

Lars van der Laan

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EDUCATION

PH.D. STATISTICS

2021-Now

University of Washington, Seattle, Washington, USA

M.A. STATISTICS

2019-2020

UC Berkeley, California, USA

Cumulative GPA: 3.9

Coursework: Probability Theory I (205A), Probability Theory II (205B), Theoretical Statistics I (210A), Theoretical Statistics II (210B), Statistical Computing (243), Data Structures and Algorithms (CS61B), M.A. Capstone Project

B.SC. MATHEMATICS

2016-2019

University of Groningen, Groningen, Netherlands

Cumulative GPA: 3.95 (cum laude)

Coursework (see transcript for a complete list): Functional Analysis, Measure Theory and Integration, Real Analysis, Analysis on Manifolds,

Ordinary and Partial Differential Equations, Numerical Mathematics and Algorithms,

Generalized (mixed) Linear Models, Large Sample Statistics, Probability Theory,

Systems Theory, Dynamical Systems, Metric Differential Geometry

B.SC. PHYSICS

2016-2019

University of Groningen, Groningen, Netherlands

Cumulative GPA: 3.95 (cum laude)

Coursework (see transcript for a complete list): Advanced (Lagrangian and Hamiltonian) Mechanics, Electricity and Magnetism, Statistical Physics and Thermodynamics,

Quantum Physics I, II; Physics Laboratory I, II, III, IV; Electronics and Signal Processing

PUBLICATIONS

Link to google scholar: <https://scholar.google.com/citations?user=0bwP0i4AAAAJ&hl=en>

Peer-Reviewed Publications

1. **Nonparametric estimation of the causal effect of a stochastic threshold-based intervention** - Lars van der Laan, Wenbo Zhang, Peter Gilbert [*Biometrics*, 2022]
2. **Immune correlates analysis of the mRNA-1273 COVID-19 vaccine efficacy clinical trial** - Peter B Gilbert, David C Montefiori, Adrian B McDermott, Youyi Fong, David Benkeser, Weiping Deng, Honghong Zhou, Christopher R Houchens, Karen Martins, Lakshmi Jayashankar, Flora Castellino, Britta Flach, Bob C Lin, Sarah O'Connell, Charlene McDanal, Amanda Eaton, Marcella Sarzotti-Kelsoe, Yiwen Lu, Chenchen Yu, Bhavesh Borate, **Lars WP van der Laan**, Nima S Hejazi, Chuong Huynh, Jacqueline Miller, Hana M El Sahly, Lindsey R Baden, Mira Baron, Luis De La Cruz, Cynthia Gay, Spyros Kalams, Colleen F Kelley, Michele P Andrasik, James G Kublin, Lawrence Corey, Kathleen M Neuzil, Lindsay N Carpp, Rolando Pajon, Dean Follmann, Ruben O Donis, Richard A Koup, Immune Assays Team §, Moderna, Inc. Team §, Coronavirus Vaccine Prevention Network (CoVPN)/Coronavirus Efficacy (COVE) Team §, United States Government (USG)/CoVPN Biostatistics Team § [*Science*, 2022]

3. **Immune Correlates Analysis of a Single Ad26.COVID-19 Vaccine Efficacy Clinical Trial.** Fong Y, McDermott B, Benkeser D, Roels S, Stieh DJ, Vandebosch A, Le Gars M, Van Roey GA, Houchens CR, Martins K, Jayashankar L, Castellino F, Amoa-Awua O, Basappa M, Flach B, Lin BC, Moore C, Naisan M, Naqvi M, Narpala S, O'Connell S, Mueller A, Serebryanny L, Castro M, Wang J, Petropoulos CJ, Luedtke A, Hyrien O, Lu Y, Yu C, Borate B, **van der Laan LWP**, Hejazi NS, Kenny A, Carone M, Wolfe DN, Sadoff J, Gray GE, Grinsztejn B, Goepfert PA, Little SJ, de Sousa LP, Maboia R, Randhawa AK, Andrasik MP, Hendriks J, Truysers C, Struyf F, Schuitemaker H, Douoguih M, Kublin JG, Corey L, Neuzil KM, Carpp LN, Follmann D, Gilbert PB, Koup RA, and Donis RO on behalf of the Immune Assays Team, the Janssen Team, the Coronavirus Vaccine Prevention Network (CoVPN)/ENSEMBLE Team, and the United States Government (USG)/CoVPN Biostatistics Team. [Nature Microbiology, in press.]
4. **Epigenetic Aging Biomarkers and Occupational Exposure to Benzene, Trichloroethylene and Formaldehyd - Lars van der Laan,** Andres Cardenas, Roel Vermeulen, Raj P. Fadadu, Alan E. Hubbard, Rachael V. Phillips, Luoping Zhang, Charles Breeze, Wei Hu, Cuiju Wen, Yongshun Huang, Xiaojiang Tang, Martyn T. Smith, Nathaniel Rothman, Qing Lan; 2020 [*Environment international*, 2021]
5. **Maternal adverse childhood experiences before pregnancy are associated with epigenetic aging changes in their children -** Jamaji C Nwanaji-Enwerem, **Lars Van Der Laan**, Katherine Kogut, Brenda Eskenazi, Nina Holland, Julianna Deardorff, Andres Cardenas [*Aging (Albany NY)*, 2021]
6. **An epigenetic aging analysis of randomized metformin and weight loss interventions in overweight postmenopausal breast cancer survivors -** Jamaji C Nwanaji-Enwerem, Felicia Fei-Lei Chung, **Lars Van der Laan**, Alexei Novoloaca, Cyrille Cuenin, Harriet Johansson, Bernardo Bonanni, Alan E Hubbard, Martyn T Smith, Sheri J Hartman, Andres Cardenas, Dorothy D Sears, Zdenko Herceg [*Clinical Epigenetic*, 2021]
7. **Associations of DNA methylation mortality risk markers with congenital microcephaly from zika virus: a study of brazilian children less than 4 years of age -** Jamaji C Nwanaji-Enwerem, **Lars Van Der Laan**, Elorm F Avakame, Kristan A Scott, Heather H Burris, Andres Cardenas [*Journal of tropical pediatric*, 2021]
8. **Controlled human exposures to diesel exhaust: a human epigenome-wide experiment of target bronchial epithelial cells -** Andres Cardenas, Raj P Fadadu, **Lars Van Der Laan**, Cavin Ward-Caviness, Louis Granger, David Diaz-Sanchez, Robert B Devlin, Marie-Abèle Bind [*Environmental Epigenetics*, 2021]
9. **A longitudinal epigenetic aging and leukocyte analysis of simulated space travel: the Mars-500 mission -** Jamaji C Nwanaji-Enwerem, Uzoji Nwanaji-Enwerem, **Lars Van Der Laan**, Jonathan M Galazka, Nancy S Redeker, Andres Cardenas [*Cell reports*, 2020]

Manuscripts under Review

10. **Higher order targeted maximum likelihood estimation -** Mark van der Laan, Zeyi Wang, **Lars van der Laan** [arXiv, 2021]
11. **Immune Correlates Analysis of the PREVENT-19 COVID-19 Vaccine Efficacy Clinical Trial.** Fong Y, Huang Y, Benkeser D, Carpp LN, Áñez G, Woo W, McGarry A, Dunkle LM, Cho I, Houchens C, Martins K, Jayashankar L, Castellino F,

Petropoulos CJ, Leith A, Haugaard D, Webb B, Lu Y, Yu C, Borate B, **van der Laan LWP**, Hejazi NS, Randhawa AK, Andrasik MP, Kublin JG, Hutter J, Keshtkar-Jahromi M, Beresnev TH, Corey L, Neuzil KM, Follmann D, Ake JA, Gay CL, Kotloff KL, Koup RA, Donis RO, Gilbert PB, the Immune Assays Team, the Coronavirus Vaccine Prevention Network (CoVPN)/2019nCoV-301 Principal Investigators and Study Team, the United States Government (USG)/CoVPN Biostatistics Team. medRxiv preprint doi: <https://doi.org/10.1101/2022.06.22.22276362>. 2022 [doi.org] (Submitted for peer review).

12. **Immune Correlates Analysis of a Phase 3 Trial of the AZD1222 (ChAdOx1 nCoV-19) Vaccine.** Benkeser D, Fong Y, Janes HE, Kelly EJ, Hirsch I, Sproule S, Stanley AM, Maaske J, Villafana T, Houchens CR, Martins K, Jayashankar L, Castellino F, Ayala V, Petropoulos CJ, Leith A, Haugaard D, Webb B, Lu Y, Yu C, Borate B, **van der Laan LWP**, Hejazi NS, Carpp LN, Randhawa A, Andrasik MP, Kublin JG, Isaacs MB, Makhene M, Tong T, Robb ML, Corey L, Neuzil KM, Follmann D, Hoffman C, Falsey AR, Sobieszczyk M, Koup RA, Donis RO, Gilbert PB, on behalf of the AstraZeneca AZD1222 Clinical Study Group, the Immune Assays Team, and the United States Government (USG)/CoVPN Biostatistics Team. (Submitted for peer review)
13. **Comparing and combining antibody assays as correlates of protection against symptomatic COVID-19 in the COVE mRNA-1273 vaccine efficacy clinical trial.** Benkeser D, Montefiori DC, McDermott AB, Fong Y, Janes HE, Deng W, Zhou H, Houchens CR, Martins K, Jayashankar L, Castellino F, Flach B, Lin BC, O'Connell S, McDanal C, Eaton A, Sarzotti-Kelsoe M, Lu Y, Yu C, Borate B, **van der Laan LWP**, Hejazi NS, Kenny A, Carone C, Garver J, Altonen E, Rudge T, Huynh C, Miller J, El Sahly HM, Baden LR, Frey S, Malkin E, Spector SA, Andrasik MP, Kublin JG, Corey L, Neuzil KM, Carpp LN, Pajon R, Follmann D, Donis RO, Koup RA, Gilbert PB, on behalf of the Immune Assays; Moderna, Inc.; Coronavirus Vaccine Prevention Network (CoVPN)/Coronavirus Efficacy (COVE); and United States Government (USG)/CoVPN Biostatistics Teams. (Submitted for peer review).
14. **Antibody Correlates of Protection from Severe RSV Disease in a Vaccine Efficacy Trial** Fong Y, Huang Y, Borate B, **van der Laan LWP**, Zhang W, Carpp LC, Cho I, Glenn G, Fries L, Gottardo R, Gilbert PB. (Submitted for peer review)

Manuscripts in Progress

11. **Improved nonparametric estimation of heterogeneous treatment effects using empirical risk minimization and data-adaptive sieve estimation** - Lars van der Laan, Marco Carone, Alex Luedtke [in progress, expect 2023]
12. **Targeted semiparametric estimation of the relative strain-specific subgroup-stratified vaccine-efficacy in observational studies with cases-only data** - Lars van der Laan, Peter B. Gilbert [in progress, expect 2022]
13. **Causal isotonic calibration** - Lars van der Laan, Ernesto Ulloa, Alex Luedtke [in progress, expect 2022]
14. **General theory of inference for univariate convex functions with causal inference applications** - Lars van der Laan, Alex Luedtke, Marco Carone [in progress, expect 2023]
15. **Superefficient model-robust sieve-based causal inference for parameters linear in the outcome regression in semiparametric models** - Lars van der Laan, Alex Luedtke, Mark van der Laan [in progress, expect 2022]

PROJECT AND RESEARCH EXPERIENCE

PH.D. STUDENT AT UNIVERSITY OF WASHINGTON, WASHINGTON SEATTLE

SEP 2021-NOW

I work on developing theory and methods for causal inference and machine-learning with applications to clinical trials. Projects I have worked on include: Inference for the causal effect of a stochastic threshold-based biomarker with applications to the COVID vaccine trials correlates of risk analysis; Efficient semiparametric estimation and inference of the conditional strain-specific relative vaccine-efficacy in observational settings; Robust and flexible estimation of the conditional treatment effect and relative risk function using machine-learning tools; Parametric working-model-based nonparametric estimation and inference for treatment effect parameters including the conditional relative risk; General theory and methods for estimation and inference for shape-constrained functions (isotonic, convex) in causal inference; A novel robust asymptotically-linear estimator for the average treatment-effect with provably superior finite-sample performance under conditions. Multiple papers are currently in progress.

INTERN AT FRED HUTCHINSON RESEARCH CENTER, WASHINGTON SEATTLE

SEP 2020-SEP 2021

Throughout the Fall of 2020, I worked as a part-time intern at the Fred Hutchinson Research center under the guidance of Professors Peter Gilbert, Marco Carone and Alex Luedtke. As part of the internship, I attended meetings and assisted with the statistical analysis preparation/design of the COVID-19 vaccine trials under Operation Warp-Speed. As part of my project with Professor Gilbert, we developed an efficient estimator for the so-called covariate-adjusted threshold-response function, which aims to capture the causal effect of a continuous treatment when the treatment is set to be above a certain threshold. This extended the previous work of Donovan, Hudgens, Gilbert (2019) where they developed the nonparametric MLE for the unadjusted threshold-response function. The method was applied in the COVID-19 setting to statistically estimate biomarker thresholds that give rise to a specified risk level of disease.

INTERN AT GENENTECH, BIOMEDICAL AFFAIRS - ONCOLOGY

JUNE 2020-SEP-2020

Throughout a 3-month long internship, I worked on a number of projects applying machine learning and targeted learning to biomedical data, specifically survival data from the Flatiron database. The projects include targeted minimum loss-based estimation to estimate the causal effect of treatment on survival. As part of this, I implemented (in R) the One-Step universal targeted minimum loss-based estimator for simultaneously targeting the conditional survival curve (at a discrete time scale) given treatment at any number of specified time points. We also implemented methods that non-parametrically and efficiently estimate simultaneous confidence bands for the conditional survival curves. The implementation was tailored to be computationally efficient for very large datasets and a large time grid. Other projects include using machine learning and causal inference to obtain nonparametric measures of variable importance for prediction algorithms.

GRADUATE STUDENT RESEARCHER/RESEARCH ASSISTANT APPOINTMENT AT UC BERKELEY

DEC 2019-JULY 2021

Working with Professor Andres Cardenas of the Department of Environmental and Health Sciences at UC Berkeley, I worked on a variety of projects regarding epigenetics and the effect of exposures on health. I was tasked with analyzing DNA methylation data and epigenetic clocks/biological age predictors to understand the effect of certain exposures on health. As part of the appointment, I implemented various pipelines in R to streamline the analysis of the epigenetic data and clocks. Much of this work was done in collaboration with scientists at the NCI/NIH.

BACHELOR'S THESIS: RIGGED HILBERT SPACE THEORY FOR HERMITIAN AND QUASI-HERMITIAN OBSERVABLES

2019

Over an 8-week period during my bachelors, I performed research on the rigged Hilbert space formulation of Quantum Mechanics, a formulation that aims to put quantum mechanics on a mathematically rigorous footing. In my thesis, I explored and proved results that extend the theory to quasi-hermitian/quasi-self-adjoint operators and offer a generalization of the nuclear spectral theorem to these cases. The thesis heavily relied on the tools of topology and functional analysis. I concluded the thesis project with a presentation to various students and professors.

LEADERSHIP/TEACHING EXPERIENCE

TUTOR FOR STATISTICS COURSES (UC BERKELEY)

2019

In the Fall semester, I was hired as a tutor for the division of Biostatistics for introductory graduate courses in probability and statistics (STAT 201A/B). This involved giving two-hour tutoring sessions twice a week where I gave mini-lectures and answered any questions students had.

TEACHING ASSISTANT FOR COURSE "MATHEMATICS FOR LIFE SCIENCES" (UNIVERSITY OF GRONINGEN)

2019

I was hired as a teaching assistant for a 3-week intensive course where I held daily 3-hour tutorial sessions. I also assisted in grading homework, midterms, and exams. Due to my class being relatively small with only 10 or so people, I was able to work closely with all the students. This was an invaluable experience which allowed me to work with a very diverse set of students from a variety of backgrounds. Each student was at a different level of mathematical maturity, which required me to be flexible in my assistance and in-tune with their needs.

PRACTICE EXAM COMMITTEE (UNIVERSITY OF GRONINGEN)

2018-2019

I was part of the Practice Exam committee for physics student association. As part of this, I helped develop and proctor practice exams for hundreds of students in the physics and mathematics programs. This involved personally tutoring a large number of students.

PROGRAM COMMITTEE (UNIVERSITY OF GRONINGEN)

2018-2019

I was student chairman of the Program Committee. The committee deals with evaluating courses and teaching for the physics program. This involved helping lead biweekly meetings where we discussed any issues that students brought up during the semester, and addressing all course evaluations at the end of each course.

EXTRACURRICULAR PROJECTS

STATISTICAL SOFTWARE DEVELOPMENT AS PART OF TLVERSE TEAM (<https://github.com/tlverse>, <https://tlverse.org>)

2020-Now

- `tlverse/causalglm` - Designed and developed package and methods implemented
- `tlverse/hal9001` - Extended to general smoothness and shape-constrained constraints, designed formula interface, computational speed up by allowing specification of number of knot points
- `tlverse/tmle3` - Implemented numerous targeted maximum likelihood estimators
- In development:
 - Larsvanderlaan `EPlearner` - a novel robust machine-learning approach for conditional average treatment effect and conditional relative risk estimation

- Larsvanderlaan/autocausalML - Superefficient sieve-based automatic causal machine-learning and inference for conditional treatment effect parameters with robust variance estimation.
- Larsvanderlaan/EPlearner - a novel robust machine-learning approach for conditional average treatment effect and conditional relative risk estimation
- Larsvanderlaan/causalCalibration - Causal isotonic calibration for conditional treatment effect predictors

SKILLS

- Advanced in R, Java, Python, SQL, Latex
- Proficient in C++, MatLab, Mathematica
- Mathematical and Statistical Modeling
- Implementation of Algorithms and Numerical Methods
- Communication and Presentation