Sample Size Estimation for Outlier Detection

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1. INTRODUCTION

- To use medical imaging techniques (e.g. DTI) for diagnostics, they need to be able to detect **subject-specific anomalies**
- Common approach: the **atlas method** (see **figure 1**)
- Detection of SSAs becomes a problem of **outlier detection**
- Outlier detection can be done by setting a threshold on the **z-score** value (e.g. z_0=1.96)
- Problem: z-score is calculated using estimates for the population parameters, which have **associated uncertainties**
- This affects the statistical power of outlier detection

2. OBJECTIVES

- Estimate a **confidence interval (CI) for the z-score**
- Use the CI to estimate the **minimum sample size** required for a desired statistical power
- Analyze how the CI affects our ability to detect SSAs in patients with **mild traumatic brain injury (mTBI)**

3. METHODS

- Applying **Gaussian Error Propagation** to the definition of the z-score gave the following CI:

$$I_{z_0} = \left[z_0 - \frac{1}{\sigma}\sqrt{u_\mu^2 + z_0^2 u_{\sigma,l}^2}\,,\; z_0 + \frac{1}{\sigma}\sqrt{u_\mu^2 + z_0^2 u_{\sigma,r}^2} \right]$$

- Uncertainties were estimated with two different methods:
  1. **Parametric Approach**
  2. **Resampling Approach (Bootstrap)**
- The parametric approach gives the half-width of the CI as:

$$\varepsilon = \sqrt{\frac{1}{N}\cdot t^2_{(1-\frac{\alpha}{2};N-1)} + z_0^2 \cdot \left(1 - \sqrt{\frac{N-1}{\chi^2_{(\frac{\alpha}{2};N-1)}}}\right)^2}$$

4. APPLICATIONS AND RESULTS

- We always used α=5%, i.e. **95% confidence intervals**
- Monte Carlo simulation shows that both the parametric and the bootstrap approach return similar results (see **figure 2**)
- Putting a threshold on ε allows to solve numerically for the sample size N. Results are given in **figure 3**.
- We reused data from (Bouix et al., 2013) to investigate the effect of the CI in the finding of SSAs. The atlas was calculated from 45 HC in 145 ROIs. For the outlier detection, we used 11 patients with mTBI. Our findings are given in **figure 4**.

5. MAIN CONCLUSIONS

- Small CI widths require **relatively large samples** ($N \sim 10^2$)
- Uncertainties associated with detecting SSAs are significant enough that they **should be taken into account** when designing an experiment or at least **acknowledged when reporting results**

6. REFERENCES

- S. Bouix et al. *Increased gray matter diffusion anisotropy in patients with persistent post-concussive symptoms following mild traumatic brain injury.* PLoS ONE, 8(6):e66205, 2013.

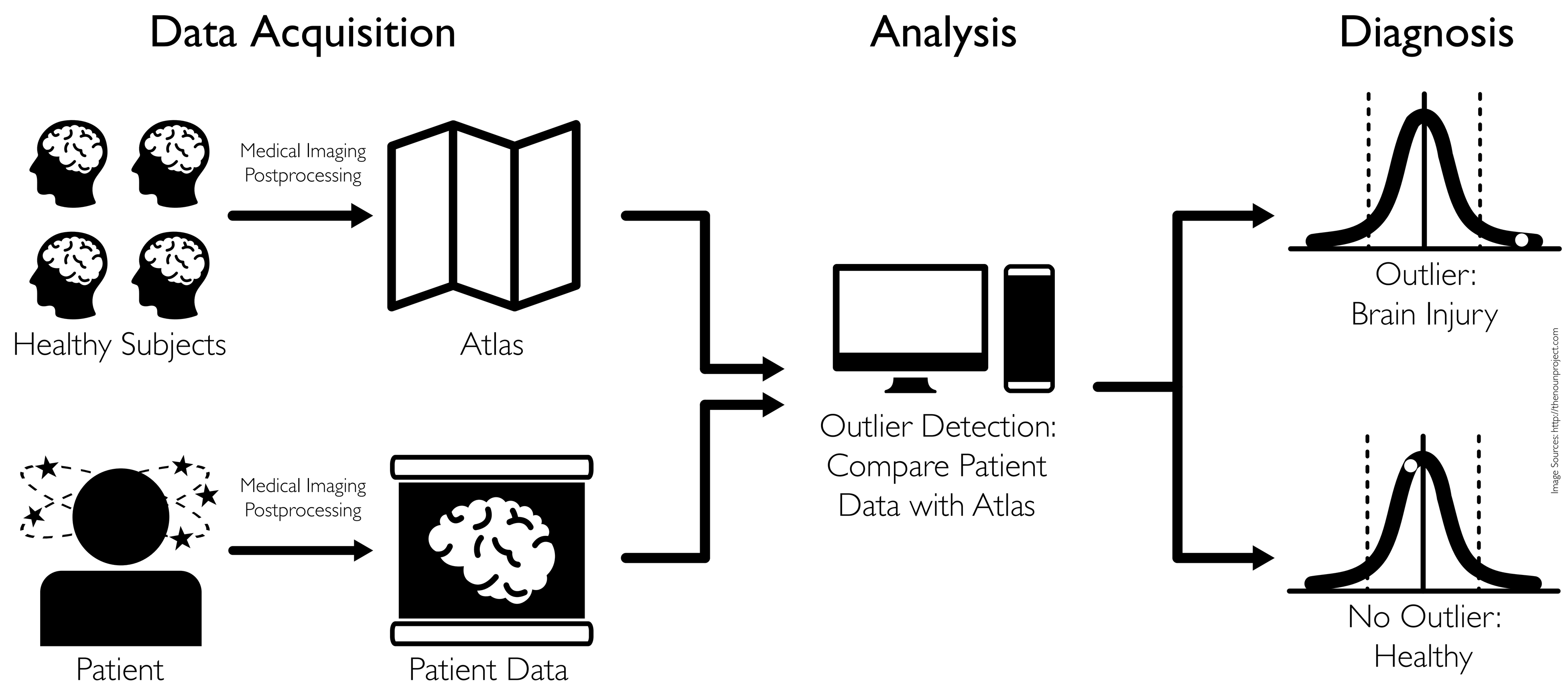

Figure 1: The atlas method, which can be used to detect subject-specific anomalies

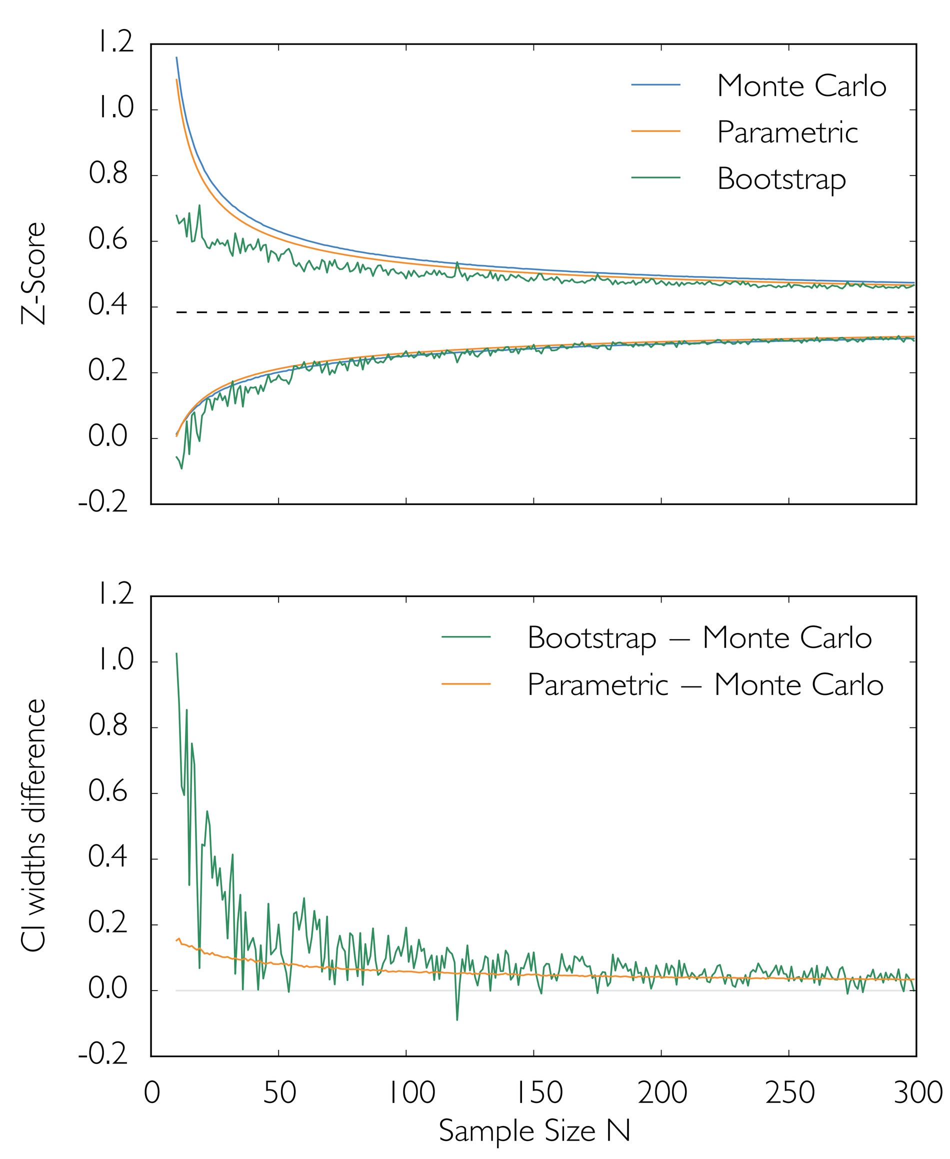

Figure 2: Monte Carlo results for z_0=1.96

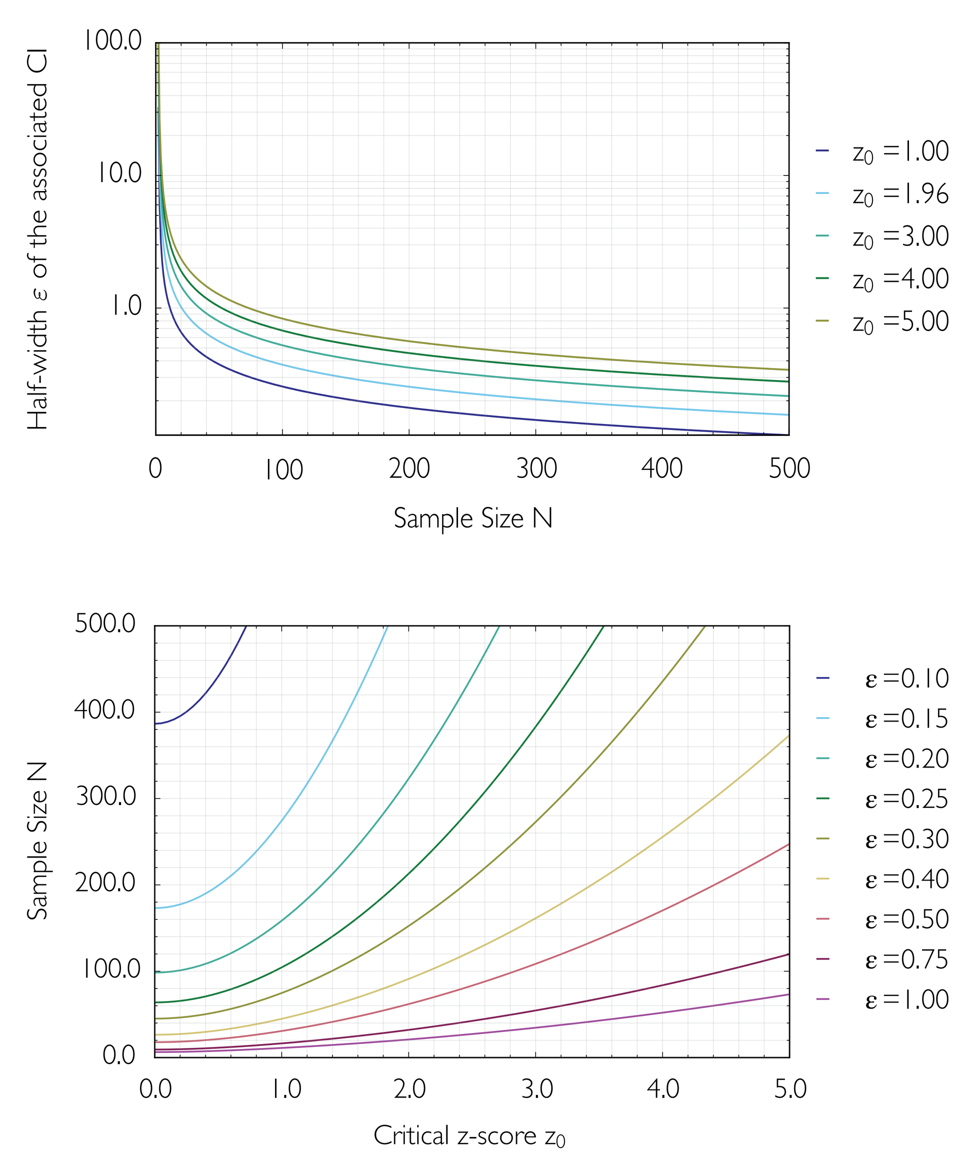

Figure 3: Minimum Sample Size Estimates

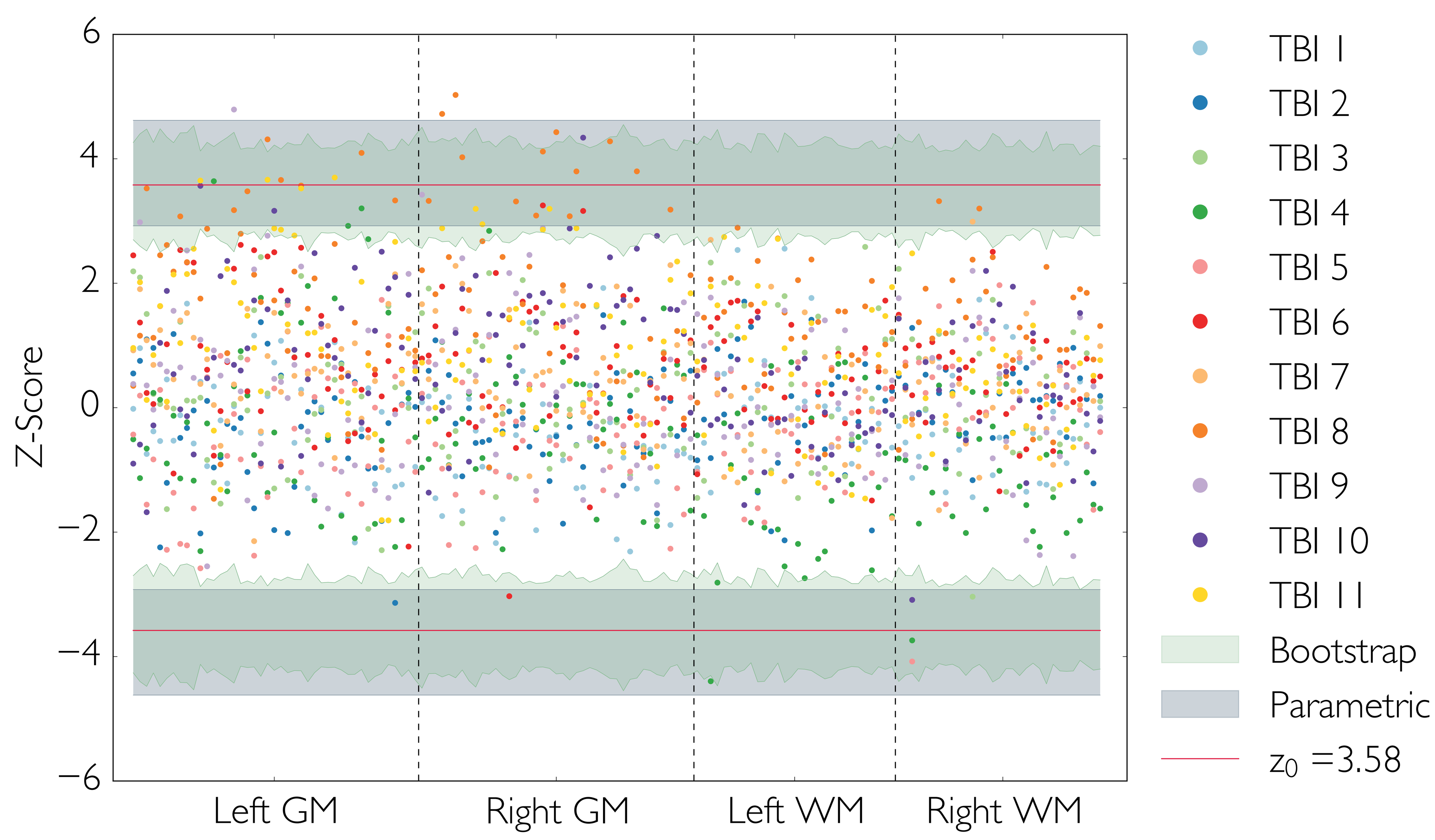

Figure 4: Confidence intervals associated with results from (Bouix et al., 2013)

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