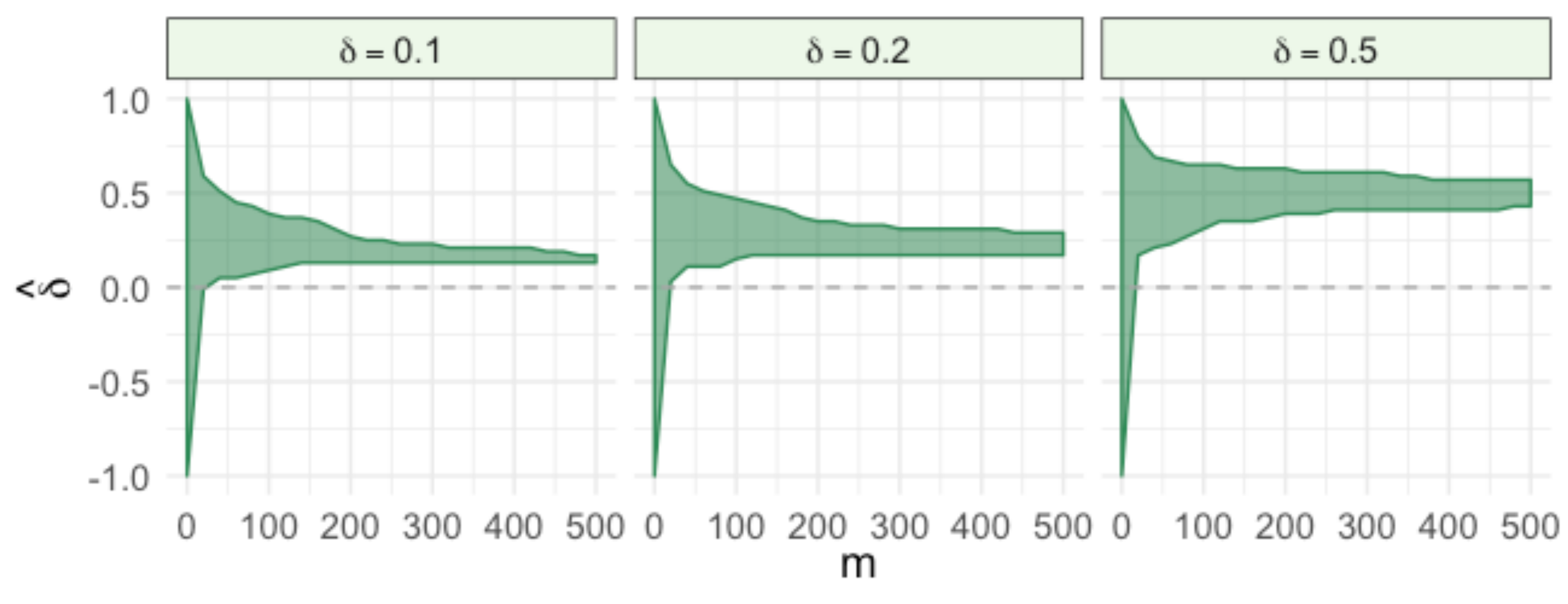
Simulations: risk difference



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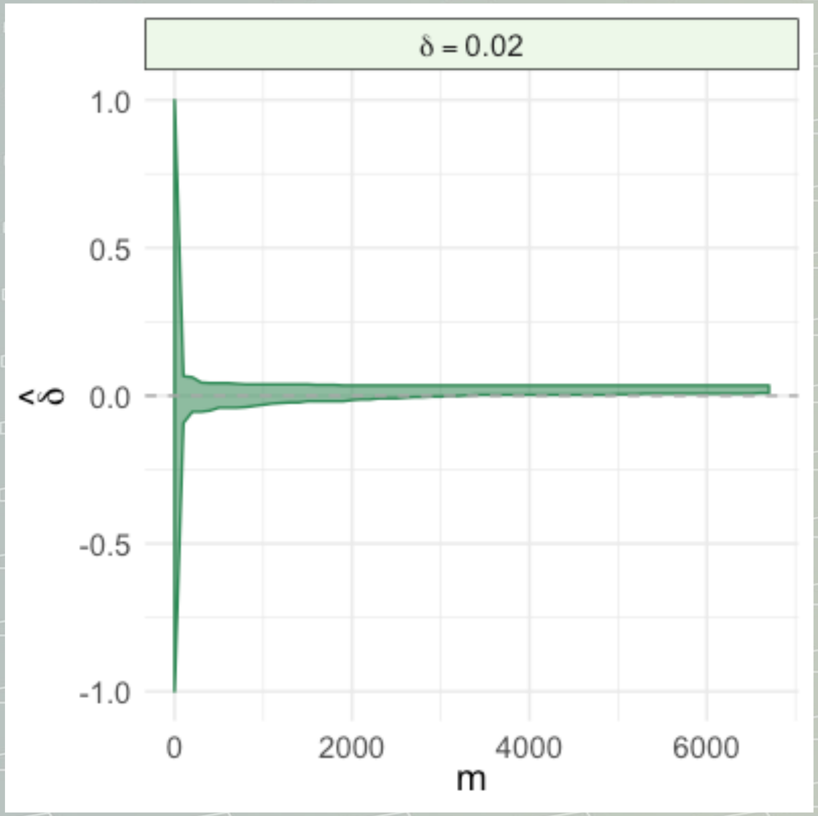
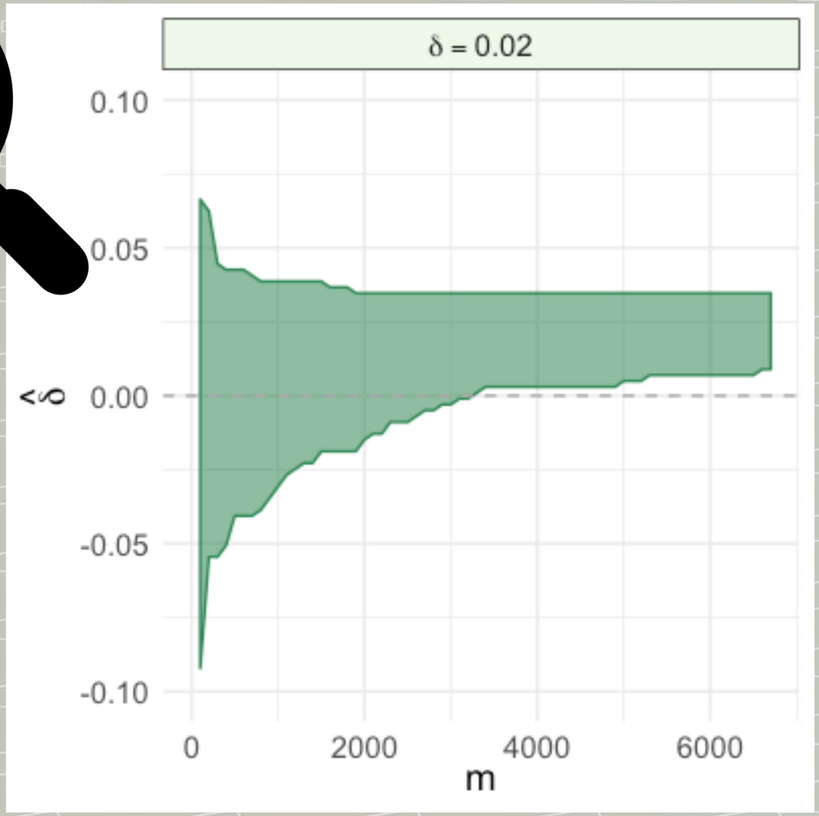
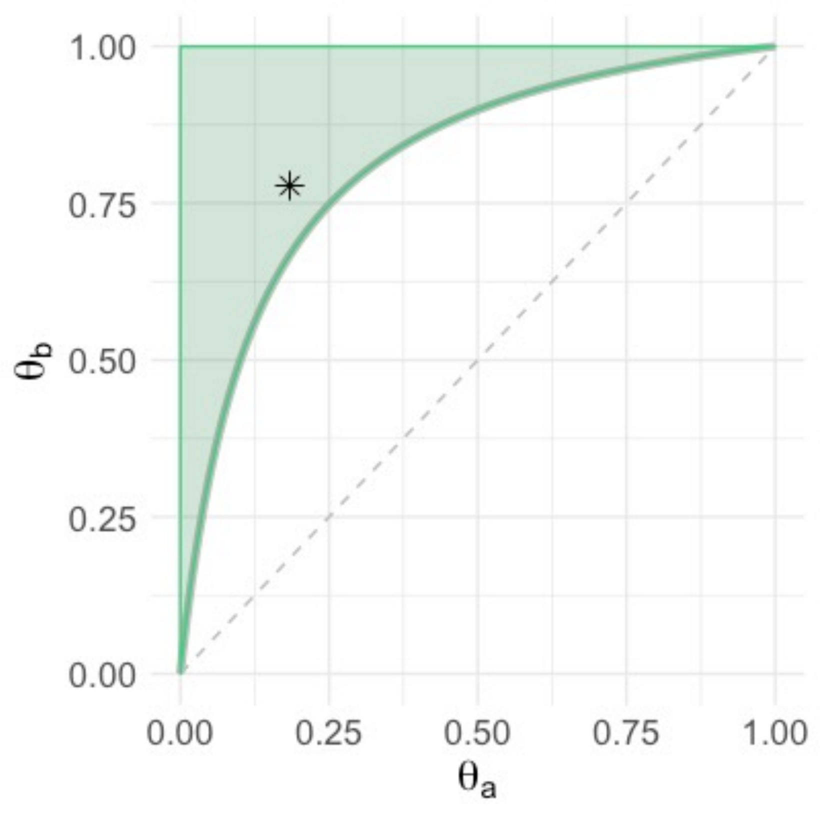
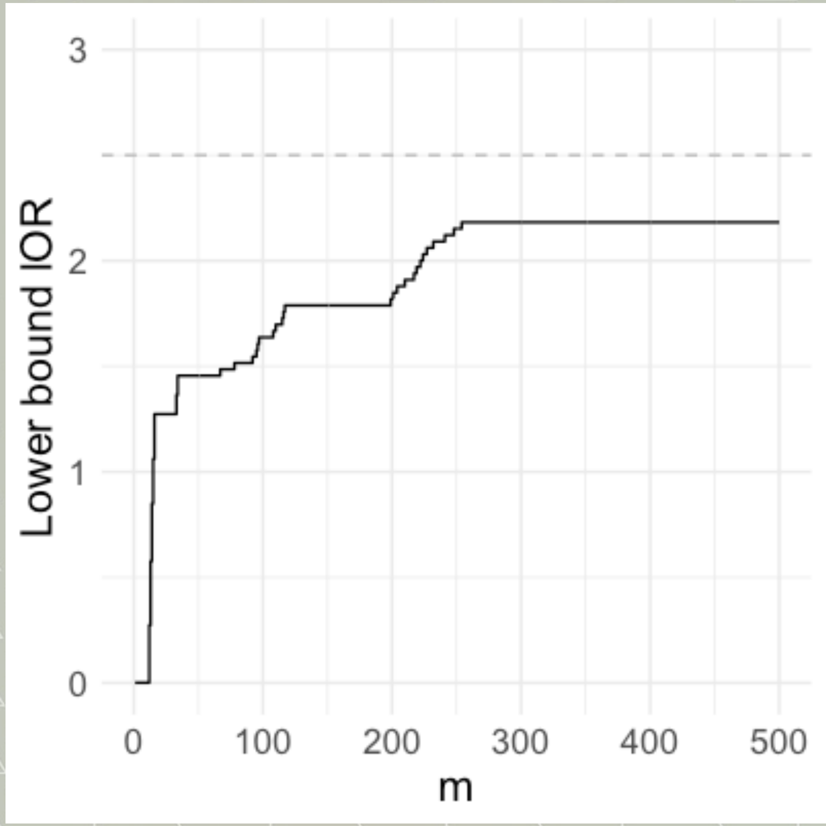




Simulation: log of the odds ratio



One-sided CS^+ at data block $m = 500$



lower bound over time

Figure adapted from Turner et al., 2022

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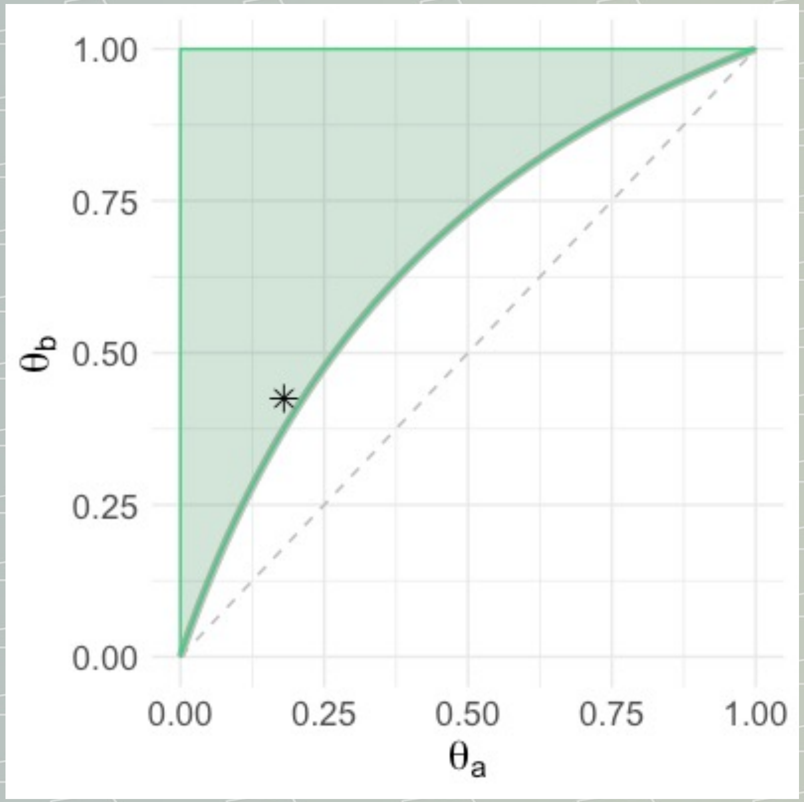

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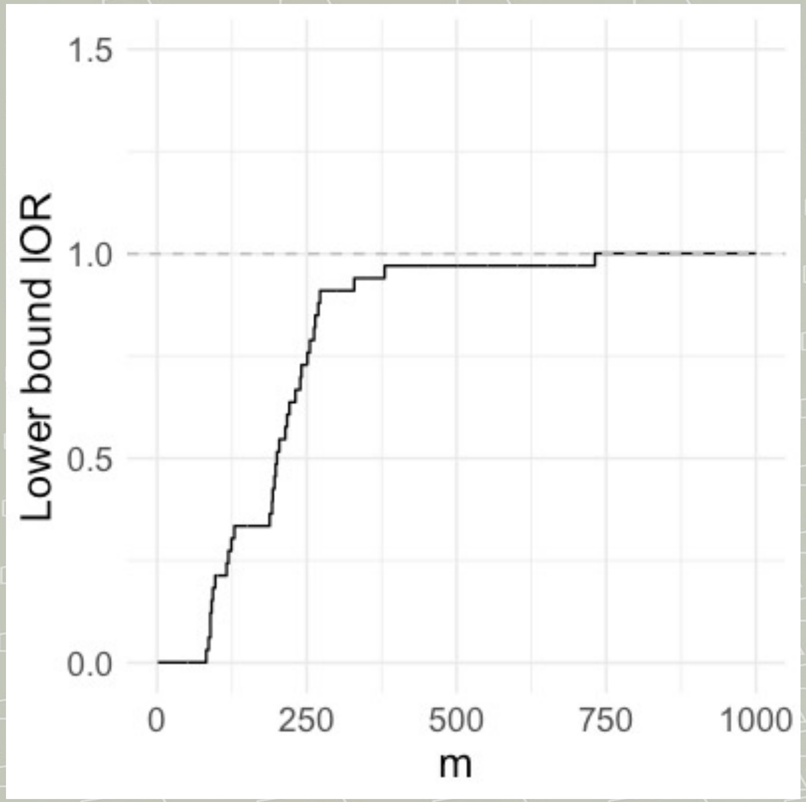

lower bound over time

Figure adapted from Turner et al., 2022

Conclusion and novelty

- To our knowledge, really new:
  - **flexibility** (block size, user-specified notions of effect size)
  - **growth rate optimality**: expect evidence for H1 to **grow as fast as possible** during data collection
- Wald's sequential probability ratio test:
  - Probability ratios can be interpreted as "alternative" E-variables
  - Not growth-rate optimal
  - Only allow for testing odds ratio effect size

Extensions

- Beyond Bernoulli: GRO property? (work by Y. Hao and others)
- Stratified data and conditional independence
  - Use case at UMC Utrecht: real-time psychiatry research and recommendations

		Strategy A	Strategy B
Stratum 1	Success	S(A1)	S(B1)
	Failure	F(A1)	F(B1)
Stratum 2	Success	S(A2)	S(B2)
	Failure	F(A2)	F(B2)
Stratum 3	Success	S(A3)	S(B3)
	Failure	F(A3)	F(B3)

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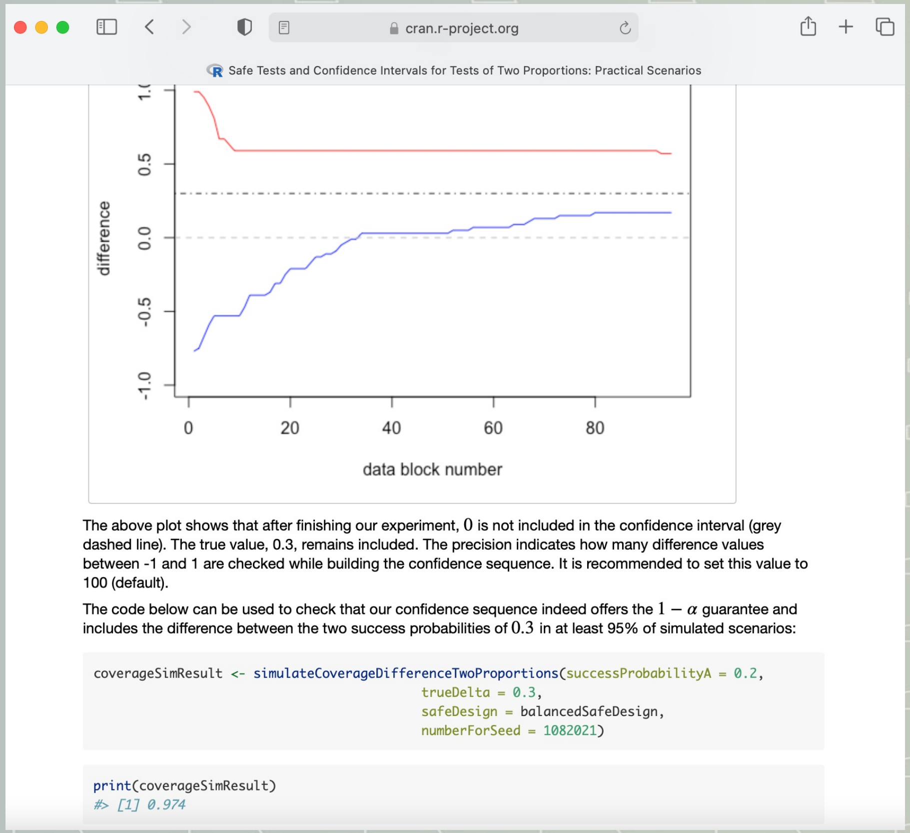
R Package and Vignettes



- In R console: `install.packages(“safestats”)`
- https://CRAN.R-project.org/package=safestats

Further reading and references

- On the theory of E-values:
  - P.D. Grünwald, R. de Heide and W. Koolen (2019) on ArXiv:
  - V. Vovk and R. Wang (2021). E-values: Calibration, combination, and applications. Annals of Statistics.
  - G. Shafer (2021). Testing by betting: A strategy for statistical and scientific communication. Journal of the Royal Statistical Society, Series A.
- On implementations of E-values:
  - R.J. Turner, A. Ly and P.D. Grünwald (2021) on ArXiv:2106.02693
  - R.J. Turner and P.D. Grünwald (2022) on ArXiv:2203.09785
  - R software: https://CRAN.R-project.org/package=safestats