Brice Ozenne May 16, 2020



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# **Current position**

November 2015- Now: Postdoctoral researcher in biostatistics with a shared position between

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

- a research unit in neuroscience

Neurobiology Research Unit

Copenhagen University Hospital, Rigshospitalet

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

My research work is organized around three topics:

- the development of latent variable models for data analysis in neuroscience see publications Ebert et al. [2019], Stenbæk et al. [2017], Fisher et al. [2017]. From a methodological point of view, I study how to perform statistical estimation and inference in small samples [Brice Ozenne et al., 2020a] as well as efficient corrections for multiple testing [Brice Ozenne et al., b]. These developments are available in the R package lavaSearch2.
- 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 [Staerk et al., 2016, 2017b,a]. Based on the **semi-parametric theory**, I have developed a robust estimator of the average treatment effect and derived its asymptotic distribution via its influence function [**Brice Ozenne** et al., 2020b]. This has been implemented in the ate function of the **riskRegression** R package.

• the extension of **generalized pairwise comparisons** (GPC) to right-censoring [Péron et al., 2016a]. 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. I am now working on deriving the asymptotic distribution of some of the estimators implemented in the BuyseTest using the U-statistique theory.

## Other domains of interest in statistics:

- Smoothing splines and functional data analysis
- Causal inference and dynamic treatment regimes
- Post-selection inference

## Language

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

## Software

Proficient in **R**, LaTeX and orgmode.

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

## **Education**

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

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**

Teaching (L : lecture, PC : practical classes)

2015 - 2020: Statistical analysis of repeated measurements for Phd students in medical sciences (18h, PC)

2016 - 2017 : Structural Equation Models for Master students in statistics (2h, L).

2014 - 2015: Bayesian statistics for Master students in public health (6h, PC).

2013 - 2015: Survival Analysis for Master students in public health (18h, PC).

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).

#### Co-supervision of master 2 student:

2014 : Ceren Tozlu

Comparison of classification methods for tissue outcome after ischemic stroke [Tozlu et al., 2019].

2019: Alice Brouquet-Laglaire

Comparison of inference methods for generalized pairwise comparisons.

### **Grants**

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

Scientific output

# Scientific output

link google scholar

# $Publications \ (methodological)$

### Published:

- 1. **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
- 2. Johan Verbeeck, **Brice Ozenne**, and William N Anderson. Evaluation of inferential methods for the net benefit and win ratio statistics. *Journal of Biopharmaceutical Statistics*, pages 1–18, 2020. URL https://doi.org/10.1080/10543406.2020.1730873
- 3. **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
- 4. Martin Nørgaard, **Brice Ozenne**, Claus Svarer, Stephen C. Strother, Vibe G. Frokjaer, Gitte M. Knudsen, and Melanie Ganz. Preprocessing, prediction and significance:

Framework and application to brain imaging. Information Processing in Medical Imaging (IPMI) conference 2019, 2019. URL

https://link.springer.com/chapter/10.1007/978-3-030-32251-9 22

5. **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

6. Julien Péron, Marc Buyse, **Brice Ozenne**, Laurent Roche, and Pascal Roy. An extension of generalized pairwise comparisons for prioritized outcomes in the presence of censoring. *Statistical methods in medical research*, 27(4):1230–1239, 2016a. URL https://doi.org/10.1177%2F0962280216658320

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

#### In revision:

- 1. **Brice Ozenne**, Sebastian Elgaard Ebert, and Esben Budtz-Jørgensen. Controlling the familywise error when performing multiple comparisons in a linear latent variable model. *Psychometrika*, b
- 2. Julien Péron, Maryam Idlhaj, Marc Buyse, Joris Giai, Pascal Roy, Laurence Collette, Delphine Maucort-Boulch, and **Brice Ozenne**. An unbiased estimation of the net survival benefit in the presence of censored observations. *Biometrical Journal*
- 3. Eva Cantagallo, Michaël De Backer, Michal Kicinski, **Brice Ozenne**, Laurence Collette, Catherine Legrand, Marc Buyse, and Julien Péron. A new measure of treatment effect in clinical trials involving competing risks based on generalized pairwise comparisons. *Biometrical Journal*

#### In preparation

1. **Brice Ozenne**, Esben Budtz-Jørgensen, and Julien Péron. The asymptotic distribution of the net benefit estimator in presence of right-censoring. a

# Publications (clinical applications)

#### Published:

- 1. VH Dam, DS Stenbæk, K Köhler-Forsberg, C Ip, B Ozenne, BJ Sahakian, GM Knudsen, MB Jørgensen, and VG Frokjaer. Hot and cold cognitive disturbances in antidepressant-free patients with major depressive disorder: a neuropharm study. *Psychological Medicine*, pages 1–10, 2020
- Liv Vadskjær Hjordt, Brice Ozenne, Sophia Armanda, Vibeke H Dam, Christian Gaden Jensen, Köhler-Forsberg Kristin, Gitte M Knudsen, and Dea Siggaard Stenbæk.
   Psychometric properties of the verbal affective memory test-26 and evaluation of affective biases in major depressive disorder. Frontiers in Psychology, 11:961, 2020
- 3. Vincent Beliveau, **Brice Ozenne**, Stephen Strother, Douglas N Greve, Claus Svarer, Gitte Moos Knudsen, and Melanie Ganz. The structure of the serotonin system: A pet imaging study. *NeuroImage*, 205:116240, 2020. URL https://doi.org/10.1016/j.neuroimage.2019.116240
- 4. Martin Korsbak Madsen, Patrick MacDonald Fisher, Dea Siggaard Stenbæk, Sara Kristiansen, Daniel Burmester, Szabolcs Lehel, Tomas Páleníček, Martin Kuchař, Claus Svarer, **Brice Ozenne**, et al. A single psilocybin dose is associated with long-term increased mindfulness, preceded by a proportional change in neocortical 5-ht2a receptor binding. *European Neuropsychopharmacology*, 2020. URL https://doi.org/10.1016/j.euroneuro.2020.02.001
- 5. **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
- 6. 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
- 7. Martin K Madsen, Patrick M Fisher, Daniel Burmester, Agnete Dyssegaard, Dea S Stenbæk, Sara Kristiansen, Sys S Johansen, Sczabolz Lehel, Kristian Linnet, Claus Svarer, **Brice Ozenne**, and Gitte Moos Knudsen. Psychedelic effects of psilocybin correlate with serotonin 2a receptor occupancy and plasma psilocin levels. *Neuropsychopharmacology*, page 1, 2019. URL https://doi.org/10.1038/s41386-019-0324-9

- 8. Ceren Tozlu, **Brice Ozenne**, Tae-Hee Cho, Norbert Nighoghossian, Irene Klærke Mikkelsen, Laurent Derex, Marc Hermier, Salvador Pedraza, Jens Fiehler, Leif Østergaard, et al. Comparison of classification methods for tissue outcome after ischaemic stroke. *European Journal of Neuroscience*, 50(10):3590–3598, 2019
- 9. Cheng-Teng Ip, Melanie Ganz, **Brice Ozenne**, Lasse B Sluth, Mikkel Gram, Geoffrey Viardot, Philippe l'Hostis, Philippe Danjou, Gitte M Knudsen, and Søren R Christensen. Pre-intervention test-retest reliability of EEG and ERP over four recording intervals. *International Journal of Psychophysiology*, 134:30–43, 2018. URL https://doi.org/10.1016/j.ijpsycho.2018.09.007
- 10. Camilla Borgsted, Brice Ozenne, Brenda Mc Mahon, Martin K Madsen, Liv V Hjordt, Ida Hageman, William FC Baaré, Gitte M Knudsen, and Patrick M Fisher. Amygdala response to emotional faces in seasonal affective disorder. *Journal of affective disorders*, 229:288–295, 2018. URL https://doi.org/10.1016%2Fj.jad.2017.12.097
- 11. Liv Vadskjær Hjordt, Vibeke H Dam, **Brice Ozenne**, Ida Hageman, Brenda Mc Mahon, Erik Lykke Mortensen, Gitte M Knudsen, and Dea Siggaard Stenbæk. Self-perceived personality characteristics in seasonal affective disorder and their implications for severity of depression. *Psychiatry research*, 262:108–114, 2018. URL https://doi.org/10.1016%2Fj.psychres.2018.02.015
- 12. Mette Thrane Foged, Kirsten Vinter, Louise Stauning, Troels W Kjær, **Brice Ozenne**, Sándor Beniczky, Olaf B Paulson, Lars H Pinborg, et al. Verbal learning and memory outcome in selective amygdalohippocampectomy versus temporal lobe resection in patients with hippocampal sclerosis. *Epilepsy & Behavior*, 79:180–187, 2018. URL https://doi.org/10.1016%2Fj.yebeh.2017.12.007
- 13. 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
- 14. Liv Vadskjær Hjordt, Dea Siggaard Stenbæk, **Brice Ozenne**, Brenda Mc Mahon, Ida Hageman, Steen Gregers Hasselbalch, and Gitte Moos Knudsen. Season-independent cognitive deficits in seasonal affective disorder and their relation to depressive symptoms. *Psychiatry research*, 257:219–226, 2017. URL https://doi.org/10.1016%2Fj.psychres.2017.07.056
- 15. Vincent Beliveau, Melanie Ganz, Ling Feng, **Brice Ozenne**, Liselotte Højgaard, Patrick M Fisher, Claus Svarer, Douglas N Greve, and Gitte M Knudsen. A high-resolution in vivo atlas of the human brain's serotonin system. *Journal of Neuroscience*, 37(1):120–128, 2017. ISSN 0270-6474. URL http://www.jneurosci.org/content/37/1/120

- 16. 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
- 17. Laila Staerk, Emil Loldrup Fosbøl, Morten Lamberts, Anders Nissen Bonde, Kasper Gadsbøll, Caroline Sindet-Pedersen, Ellen A Holm, Thomas Alexander Gerds, **Brice Ozenne**, Gregory YH Lip, et al. Resumption of oral anticoagulation following traumatic injury and risk of stroke and bleeding in patients with atrial fibrillation: a nationwide cohort study. *European heart journal*, 39(19):1698–1705a, 2017b. URL https://doi.org/10.1093%2Feurheartj%2Fehx598
- 18. PM Fisher, **Ozenne**, **B**, C Svarer, D Adamsen, S Lehel, WFC Baaré, PS Jensen, and GM Knudsen. Bdnf val66met association with serotonin transporter binding in healthy humans. *Translational psychiatry*, 7(2):e1029–e1029, 2017. URL https://doi.org/10.1038%2Ftp.2016.295
- 19. Mette Thrane Foged, Ulrich Lindberg, Kishore Vakamudi, Henrik BW Larsson, Lars H Pinborg, Troels W Kjær, Martin Fabricius, Claus Svarer, **Brice Ozenne**, Carsten Thomsen, et al. Safety and eeg data quality of concurrent high-density eeg and high-speed fmri at 3 tesla. *PloS one*, 12(5):e0178409, 2017. URL https://doi.org/10.1371%2Fjournal.pone.0178409
- 20. Julien Péron, Pascal Roy, **Brice Ozenne**, Laurent Roche, and Marc Buyse. The net chance of a longer survival as a patient-oriented measure of treatment benefit in randomized clinical trials. *JAMA oncology*, 2(7):901, 2016b. URL https://doi.org/10.1001%2Fjamaoncol.2015.6359
- 21. Laila Staerk, Emil Loldrup Fosbøl, Gregory YH Lip, Morten Lamberts, Anders Nissen Bonde, Christian Torp-Pedersen, **Brice Ozenne**, Thomas Alexander Gerds, Gunnar Hilmar Gislason, and Jonas Bjerring Olesen. Ischaemic and haemorrhagic stroke associated with non-vitamin k antagonist oral anticoagulants and warfarin use in patients with atrial fibrillation: a nationwide cohort study. *European heart journal*, page ehw496, 2016. URL https://doi.org/10.1093%2Feurheartj%2Fehw496
- 22. Julien Péron, Pascal Roy, Thierry Conroy, Françoise Desseigne, Marc Ychou, Sophie Gourgou-Bourgade, Trevor Stanbury, Laurent Roche, **Brice Ozenne**, and Marc Buyse. An assessment of the benefit-risk balance of folfirinox in metastatic pancreatic adenocarcinoma. *Oncotarget*, 7(50), 2016c. URL https://doi.org/10.18632%2Foncotarget.12761
- 23. **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

24. Laure Hermitte, Tae-Hee Cho, **Brice Ozenne**, Norbert Nighoghossian, Irene Klærke Mikkelsen, Lars Ribe, Jean-Claude Baron, Leif Østergaard, Laurent Derex, Niels Hjort, et al. Very low cerebral blood volume predicts parenchymal hematoma in acute ischemic stroke. *Stroke*, 44(8):2318–2320, 2013. URL

https://doi.org/10.1161%2Fstrokeaha.113.001751

# Software development

Packages for the R software:

- BuyseTest (author and maintainer): generalized pairwise comparisons. Implementation of the extension described in [Péron et al., 2016a, Péron et al.]. Available on CRAN and on Github.
- lavaSearch2 (author and maintainer): Inference and diagnostic tools for latent variable models. Methodology described in [Brice Ozenne et al., 2020a] and [Brice Ozenne et al., b]. Available on CRAN and on Github.
- **riskRegression** (contributor): computation of absolute risks and average treatment effects. Methodology described in [**Brice Ozenne** et al., 2017] and [**Brice Ozenne** et al., 2020b]. Available on CRAN and 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 sur sur Github.

### Peer review

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

#### **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)

Invited speaker at an internation conference:

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

december 2020: Robust estimation of the average treatment effects in presence of right-censoring

and competing risks

CMStatistics, London, England

Chairman at international conferences:

2019 : Mathematical Statistics

Survival analysis for junior researcher, Copenhagen, Denmark