



Universiteit
Leiden
The Netherlands

Optimal cardiovascular treatment strategies in kidney disease: casual inference from observational data

Fu, E.L.

Citation

Fu, E. L. (2021, October 28). *Optimal cardiovascular treatment strategies in kidney disease: casual inference from observational data*. Retrieved from <https://hdl.handle.net/1887/3221348>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/3221348>

Note: To cite this publication please use the final published version (if applicable).

Dankwoord (Acknowledgments)

Dit proefschrift had niet tot stand kunnen komen zonder de hulp en steun van een groot aantal mensen. Ik wil daarom graag mijn dank uitspreken aan eenieder die heeft bijgedragen aan dit proefschrift, waarvan een aantal mensen in het bijzonder.

Friedo, als eerstejaars geneeskunde student heb je me al onder je hoede genomen. In de afgelopen vijf jaar heb je me niet alleen veel over onderzoek geleerd, maar ook veel daarbuiten. Ik ben je zeer dankbaar voor de mogelijkheden die je me hebt gegeven om mezelf te ontwikkelen en de vrijheid die je mij gunde bij de invulling van dit promotietraject.

Merel, je begeleiding, steun en alle gezelligheid de afgelopen jaren waren van onschatbare waarde. In het bijzonder dank voor je extra steun tijdens de coronaperiode. Stressvolle situaties wist jij goed te relativëren, waar ik veel aan heb gehad.

Juan, we connected from the very first day and I enjoy our efficient, fast and fun working ethic. Even if separated by a thousand kilometers, we form a great team together. I cherish great memories from our collaboration and I am grateful for the opportunities you have given me in the past years.

Alle collega's van de afdeling Klinische Epidemiologie wil ik bedanken voor de fijne werksfeer. Roommates of C7-82: our chit-chat and your support made me come to work with much joy. Leden van het nierclubje, de afgelopen jaren heb ik veel geleerd tijdens de leerzame journal clubs. Rolf, ik ben je dankbaar voor wat je me allemaal hebt geleerd over causaliteit. Maarten, je deur stond altijd open voor een goed gesprek of waardevol advies, veel dank daarvoor. Tamara, door jou voelde ik me meteen thuis op de afdeling als eerstejaars geneeskunde student.

I would like to thank Catherine and Marie for their great collaboration and valuable input. Catherine, you always took the time to review my work with much care and detail. Marie, thank you for your input on my work and help with the Swedish Renal Registry.

De Raad van Bestuur, de MD/PhD selectiecommissie en in het bijzonder Professor Pancras Hogendoorn wil ik bedanken voor de kans die zij mij hebben gegeven om dit promotietraject te starten.

Marco, my good Italian friend, thank you for teaching me so much about R and routinely collected healthcare data. You made me feel at home at Karolinska and I am grateful for our friendship.

Bas, Fas, Floris, Michael, Niels, Tjerk, dank voor jullie steun de afgelopen jaren. Ik zie jullie gauw in de kliniek!

Layla en Sophie, wat begon als de CAT is uitgemonnd in een ware vriendschap. Ik heb genoten van de taart en etentjes de afgelopen jaren. Sophie, dank dat je mijn paranimf wil zijn op deze bijzondere dag.

Maxim, via de GDT, het SGL en de uni zijn we al 17 jaar goede vrienden. Ik koester bijzondere herinneringen aan onze vriendschap, waaronder Hei- en Boeicop, onze vakanties en de aanval van de Schotse Hooglander. Ik prijs mij gelukkig deze langdurige vriendschap te hebben.

Papa en mama, jullie hebben mij geleerd om hard te werken om iets te bereiken in het leven. Ik realiseer me hoeveel beter de kansen zijn die jullie mij hebben gegeven dan de kansen die jullie zelf hadden. Zonder jullie steun had ik hier niet gestaan. Dit proefschrift is dan ook aan jullie opgedragen.

Victor, quel bonheur om jou als broer te hebben. Ik ben dankbaar dat je altijd voor je kleine broertje klaar staat, of dat nu urenlange telefoongesprekken, broodnodige ontspanmomenten of een reddingsmissie naar Stockholm zijn. Je goede adviezen zijn van onschatbare waarde geweest de afgelopen jaren.

Tot slot mijn lieve Anne. Zonder jou was dit proefschrift niet tot stand gekomen. Dank voor alle liefde en steun de afgelopen jaren, waarbij je me stimuleert om het beste uit mezelf te halen en ook zorgt voor balans in mijn leven. Ik ben gelukkig dat ik deze mooie momenten met jou kan delen en dat je aan mijn zijde staat op deze bijzondere dag.

List of publications

Published articles included in this thesis

1. **Fu EL**, van Diepen M, Xu Y, Trevisan M, Dekker FW, Zoccali C, Jager KJ and Carrero JJ. Pharmacoepidemiology for nephrologists (part 2): potential biases and how to overcome them. *Clin Kidney J.* 2020;14:1317-1326.
2. **Fu EL**, Groenwold RHH, Zoccali C, Jager KJ, van Diepen M and Dekker FW. Merits and caveats of propensity scores to adjust for confounding. *Nephrol Dial Transplant.* 2019;34:1629-1635.
3. **Fu EL**, van Diepen M. Comment on Kwon et al. The Long-term Effects of Metformin on Patients With Type 2 Diabetic Kidney Disease. *Diabetes Care* 2020;43:948-955. *Diabetes Care.* 2020;43:e190.
4. **Fu EL**, Trevisan M, Clase CM, Evans M, Lindholm B, Rotmans JI, van Diepen M, Dekker FW and Carrero JJ. Association of Acute Increases in Plasma Creatinine after Renin-Angiotensin Blockade with Subsequent Outcomes. *Clin J Am Soc Nephrol.* 2019;14:1336-1345.
5. **Fu EL**, Uijl A, Dekker FW, Lund LH, Savarese G and Carrero JJ. Association Between beta-Blocker Use and Mortality/Morbidity in Patients With Heart Failure With Reduced, Midrange, and Preserved Ejection Fraction and Advanced Chronic Kidney Disease. *Circ Heart Fail.* 2020;13:e007180.
6. **Fu EL**, Clase CM, Evans M, Lindholm B, Rotmans JI, Dekker FW, van Diepen M and Carrero JJ. Comparative Effectiveness of Renin-Angiotensin System Inhibitors and Calcium Channel Blockers in Individuals With Advanced CKD: A Nationwide Observational Cohort Study. *Am J Kidney Dis.* 2020;77:719-729.
7. **Fu EL**, Evans M, Clase CM, Tomlinson LA, van Diepen M, Dekker FW and Carrero JJ. Stopping Renin-Angiotensin System Inhibitors in Patients with Advanced CKD and Risk of Adverse Outcomes: A Nationwide Study. *J Am Soc Nephrol.* 2021;32:424-435.

Other publications

8. **Fu EL**, Franko MA, Oberfell A, Dekker FW, Gabrielsen A, Jernberg T and Carrero JJ. High-sensitivity C-reactive protein and the risk of chronic kidney disease progression or acute kidney injury in post-myocardial infarction patients. *Am Heart J.* 2019;216:20-29.
9. **Fu EL**, Janse RJ, de Jong Y, van der Endt VHW, Milders J, van der Willik EM, de Rooij ENM, Dekkers OM, Rotmans JI and van Diepen M. Acute kidney injury and kidney replacement therapy in COVID-19: a systematic review and meta-analysis. *Clin Kidney J.* 2020;13:550-563.
10. Clase CM, **Fu EL**, Joseph M, Beale RCL, Dolovich MB, Jardine MJ, Mann JFE, Pecoits-Filho R, Winkelmayer WC and Carrero JJ. Cloth Masks May Prevent Transmission of COVID-19: An Evidence-Based, Risk-Based Approach. *Ann Intern Med.* 2020;173:489-491.
11. Clase CM, **Fu EL**, Ashur A, Beale RCL, Clase IA, Dolovich MB, Jardine MJ, Joseph M, Kansime G, Mann JFE, Pecoits-Filho R, Winkelmayer WC and Carrero JJ. Forgotten Technology in the COVID-19 Pandemic: Filtration Properties of Cloth and Cloth Masks-A Narrative Review. *Mayo Clin Proc.* 2020;95:2204-2224.

12. Bidulka P, **Fu EL**, Leyrat C, Kalogirou F, McAllister KSL, Kingdon EJ, Mansfield KE, Iwagami M, Smeeth L, Clase CM, Bhaskaran K, van Diepen M, Carrero JJ, Nitsch D and Tomlinson LA. Stopping renin-angiotensin system blockers after acute kidney injury and risk of adverse outcomes: parallel population-based cohort studies in English and Swedish routine care. *BMC Med.* 2020;18:195.
13. Trevisan M, **Fu EL**, Xu Y, Jager KJ, Zoccali C, Dekker FW and Carrero JJ. Pharmacoepidemiology for nephrologists (part 1): concept, applications and considerations for study design. *Clin Kidney J.* 2020;14:1307-1316.
14. Trevisan M, **Fu EL**, Szummer K, Norhammar A, Lundman P, Wanner C, Sjolander A, Jernberg T and Carrero JJ. Glucagon-like peptide-1 receptor agonists and the risk of cardiovascular events in diabetes patients surviving an acute myocardial infarction. *Eur Heart J Cardiovasc Pharmacother.* 2021;7:104-111.
15. de Jong Y, **Fu EL**, van Diepen M, Trevisan M, Szummer K, Dekker FW, Carrero JJ and Ocak G. Validation of risk scores for ischaemic stroke in atrial fibrillation across the spectrum of kidney function. *Eur Heart J.* 2021;42:1476-1485.
16. Windahl KM, Faxén Irving G, Almquist T, Lidén MK, Stenvinkel P, Chesnaye NC, Drechsler C, Szymczak M, Krajewska M, **Fu EL**, Torino C, Porto G, Roderick PJ, Caskey FJ, Wanner C, Dekker FW, Jager KJ and Evans M. Patient-reported measures and life-style are associated with deterioration in nutritional status in CKD stage 4-5: the EQUAL cohort study. *J Ren Nutr.* 2021.
17. Zhang JLH, Appelman-Dijkstra N, **Fu EL**, Rotmans JI and Schepers A. Practice variation in treatment of patients with renal hyperparathyroidism: a survey-based study in the Netherlands. *BMC Nephrol.* 2021;22:150.
18. Trevisan M, **Fu EL**, Xu Y, Savarese G, Dekker FW, Lund LH, Sjolander A and Carrero JJ. Stopping mineralocorticoid receptor antagonists after hyperkalemia is associated with lower recurrence of hyperkalemia but greater risk of cardiovascular events and death. *Eur J of Heart Fail.* 2021.
19. Clase CM, **Fu EL**, Jardine M, Mann JFE, Carrero JJ. Cloth Masks May Prevent Transmission of COVID-19. *Ann Intern Med.* 2021;174:580.
20. Chesnaye NC, Stel VS, Tripepi G, Dekker FW, **Fu EL**, Zoccali C, Jager KJ. An introduction to inverse probability of treatment weighting in observational research. *Clin Kidney J.* 2021.

Submitted

21. **Fu EL**, Evans M, Carrero JJ, Putter H, Clase CM, Caskey FJ, Szymczak M, Torino C, Chesnaye NC, Jager KJ, Wanner C, Dekker FW and Van Diepen M. When to initiate dialysis to reduce mortality and cardiovascular events in advanced chronic kidney disease: nationwide cohort study.
22. **Fu EL**, Clase CM, Janse RJ, Lindholm B, Dekker FW, Jardine MJ, Carrero JJ. Comparative effectiveness of SGLT2i versus GLP1-RA on cardiovascular outcomes in routine clinical practice.
23. **Fu EL**, Trevisan M, Lanka V, Clase CM, Xu Y, Van Diepen M, Dekker FW, Jardine MJ, Carrero JJ. Comparative effectiveness of SGLT2i versus DPP4i on cardiovascular, kidney and hyperkalemia outcomes in individuals from routine clinical practice: observational cohort study.
24. Xu Y, **Fu EL**, Trevisan M, Jernberg T, Sjolander A, Clase CM and Carrero JJ. Stopping renin-angiotensin system inhibitors after hyperkalemia and risk of adverse outcomes.

PhD Portfolio

Name PhD student:	E.L. Fu
LUMC department:	Clinical Epidemiology
PhD period:	September 2018 - August 2021
Title thesis:	Optimal cardiovascular treatment strategies in kidney disease – causal inference from observational data
Promotors:	Prof. dr. F.W. Dekker Prof. dr. J.J. Carrero
Copromotor:	Dr. M. van Diepen

PhD Training	Year	Hours
Courses		
Survival analysis	2017	42
Regression analysis	2018	42
Causal inference	2018	84
PhD Introductory Meeting	2019	5
Basic Methods and Reasoning in Biostatistics	2019	42
BROK Course	2019	42
Meta analysis	2019	42
Advanced survival analysis	2019	40
Analysis of repeated measurements	2019	42
ESP48 Causal inference Rotterdam	2019	40
Prediction modelling and intervention research	2019	84
Winterschool Dutch Kidney Foundation	2020	42
Causal inference for multiple time-point (longitudinal) exposures (SER workshop)	2020	4
An introduction to transporting treatment effects from randomized clinical trials to clinical practice (SER workshop)	2021	4
Regression discontinuity designs	2021	14
Instrumental variables	2021	14
Statistical aspects of clinical trials	2021	42

PhD Training	Year	Hours
Congress attendance and poster or oral presentations		
Poster presentation ERA-EDTA congress	2018	8
Oral presentation Dutch Nephrology Days	2019	12
Oral presentation & 2 poster presentations ERA-EDTA congress	2019	28
Oral presentation & poster presentation ERA-EDTA congress	2020	30
Oral presentation ESC congress	2020	12
Oral presentation & moderated poster presentation Dutch Nephrology Days	2020	20
Oral presentation & moderated poster presentation ERA-EDTA congress	2021	20
Poster presentation Dutch Epidemiological Conference	2021	8
Teaching activities		
Academic and Scientific Training Year 1 (BSc Medicine)	2018	6
CRiP - Advanced Concepts in Epidemiology (MSc Biomedical Sciences)	2018	3
Academic and Scientific Training Year 1 (BSc Medicine)	2019	3
Academic and Scientific Training Year 2 (BSc Medicine)	2019	6
Design and Analysis of Biomedical Studies (BSc Biomedical Sciences)	2019	3
Critical Appraisal of a Topic (BSc Medicine)	2019	28
Lecture Series (Honours College Medicine)	2019	8
Lecture Series (Honours College Medicine)	2020	8
Medicine in Numbers (Pre-University College Leiden), course coordinator	2020	66
Epidemiological Data Analysis and Critical Review of Scientific Literature (Honours College Medicine)	2020	34
Academic and Scientific Training Year 1 (BSc Medicine)	2021	19
Critical Appraisal of a Topic (BSc Medicine)	2021	28
Academic and Scientific Training Year 3 (BSc Medicine)	2021	3

PhD Training	Year	Hours
Awards and prizes		
Face of Science, Royal Academy of Sciences	2019	
ERA-EDTA 2019 Travel Grant	2019	
ERA-EDTA 2019 Best Abstract presented by Young Author	2019	
ERA-EDTA 2020 Social Media Selection Award for Best Abstract	2020	
ERA-EDTA 2021 Travel Grant	2021	
ERA-EDTA 2021 Best Abstract presented by Young Author	2021	
ERA-EDTA 2021 Best Abstract of Congress	2021	
Personal grants		
Personal MD/PhD Grant, Board of Directors LUMC	2018	
Eurolife Scholarship for Early Career Researchers	2018	
Dutch Kidney Foundation Kolff PhD Fellow Abroad Grant	2018	

Curriculum vitae

Edouard Liang Fu was born on the 4th of February 1997 in Leiden, The Netherlands. In 2015 he obtained his gymnasium diploma cum laude at the Stedelijk Gymnasium Leiden and started medical school at Leiden University. As a first year medical student he developed an early interest in clinical research, and therefore started training under supervision of Prof. dr. F.W. Dekker at the department of Clinical Epidemiology. A year later he was given the opportunity to formally continue his research as part of the MD/PhD track, preparing him to combine a PhD with his medical studies. He received further training in epidemiology and statistics by following the clinical epidemiology track of the Honours College Medicine. Besides his research, Edouard was an active member of the Dutch Surgical Society for Medical Students Leiden, of which he later became a board member. Furthermore, he taught dissection courses, was year representative and participated in the Leiden Oxford Transplantation Summer School. In 2018 he received a highly competitive MD/PhD grant from the LUMC Board of Directors, allowing him to do 3-year fulltime PhD research.

After obtaining both his bachelor's degree in medicine and Honours College degree cum laude, Edouard started as a PhD student at the department of Clinical Epidemiology, under supervision of Prof. dr. F.W. Dekker and Dr. M. van Diepen. He spent part of his PhD abroad in Sweden at the department of Medical Epidemiology and Biostatistics, Karolinska Institutet, under supervision of Prof. dr. J.J. Carrero. This was supported by a grant from the Dutch Kidney Foundation and a Eurolife scholarship.

During his PhD, he has addressed clinically important questions in the fields of cardiology, nephrology and internal medicine, and has published in journals such as the Journal of the American Society of Nephrology, Annals of Internal Medicine and the European Heart Journal. He also presented his research at multiple national and international congresses where he was awarded with various prizes. Furthermore, the Royal Dutch Academy of Arts and Sciences (KNAW) gave him the opportunity to write about his research for the lay public when he was elected as a Face of Science in 2019. With the completion of his PhD he also has completed his training as clinical epidemiologist (Epidemiologist B).

Before finishing his training to become a medical doctor, Edouard will spend two years as postdoctoral researcher at the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital and Harvard Medical School. In addition, he will serve as an editorial fellow at the leading kidney journal JASN.