Brice Ozenne

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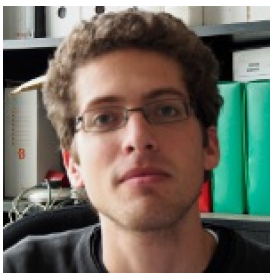

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Current position

October 2023- Now: **Associate professor in biostatistics** with a shared position between

- a research unit in biostatistics
Section of Biostatistics, University of Copenhagen (KU)
Øster Farimagsgade 5, 1014 Copenhagen, Denmark

- a research unit in neuroscience
Neurobiology Research Unit (NRU)
Copenhagen University Hospital, Rigshospitalet
Building 6931, Blegdamsvej 9, DK-2100 Copenhagen, Denmark

where I do research in biostatistics along with a consulting and teaching activity in statistics.

My research work is organized around three topics:

- the development of **multivariate models** for data analysis in neuroscience, mainly latent variable models (LVM) and mixed models (LMM) - see publications **???**. From a methodological point of view, I study how to perform statistical **estimation and inference in small samples** [**?**] as well as efficient corrections for **multiple testing** [**?**]. These developments are available in the R packages `lavaSearch2` (LVM) and `LMMstar` (LMM).

- the analysis of registry data in presence of **right-censoring**, **competing risks**, and **confounding competing risks**. A typical application is the comparison of preventive treatments of cardiovascular diseases [**???**]. Based on the **semi-parametric theory**, I have developped a robust estimator of the average treatment effect and derived its asymptotic distribution via its influence function [**?**]. This has been implemented in the `ate` function of the `riskRegression` R package.

- the extension of **generalized pairwise comparisons** (GPC), e.g. to handle right-censoring [**Brice Ozenne** et al., 2021], restriction time [**?**], or perform reliable statistical inference with more than two groups. GPC is a method able to handle multiple and heterogeneous endpoints which is especially relevant to assess the benefit-risk balance of a treatment. A typical application is the evaluation of chemotherapies where jointly considering gains in survival and side effects is critical [**??**].

- Handling delayed endpoint when designing and analyzing **group sequential trials**. A typical application would be a trial on anti-depressant where the outcome is the depression score after 1 month of treatment and one would like to have one or several interim analyzes to have the possibility to stop early for efficacy of futility. This work has lead to a tutorial paper [**?**] and a companion software package called `delayedGSD` hosted on Github. It includes sample size calculation, determination of efficacy/futility/decision boundaries, p-values, confidence intervals, and median unbiased estimates.

Other domains of interest in statistics:

- Mediation analysis
- Causal inference
- Smoothing splines
- Multiple testing

Skills

Language

French (native language), english (fluent), danish (intermediate), basics in italian.

Software

Proficient in , LaTeX and orgmode.
Basic knowledge but common use of C++, lisp (for GNU Emacs) and git/github (via magit).

Education and research carrier

2022 - 2023 : Course in teaching and learning in higher education (Universitetspædagogikum)

2020 - 2023 : Assistant professor in biostatistics with a shared positive between:
University of Copenhagen: researcher and teacher at the Graduate School of Health and Medical Sciences
Copenhagen University Hospital: consultant
Development of a 'user-friendly' mixed model package (`LMMstar` package), a package for designing and analyzing groups sequential trials (`DelayedGSD` package), and extension of the `BuyseTest` package (H-decomposition, restriction time)

2020 - 2015 : Post-doc in biostatistics with a shared positive between:
University of Copenhagen: researcher and teacher at the Graduate School of Health and Medical Sciences
Copenhagen University Hospital: consultant and leader of the data analysis work package of the Neuropharm project
Development of small sample corrections and multiple testing adjustment for LVM and robust estimators of treatment effect for registry data analysis (respective R packages: `lavaSearch2` and `riskRegression`)

2012 - 2015 : Ph.D. in biostatistics, University Lyon 1, Lyon, France.
Thesis Title: Statistical modelling for the prognosis of stroke patients.
Advisor: Pr. Delphine Maucort-Boulch and Pr. Norbert Nighoghossian
Start of the `BuyseTest` package emulating a SAS macro.

2011 - 2012 : Master's degree in biostatistics (M2 B3S), University lyon, Lyon, France.
Carried out in double degree with the École Centrale de Lyon.

2009 - 2012 : Engineering diploma from the École Centrale de Lyon, Lyon, France.
Erasmus at Politecnico di Milano (2nd semester 2011).

Teaching and supervision

Current teaching activity for Phd students in medical sciences:

2015 - 2023 : Statistical analysis of repeated measurements (course director Julie Forman).
3 lectures of 3 hours and 6 practicals of 3 hours
Development of a dedicated R package for the course (LMMstar)

2021 - 2023 : Epidemiological methods in medical research as course director.
3.5 lectures of 3 hours, 7 practical of 3 hours, 1/2 day student presentations

2021 - 2023 : Basic statistics (course director Paul Blanche).
1 lecture of 3 hours, 1 practical of 3 hours, 1 day student presentations

More in depth presentation of the present and past teaching activity as well as the pedagocial approach can be found in my teaching portofilio.

I now also teach Master students in statistics:
2023 - 2024 : Survival analysis (course director Frank Eriksson).
6 lectures of 4 hours and 6 practicals of 1 or 2 hours

Co-supervision of students:

2023 : Tanne Ebert Jørgensen and Johanne Triantafyllou Lorenzen (Master in epidemiology)
Childcare and symptoms of ADHD in the Danish population.

2021-2024 : Simon Christoffer Ziersen (Ph.D in biostatistics)
Causal inference in time to event analysis with competing risks

2021 : Ramlah Sara Rehman (Bachelor in data science)
An Analysis of Clustering Algorithms: Clustering Trajectories of the Cortisol Concentration.

2019 : Alice Brouquet-Laglaire (Master 2 in biostatistics)
Comparison of inference methods for generalized pairwise comparisons.

2014 : Ceren Tozlu (Master 2 in biostatistics)
Comparison of classification methods for tissue outcome after ischemic stroke [**?**].

Pedagogical talks for researchers in neuroscience on specific statistical tools/issues:

- Do we need more power? (NRU Christmas Symposium 2017).
- To adjust or not adjust, that is the question (NRU Christmas Symposium 2018).
- A refresher on multiple comparisons? (NRU Christmas Symposium 2019).
- The data-processing multiverse: achieving reconciliation for Christmas (NRU Christmas Symposium 2022).

Grants

2017-2019: MARIE CURIE Individual Fellowships (200 000€, EU H2020-MSCA-IF-2016 746850)
2017-2020: Lundbeck Fellowships (140 000€, R231-2016-3236)

Publications in peer reviewed scientific journals — link google scholar

Methodological (selected publications - 8/14)

1. Thomas H Scheike, Torben Martinussen, and **Brice Ozenne**. Efficient estimation in the fine and gray model. *Journal of the American Statistical Association*, pages 1–9, 2022. URL https://doi.org/10.1080/01621459.2022.2057860

2. **Brice Ozenne**, Esben Budtz-Jørgensen, and Sebastian Elgaard Ebert. Controlling the familywise error rate when performing multiple comparisons in a linear latent variable model. *Computational Statistics*, pages 1–23, 2022. URL https://doi.org/10.1007/s00180-022-01214-7

3. **Brice Ozenne**, Esben Budtz-Jørgensen, and Julien Péron. The asymptotic distribution of the net benefit estimator in presence of right-censoring. *Statistical Methods in Medical Research*, 30(11):2399–2412, 2021. URL https://doi.org/10.1177/09622802211037067

4. **Brice Ozenne**, Patrick Fisher, and Esben Budtz-Jørgensen. Small sample maximum likelihood inference in latent variable models. *JRSS-C*, 2020a. URL https://doi.org/10.1111/rssc.12414

5. **Brice Ozenne**, Thomas Harder Scheike, Laila Stærk, and Thomas Alexander Gerds. On the estimation of average treatment effects with right-censored time to event outcome and competing risks. *Biometrical Journal*, Epub ahead of print, 2020b. URL https://doi.org/10.1002/bimj.201800298

6. **Brice Ozenne**, Anne Lyngholm Sørensen, Thomas Scheike, Christian Torp-Pedersen, and Thomas Alexander Gerds. riskregression: Predicting the risk of an event using cox regression models. *R Journal*, 9(2):440–460, 2017. URL https://journal.r-project.org/archive/2017/RJ-2017-062/index.html

7. **Brice Ozenne**, Fabien Subtil, and Delphine Maucort-Boulch. The precision–recall curve overcame the optimism of the receiver operating characteristic curve in rare diseases. *Journal of clinical epidemiology*, 68(8):855–859, 2015b. URL https://doi.org/10.1016%2Fj.jclinepi.2015.02.010

8. **Brice Ozenne**, Fabien Subtil, Leif Østergaard, and Delphine Maucort-Boulch. Spatially regularized mixture model for lesion segmentation with application to stroke patients. *Biostatistics*, 16(3):580–595, 2015c. URL https://doi.org/10.1093%2Fbiostatistics%2Fkxv004

Clinical applications (selected publications - 10/54)

9. Kristin Köhler-Forsberg, Vibeke H Dam, **Brice Ozenne**, Anjali Sankar, Vincent Beliveau, Elizabeth B Landman, Søren V Larsen, Asbjørn S Poulsen, Cheng-Teng Ip, Anders Jørgensen, et al. Serotonin 4 receptor brain binding in major depressive disorder and association with memory dysfunction. *JAMA psychiatry*, 2023

10. Arafat Nasser, **Brice Ozenne**, Emma Sofie Høgsted, Peter Steen Jensen, and Vibe G Frokjaer. Reliability of three versus five saliva sampling times for assessing the cortisol awakening response. *Psychoneuroendocrinology*, page 105950, 2022. URL https://doi.org/10.1016/j.psyneuen.2022.105950

11. Kristin Köhler-Forsberg, **Brice Ozenne**, Søren V Larsen, Asbjørn S Poulsen, Elizabeth B Landman, Vibeke H Dam, Cheng-Teng Ip, Anders Jørgensen, Claus Svarer, Gitte M Knudsen, et al. Concurrent anxiety in patients with major depression and cerebral serotonin 4 receptor binding. a neuropharm-1 study. *Translational psychiatry*, 12(1):1–8, 2022. URL https://doi.org/10.1038/s41398-022-02034-5

12. Emily Eufaula Beaman, Anders Nissen Bonde, Sara Marie Ulv Larsen, **Brice Ozenne**, Terhi Johanna Lohela, Maiken Nedergaard, Gunnar Hilmar Gíslason, Gitte Moos Knudsen, and Sebastian Camillo Holst. Blood–brain barrier permeable β-blockers linked to lower risk of alzheimer's disease in hypertension. *Brain*, 2022. URL https://doi.org/10.1093/brain/awac076

13. Søren Vinther Larsen, **Brice Ozenne**, Kristin Köhler-Forsberg, Asbjørn Seenithamby Poulsen, Vibeke Høyrup Dam, Claus Svarer, Gitte Moos Knudsen, Martin Balslev Jørgensen, and Vibe Gedso Frokjaer. The impact of hormonal contraceptive use on serotonergic neurotransmission and antidepressant treatment response: Results from the neuropharm 1 study. *Frontiers in endocrinology*, 13, 2022. URL https://doi.org/10.3389/fendo.2022.799675

14. **Brice Ozenne**, Tae-Hee Cho, Irene Klærke Mikkelsen, Marc Hermier, Götz Thomalla, Salvador Pedraza, Pascal Roy, Yves Berthezène, Norbert Nighoghossian, Leif Østergaard, et al. Individualized quantification of the benefit from reperfusion therapy using stroke predictive models. *European Journal of Neuroscience*, 50(8):3251–3260, 2019. URL https://doi.org/10.1111/ejn.14505

15. Sebastian Elgaard Ebert, Per Jensen, **Brice Ozenne**, Sophia Armand, Claus Svarer, Dea Siggaard Stenbaek, Kirsten Moeller, Agnete Dyssegaard, Gerda Thomsen, Jacob Steinmetz, et al. Molecular imaging of neuroinflammation in patients after mild traumatic brain injury: a longitudinal 123i-clinde single photon emission computed tomography study. *European journal of neurology*, 26(12):1426–1432, 2019. URL https://doi.org/10.1111/ene.13971

16. L. Staerk, T. A. Gerds, G. Y. H. Lip, **B. Ozenne**, A. N. Bonde, M. Lamberts, E. L. Fosbøl, C. Torp-Pedersen, G. H. Gislason, and J. B. Olesen. Standard and reduced doses of

dabigatran, rivaroxaban and apixaban for stroke prevention in atrial fibrillation: a nationwide cohort study. *Journal of Internal Medicine*, 283(1):45–55, 2017a. URL https://doi.org/10.1111%2Fjoim.12683

17. Dea S Stenbæk, Patrick M Fisher, **Brice Ozenne**, Emil Andersen, Liv V Hjordt, Brenda McMahon, Steen G Hasselbalch, Vibe G Frokjaer, and Gitte M Knudsen. Brain serotonin 4 receptor binding is inversely associated with verbal memory recall. *Brain and behavior*, 7 (4):e00674, 2017. URL https://doi.org/10.1002%2Fbrb3.674

18. **Brice Ozenne**, Tae-Hee Cho, Irene Klærke Mikkelsen, Marc Hermier, Lars Ribe, Götz Thomalla, Salvador Pedraza, Jean-Claude Baron, Pascal Roy, Yves Berthezène, et al. Evaluation of early reperfusion criteria in acute ischemic stroke. *Journal of Neuroimaging*, 25(6):952–958, 2015a. URL https://doi.org/10.1111%2Fjon.12255

Software development

Packages for the R software:

- **BuyseTest** (author and maintainer): implementation of generalized pairwise comparisons, including recent developments to handle right-censoring [**Brice Ozenne** et al., 2021]. Available on CRAN and on Github.
- **lavaSearch2** (author and maintainer): Inference and diagnostic tools for latent variable models. Methodology described in [**?**] and [**?**]. Available on CRAN and on Github. .
- **LMMstar** (author and maintainer) : linear mixed model via covariance structure (marginal formulation). Inference in small sample, test linear and non-linear combinations of parameters, multiple comparisons adjustment. Available on CRAN and on Github.
- **riskRegression** (contributor): computation of absolute risks and average treatment effects. Methodology described in [**?**] and [**?**]. Available on CRAN and on Github.
- **DelayedGSD** (author and maintainer): design and analysis for group sequential trial with repeated measurements of a continous outcome. Methodology described in [**?**] (to appear). Available on Github.

Package for emacs:

- **emacs-config** (author and maintainer) : Configuration files for emacs to ease the interaction with R/C++/orgmode/latex/git. Disponible on Github.

Peer review

I have reviewed papers for Biometrical Journal, Biometrics, Journal of statistical software, Statistics in Medicine, and the International Journal of Biostatistics.

I am also in the Data and Safety Monitoring Board (DSMB) of the clinical trial TRAUMOX2 (1420 patients, 5 sites in europe).

Oral communications

Oral presentation at international conferences:

2014 : Lesion Segmentation using a Spatially Regularized Mixture Model
Applied Statistics, Ribno, Slovenia (slides)

2015 : MRIaggr : un package pour la gestion et le traitement de données multivariées d'imagerie
Rencontres R, Grenoble, France (slides)

2016 : Penalized latent variable models
Computational statistics, Oviedo, Spain (slides)

2017 : Assessing treatment effects on registry data in presence of competing risks
ISCB, Vigo, Spain (slides)

2019 : Generalized pairwise comparisons for right-censored time to event outcomes
Survival analysis for junior researcher, Copenhagen, Denmark (slides)

2019 : Multiple testing in latent variable models
ISCB, Leuven, Belgium (slides)

2024 : Ordering the sample space in group sequential trials with delayed outcome
ADMTP Workshop, Ibiza, Spain (slides)

Invited speaker at an international conference:

2019 : Region-Based and Voxel-Wise Analysis of Medical Images Using Latent Variables
7th NBBC, Vilnius, Lithuania

2020 : Robust estimation of the average treatment effects in presence of right-censoring and competing risks
CMStatistics, London, England

2022 : Benefit-risk assessment via generalized pairwise comparisons
CMStatistics, London, England

Chairman at international conferences:

2019 : Mathematical Statistics
Survival analysis for junior researcher, Copenhagen, Denmark

Organisation of a workshop:

2021 : Analysis of repeated measurements with mixed models using the R package LMMstar (1h+3h)
Methods Week, Karolinska institute, Stockholm, Sweden