Marie-Karelle RIVIERE, PhD

Director, statistical methodologist

07/19/1988 | French | Paris, France | +336 73 28 58 57 | eldamjh@gmail.com

CAREER HIGHLIGHTS

- Statistician with strong technical skills, driving innovation for more than 15 years in both industry and academia, from early to late phases clinical trials, especially in oncology.
- Experienced in managing a growing team of statistical methodologists, mentoring and supervising PhD students.

PROFESSIONAL EXPERIENCE

2022 – present

Director, Statistical methodologist.
SARYGA, Statistics & Methodology, France.

- **Team & Project Management**
  - Lead and manage an internal team of 6 statistical methodologists, ensuring alignment with company objectives and project timelines.
  - Oversee day-to-day team operations: task distribution, prioritization, mentoring.
  - Supervise and coordinate external consultants and contractors, ensuring quality, consistency, and timely delivery of outputs.
  - Manage multiple statistical and methodological projects simultaneously, from scoping to final delivery.
  - Actively contribute to collaborative research projects with academic partners, combining hands-on research involvement with cross-stakeholder collaboration.
  - Contribute to the continuous improvement of processes, methodologies, and team organization.
- **Statistical methodology consulting for projects.**
  - Seamless Phase II/III trials with interim analysis, sub-populations testing, enrichment strategies.
  - Design evaluation of complex late phase clinical trials.
  - Prediction of time recruitment and prediction of events.
  - Decision-making frameworks.
  - Bayesian adaptive dose-escalation procedures and oncology Phase I trials dose-optimization in the context of Optimus.
  - Biomarker analysis: descriptive, modeling, cut-offs determination, and

evaluation of the predictive value of a biomarker.
    - Biomarker-based design with population selection.
    - Bayesian analysis and predictive probability of success.
- Research activities related to projects and participation to working groups.
- Statistical trainings.

2016 – 2022 **Principle Research Biostatistician.**
Statistical Methodology Group / Statistical Innovation Hub, Biostatistics & Programming, SANOFI R&D, Chilly-Mazarin, France.

- Statistical support to projects.
    - Designing Bayesian oncology dose-finding trials, discussions with project team, protocol writing, end of cohorts' meetings, and FDA questions.
    - Planning of several enrichment strategies for phases III trials.
    - Identification of predictive covariates in phase III trials databases.
    - Multiplicity issues.
    - Predictive probability of success.
    - Decision-making frameworks and applications, along with methodological advancements and development of internal tools.
- Research activities to develop expertise on identified statistical topics and participation to working groups.
- Supervision of internships and a PhD student on "Bayesian dose regimen assessment in early phase oncology incorporating pharmacokinetics and pharmacodynamics" in collaboration with PK/PD department and academia.
- Statistical trainings to the department.
- Development of several R packages to promote practical use of complex innovative methods by statisticians, supporting development of internal Rshiny applications, and development of R codes.

2014 – 2016 **Post-doctoral in Pharmacometrics.**
UMR 1137, Inserm and Université Paris Diderot, Team 'Biostatistics – Investigation – Pharmacometrics', Paris, France.

Post-doctoral on European project IDEAL (Integrated DEsign and AnaLysis of small population group trials) in WP5 led by Pr. France Mentré.

- Development of a general approach to evaluate the Fisher information matrix in non-linear mixed effect models for both discrete and continuous outcomes.
- Development of an R package (MIXFIM).

2011 – 2014 **PhD.**
INSERM UMRS 1138, Team "Information Sciences to support Personalized Medicine", Paris, France.
SERVIER, Oncology, Biostatistics department, Suresnes, France.

PhD on **early phases dose-finding designs in oncology** for combination of molecules and molecularly targeted agents.

- Development of Bayesian innovative dose-escalation methods.
- Support statisticians for the planning of several Bayesian adaptive dose-finding trials in oncology using model-based approaches.
- Provide trainings and promote the use of innovative model-based methods.

2011 **Eight-month Internship, SERVIER pharmaceutical company, Oncology Department, Suresnes, France.**
INSERM UMRS 717, Saint-Louis Hospital, biostatistics department, Paris, France.

- Comparison of several innovative designs for combination of two agents in phase I oncology dose-finding studies.

2010 **Two-month Internship, Averion international Corp. (Adptiv solutions), Boston, USA.**

- Support on current studies, performed simulations (stochastic curtailment, adaptive design, probability of being in response, non-inferiority tests).

EDUCATION

2011 – 2014 **PhD in Biostatistics, University Paris Diderot.**
INSERM UMRS 1138, Team 22, "Centre de Recherche des Cordeliers", Paris, France.
SERVIER pharmaceutical company, Biostatistics department, Oncology, Suresnes, France.

- PhD topic "Adaptive dose-finding designs in oncology for combination of molecules and molecularly targeted agents".

Grant CIFRE-ANRT N°2011/0900. Supervised by Sarah Zohar.

2008 – 2011 **Engineer's degree (*Diplôme d'ingénieur*) in Statistics, Rennes, France.**
ENSAI - National School for Statistics and Information Analysis.

- Specialty: Biostatistics.

2010 – 2011 **Master of Science in Statistics and Econometrics applied to Research, University of Rennes 1, Rennes, France.**

- Specialty "data processing, prediction and modeling", with honours.

2006 – 2008 **Post-secondary preparatory classes (*classes préparatoires aux grandes écoles*), Lycée Louis-Le-Grand, Paris, France.**

- Major: Mathematics and Physics, Option: Computer science.

SUPERVISING AND TEACHING

Supervision:

- Support PhD supervision between SERVIER pharmaceutical company, Politecnico di Torino University and SARYGA "Incorporation of pre-clinical animal data in a phase I oncology trial".
- PhD co-supervision between Sanofi-Aventis R&D and INSERM UMR 1138-INRIA team HeKA.
  "Bayesian toxicity modeling for dose regimen assessment in early phase oncology trials incorporating pharmacokinetics and pharmacodynamics".
  - Development of a dose-PK/PD-toxicity model to determine the MTD-dose regimen (defined as the combination of schedule and dose), assuming multiple administrations of increasing doses until a fixed dose reduce the risk of cytokine release syndrome.
  - Extension to include other types of toxicities: the joint probability of DLT is modelled under three different approaches to account for potential association between toxicities.

- **Internships** including:
  - "Early phases dose-finding in oncology – support development of an RShiny application".
  - "Bayesian Basket Trial Design with Flexible Information Borrowing across Cancer Types".
  - "Dynamic treatment regimens for dose finding studies in oncology".
  - "Identification of responders' subgroups to a new treatment".
  - "Development of R Shiny applications".
  - "Subgroups identification and Machine Learning data sets visualization".

Teaching and trainings:

- **SARYGA (2022-2024)**
  - Predictive biomarker - Subgroup Identification
  - Quantitative Decision-making frameworks.
  - Statistical testing: accounting for uncertainty when making decisions (for non-statisticians).
  - Hypothesis testing, type I error, power and sample size (for non-statisticians).
- **SANOFI R&D (2016-2022)**
  - Bayesian statistics (for statisticians and non-statisticians).
  - Single-agent adaptive dose-finding designs in oncology (for statisticians and non-statisticians).
  - GSED (Group Sequential enrichment designs).
  - SIDES (Subgroups identification based on Differential Effect Search).
  - Combination adaptive dose-finding designs in oncology.
  - Case studies of Bayesian adaptive trials: Bayesian Hierarchical Model and response adaptive randomization.
  - Oncology Case Studies in Master Protocols.
  - Quantitative go/no-go decision making for single or multiple endpoints.
- **ENSAI - National School for Statistics and Information Analysis (2012-2019)**
  - "Statistical methods for Phase I dose-finding studies in oncology" (Professional seminar)
  - Generalized Linear Models (Tutorial classes and Practical Works)
  - Programming with R (Practical Works)
- **CRC - "Centre de Recherche des Cordeliers" (2013-2014)**
  - "Statistical hypothesis testing for statisticians and non-statisticians" (Courses and Practical Works)
  - "Survival data analysis for statisticians and non-statisticians" (Courses and Practical Works)

REASEARCH ACTIVITIES

Statistical publications:

- **Riviere MK**, Andrillon A, Mozgunov P, Gerard E, Ursino M. *Evaluating early-stage oncology clinical trial designs in the era of project Optimus: a scoping review*, **submitted to Phar Stat.**
- **Riviere MK**, Guhl M, Hadjur H, Tanniou J. *Exact approaches to evaluate decision-making frameworks using single or multiple correlated endpoints: a tutorial*, **submitted to Pharm Stat.**
- Andrillon A, Guhl M, Tanniou J, Dubois F, **Riviere MK**. *Designing Better Trials: Group Sequential Approaches for Subpopulation Testing*, **Ongoing.**
- Hadjur H, Geronimi J, Guilleminot S, Serra A, Daniells L, **Riviere MK**, Saint-Hilary G, Mozgunov P. *Evaluating methods for biomarker cut-off detection: a comparative study in small and unbalanced samples,* **in review in Stat Med.**
- Livieratos A, Goea L, Das V, **Riviere MK**, Chlamydas S, Purkayastha D, Gerhold-Ay A, Schlieker L,

Cardner M, Gaga M, Jansen G. *Non-Oncology Biomarkers in Precision Medicine: A Narrative Review,* **in review in Therapeutic Innovation & Regulatory Science**

- Andrillon A, Micallef S, Ursino M, Mozgunov P, **Riviere MK**. *U-DESPE: a Bayesian Utility-based methodology for dosing regimen optimization in early-phase oncology trials based on Dose-Exposure, Safety, Pharmacodynamics, Efficacy*, **in review in Stat Med.**
- Barnett H, Mozgunov P, Di Stefano F, Skanji D, Guilleminot S, Saint-Hilary G, Guhl M, **Riviere MK**. *Integrating Preclinical Insights for Adaptive Dose Escalation in Phase I Oncology Trials: A Methodological Framework*, **accepted in Pharm Stat.**
- Serra A, Geronimi J, Guilleminot S, Hadjur H, **Riviere MK**, Saint-Hilary G, Mozgunov P. *A novel approach to assess the predictiveness of a continuous biomarker in early phases of drug development*, **Stat Med. 2025**, 44(5).
- Gerard E, Zohar S, Thai HT, Lorenzato C, **Riviere MK***(*co-last author), Ursino M. *Dose-finding Bayesian hierarchical design for toxicity-schedule assessment using pharmacokinetics and pharmacodynamics,* **Biometrics. 2022**, 78(1):300-312.
- Gerard E, Zohar S, Lorenzato C, Ursino M*(*co-last author), **Riviere MK**. *Bayesian joint modeling of a bivariate toxicity for dose-regimens in early phase oncology,* **Stat Med. 2021**, 40(23):5096-5114.
- Aziz M, Kaufmann E, **Riviere MK**. *On Multi-Armed Bandit Designs for Phase I Clinical Trials*, **J Mach Learn Res. 2021**, 22(14):1-38.
- Loingeville F, Nguyen TT, **Riviere MK**, Mentré F. *Robust design in longitudinal studies accounting for parameter and model uncertainties - Application to count data*, **J Biopharm Stat. 2020**, 30(1):31-4.
- Jin J, **Riviere MK**, Luo X, Dong Y. *A Bayesian Basket Trial Design with Flexible Information Borrowing across Cancer Types*, **Stat Med. 2020**, 39(25):3459-3475.
- **Riviere MK**, Yuan Y, Jourdan JH, Dubois F, Zohar S. *Phase I/II Dose-Finding Design for Molecularly Targeted Agent: Plateau Determination using Adaptive Randomization*, **Stat Methods Med Res. 2018**, 27(2):466-479.
- **Riviere MK**, Ueckert S, Mentré F. *An MCMC method for the evaluation of the Fisher information matrix for non-linear mixed effect models*, **Biostatistics. 2016**, 17(4):737-750.
- **Riviere MK**, Jourdan JH, Zohar S. *dfcomb: An R-package for phase I/II trials of drug combinations*, **Comput Methods Programs Biomed. 2016**, 125:117-33.
- **Riviere MK**, Zohar S. *Comments on 'A comparative study of adaptive dose-finding designs for phase I oncology trials of combination therapies'*, **Stat Med. 2016**, 35(3):475-478.
- **Riviere MK**, Le Tourneau C, Paoletti X, Dubois F, Zohar S. *Designs of drug-combination phase I trials in oncology: a systematic review of the literature*, **Annals of Oncology. 2014**, 26(4):669-674.
- **Riviere MK**, Dubois F, Zohar S. *Competing designs for drug combination in phase I dose-finding clinical trials*, **Stat Med. 2015**, 34(1):1-12.
- **Riviere MK**, Dubois F, Zohar S. *Response to 'Comments on Competing designs for drug combination in phase I dose-finding clinical trials' by G. Yin, R. Lin and N. Wages*, **Stat Med. 2015**, 34(1):23-26.
- **Riviere MK**, Yuan Y, Dubois F, Zohar S. *A Bayesian Dose-finding Design for Clinical Trials Combining a Cytotoxic Agent with a Molecularly Targeted Agent*, **JRSS-C. 2015**, 64(1):215–229.
- **Riviere MK**, Yuan Y, Dubois F, Zohar S. *A Bayesian dose-finding design for drug combination clinical trials based on the logistic model*, **Pharm Stat. 2014**, 13(4):247-257.

Clinical publications:

- Riviere P, Penel N, Faure K, Marie G, Najem A, **Riviere MK**, Panaget S. *Effect of medical staff training*

on vaccination coverage in outpatients with cancer: An interventional multicenter before-and-after study, **Vaccine: X**. **2023**, 13:100261.

- Riviere P, Penel N, Faure K, Marie G, Najem A, **Riviere MK**, Panaget S. Vaccination coverage in cancer outpatients: An interventional multicenter before/after study. **J Clin Oncol 2021**, 39(15).
- Simon Y, Marchadier A, **Riviere MK**, Vandamme K, Trouve A, Koenig F, Lezot F, Benhamou CL, Saffar JL, Berdal A, Nefussi JR. *Cephalometric assessment of craniofacial dysmorphologies in relation with Msx2 mutations in mouse*, **Orthod Craniofac Res. 2014**, 17(2):92-105.

Presentations & posters:

- **SnB,** Paris 2025, poster
- **PSI Conference,** London 2025, oral presentations
- **Journées de Biostatistique,** Paris 2024**,** oral presentation
- **Bayes,** Utrecht 2023, oral presentation
- **PSI Conference,** London 2023, oral presentation
- **ISCB - International Society for Clinical Biostatistics**, Milano 2023, poster
- **JSTAR - Journées de STAtistique de Rennes,** Rennes 2023, invited speaker
- **7th Early Phase Adaptive Trials Workshop,** Cambridge 2022, oral presentation
- **Epiclin**, Marseille 2021, oral presentation
- **ISCB - International Society for Clinical Biostatistics**, Lyon 2021, oral presentation
- **ISCB - International Society for Clinical Biostatistics**, Krakow 2020, oral presentation
- **IBC - International Biometric Conference**, Seoul 2020, oral presentation
- **Population Approach Group in Europe – PAGE**, Hersonissos 2015, poster
- **Population Optimum Design of Experiments – PODE**, Cambridge 2015, invited speaker
- **ISCB - International Society for Clinical Biostatistics**, Utrecht 2015, oral presentation
- **Eighth International Workshop on Simulation**, Vienna 2015, oral presentation
- **4th Early Phase Adaptive Trials Workshop,** Charleston 2014, oral presentation
- **ISCB - International Society for Clinical Biostatistics**, Munich 2013, oral presentation
- **International Meeting - Statistical Methods in Biopharmacy**, Paris 2013, oral presentation
- **Days of Biopharmacy and health** ("Journées Biopharmacie et Santé"), Paris 2012, oral presentation
- **Days of Biopharmacy and health** ("Journées Biopharmacie et Santé"), Paris 2011, oral presentation

Participation to the research community:

- Member of Special Interest Groups (SIGs)
- Reviewer for statistical journals
- Member of the scientific committee SnB2022: 9th International Meeting on Statistical Methods in Biopharmacy "When Machine Learning meets Statistics For Drug Development and Evaluation".
- Development of R packages: GSED, SIDES, MIXFIM, dfmta, dfcomb.

LANGUAGES

French: native.
English: fluent.
German: beginner.
Japanese: beginner.

INFORMATION TECHNOLOGIES

Statistics:





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Others:


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