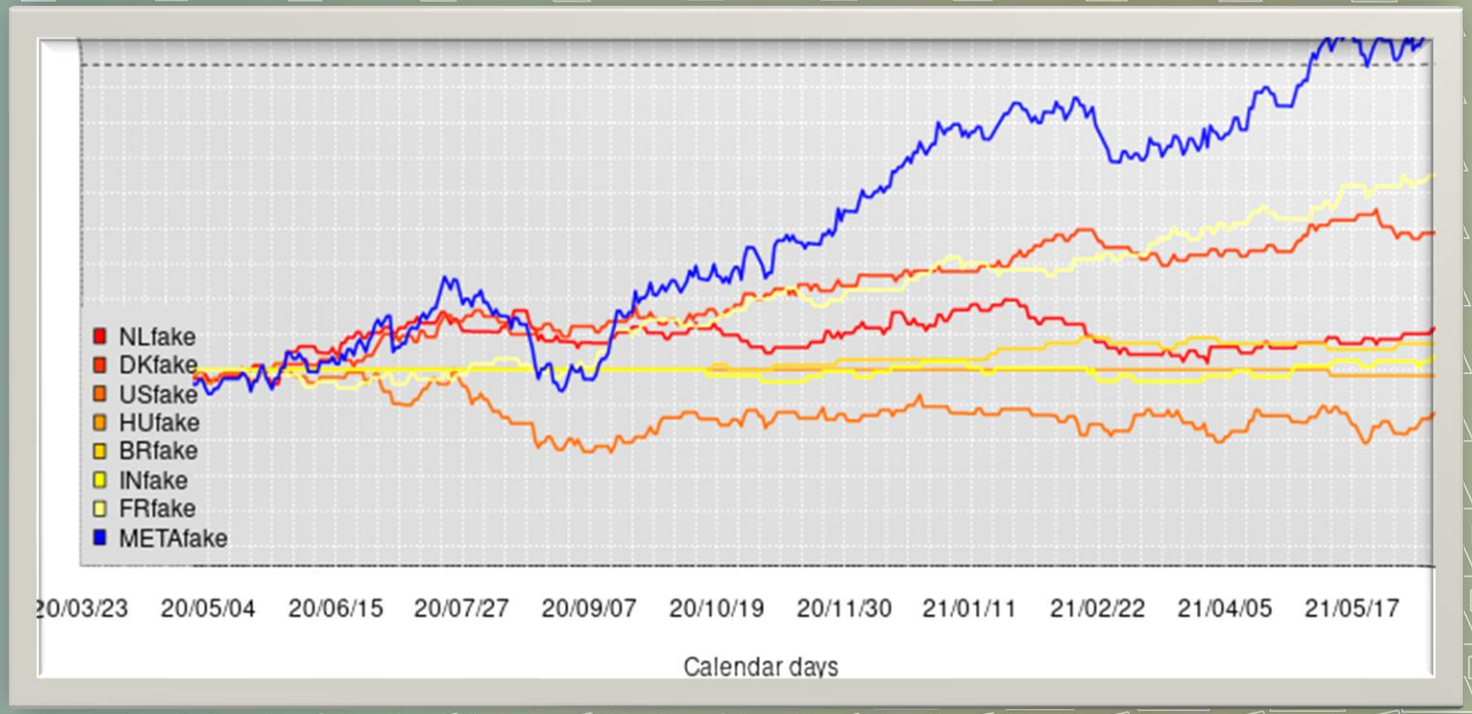
CWI Centrum Wiskunde & Informatica

MACHINE LEARNING

ALL-IN meta-analysis



Judith ter Schure

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MACHINE LEARNING

ALL-IN meta-analysis




Peter Grünwald Judith ter Schure Alexander Ly Muriel Pérez

ALL-IN meta-analysis properties

Type-I error whenever you analyze

- Continuous monitoring
- Unlimited horizon (no prespecified maximum sample size)
- Possibly 100% power
- Live meta-analysis (update after each new observation)
- Effortless cumulative meta-analysis (unlimited number of trials)

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A*nytime*
L*ive* and
L*eading*
IN*terim* meta-analysis

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I'll give an example of time-to-event analysis (logrank test)
ALL-IN-META-BCG-CORONA

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Whenever you see *e*-value, you can read: likelihood ratio

ALL-IN meta-analysis

- Meta evidence by ***multiplying*** study e-values
- **Type-I error control** under continuous monitoring and **any decision** to start, stop or expand studies
- Evidence against
  the global null (= no risk difference ***in any study***)
  contribution by any study with hazard ratio < 0.8

e-values and Ville's inequality

$$E\langle i\rangle = \frac{\boldsymbol{P}(\ \textit{observed event } i\ \mid\ \textit{hazard ratio } = 0{,}8\ )}{\boldsymbol{P}(\ \textit{observed event } i\ \mid\ \textit{hazard ratio } = 1\ )} \quad \begin{matrix} H_1 \\ H_0 \end{matrix}$$

- If $E\langle i\rangle$ is an *e-value* for a single event i

$$E^{\langle n\rangle} = \prod_{i=1}^{n} E\langle i\rangle$$

is also an *e-value* for n events

- Ville's inequality (1939)

$$\boldsymbol{P}_{\boldsymbol{events} \sim \boldsymbol{H_0}}\Big(\ E^{\langle n\rangle} \geq \frac{1}{\alpha} \ \text{ for some } \ n\ \Big) \leq \alpha$$

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$$\boldsymbol{P}_{\boldsymbol{events} \sim \boldsymbol{H_0}}\big(\ \ E^{\langle n\rangle} \geq 20 \ \text{ for some } n\ \big) \leq 0{,}05$$

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e-values and Ville's inequality

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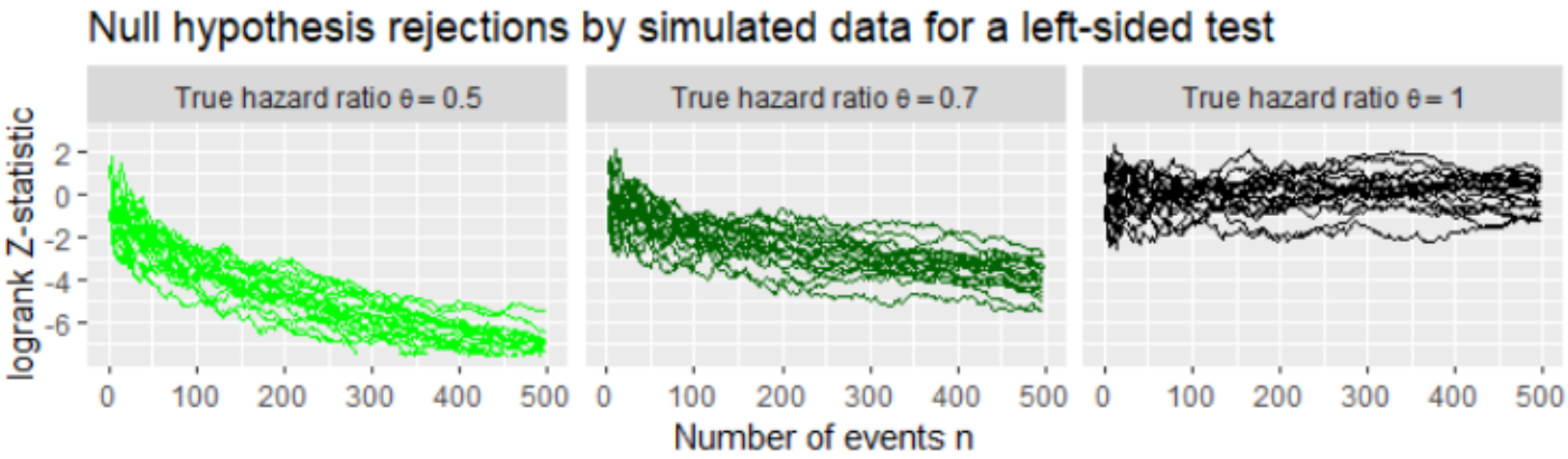

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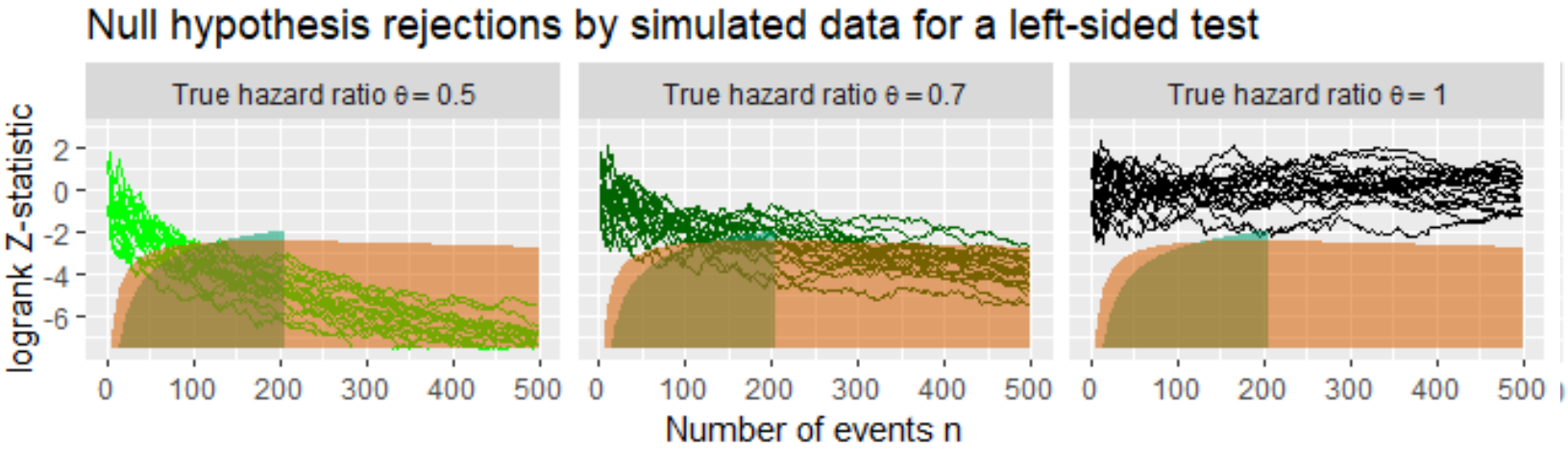

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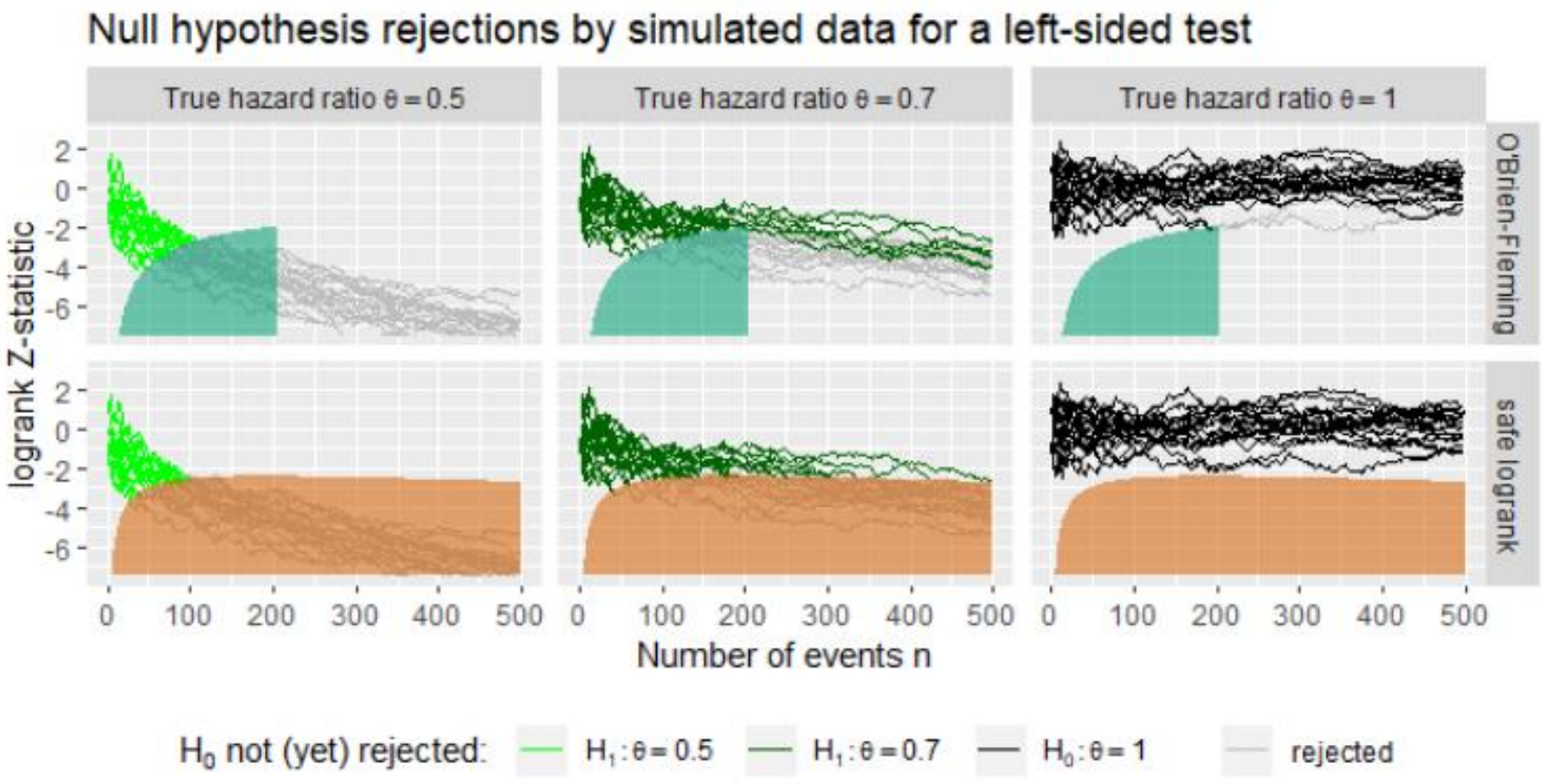
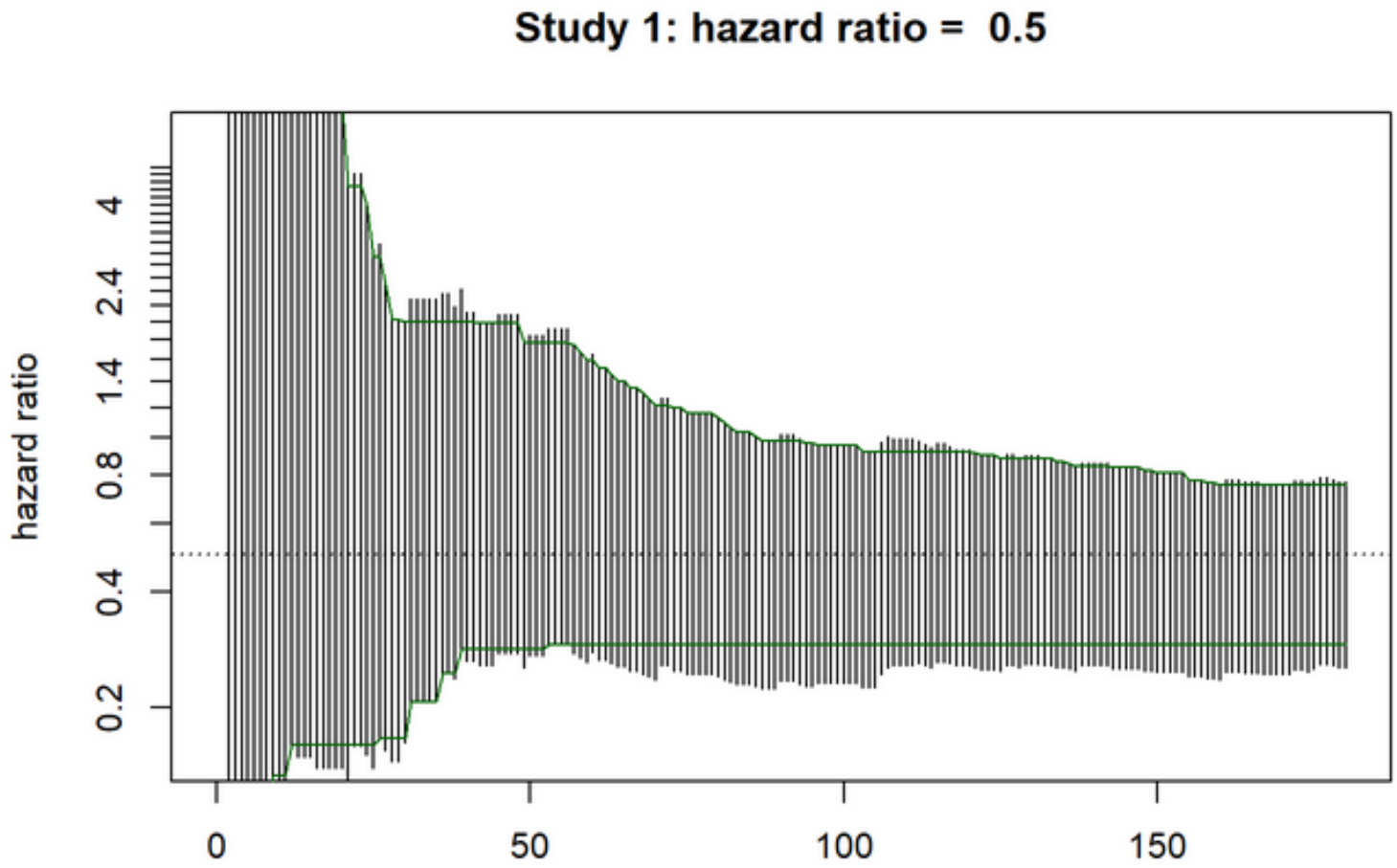


Anytime-valid confidence sequences



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Heterogeneity

Simplicity

Anytime-valid confidence sequences

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- Future work confidence sequences based on random-effects model

References

- ter Schure, J.A., Pérez-Ortiz, M.F., Ly, A., & Grünwald, P.D. (2021). The Safe Logrank Test: Error Control under Continuous Monitoring with Unlimited Horizon. arXiv:2011.06931

- ALL-IN meta-analysis webinar (2020) https://ir.cwi.nl/pub/30338
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- ter Schure, J.A, & Grünwald, P.D. (2019). Accumulation Bias in meta-analysis: the need to consider time in error control [version 1; peer review: two approved]. *F1000Research*, *8*. doi:10.12688/f1000research.19375.1

- Peto, Richard. Why do we need systematic overviews of randomized trials? (Transcript of an oral presentation, modified by the editors). *Statistics in medicine* 6.3 (1987): 233-240.

Thank you!

References

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