Curriculum vitae Siv Jönsson (PhD)

Contact

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Education

Sep 1984 – June 1988 Uppsala University, Uppsala, Sweden
Pharmacy program
M.Sc awarded by the Department of Biopharmaceutics & Pharmacokinetics
M.Sc project title: Effect of apomorphine in conscious rats during sulpiride infusion

Feb 1998 – May 2004 Uppsala University, Uppsala, Sweden
PhD student at Division of Pharmacokinetics and Drug Therapy
Dissertation date: May 19, 2004
Thesis title: Estimation of Dosing Strategies for Individualisation

15 April 2020 Uppsala University, Sweden
Docent* in Pharmacometrics
*Docent is an academic title

Employment

Jun 1988 – Aug 1989, Swedish Poison Information Centre, Apoteksbolaget, Stockholm, Sweden
Pharmacist

Sep 1989 – Dec 1990, Dep of Biopharmaceutics, Kabi Pharma, Stockholm, Sweden
Pharmacist/pharmacokineticist

Feb 1991 – Feb 1993, Dep of Pharmacokinetics, Kabi Pharmacia, Stockholm and Uppsala, Sweden
Pharmacokineticist

Feb 1993 – Jan 1998, Preclinical and Clinical Evaluation, Medical Products Agency, Uppsala, Sweden
Pharmacokinetic assessor

Feb 1998 – June 2004, Division of Pharmacokinetics and Drug Therapy, Faculty of Pharmacy, Uppsala University, Uppsala, Sweden
PhD student

Apr 2002 – Aug 2002, Division of Pharmacokinetics and Drug Therapy, Faculty of Pharmacy, Uppsala University, Uppsala, Sweden
Lecturer

Jul 2004 – Feb 2006, Division of Pharmacokinetics and Drug Therapy, Faculty of Pharmacy, Uppsala University, Uppsala, Sweden
Senior lecturer (temporary position)

Apr 2006 – Jan 2007, Clinical Pharmacology, AstraZeneca R&D Södertälje Södertälje, Sweden
Senior research scientist/Pharmacometrician

	Feb 2007 – Aug 2010, Department of Preclinical and Clinical Assessment 2, Medical Products Agency Pharmacokinetic assessor **Sep 2010 – Jun 2011, Department of Efficacy and Safety 1, Medical Products Agency** Pharmacokinetic assessor **July 2011 – August 2020, Department of Pharmaceutical Biosciences, Uppsala University** **Present positions:** **Sep 2020 – , Department of Pharmacy, Uppsala University** Researcher **Nov 2019 - , Pharmetheus AB** Senior MIDD Consultant
Skills	Good to excellent knowledge of the NONMEM data analysis program. Good knowledge in Microsoft Office programs, *i.e.* Excel, Word and Powerpoint. Basic knowledge in R graphics and scripting.
Teaching & Supervision	Participation in teaching during my time as a PhD student (appr. 40 – 60 hours per semester) at the Division of Pharmacokinetics and Drug Therapy. Lecturer (adjunkt) at the Division of Pharmacokinetics and Drug Therapy with responsibility for the B-level pharmacokinetic course (Farmakokinetik 5,5 p, B) spring semester 2002. Senior lecturer (universitetslektor) at the Division of Pharmacokinetics and Drug Therapy with responsibility for Clinical pharmacokinetics and pharmacodynamics (B/C-level, 5p) and Pharmacokinetics (C-level, 5 p) from fall 2004 until 2006. Supervisor for Katalin Matolcsi (2000) and Anders Lanner (2002) during their bachelor degree projects in pharmacokinetics (fördjupningstermin i farmakokinetik C-nivå) at the Division of Pharmacokinetics and Drug Therapy. Supervisor for Robin Svensson (2013) and Björn Clausen (2015) during their master degree projects in pharmacokinetics at the Division of Pharmacokinetics and Drug Therapy. Assistant supervisor in two PhD projects at the Division of Pharmacokinetics and Drug Therapy for Maria Kjellsson and Radojka Savic, both receiving the doctoral titles in 2008.

	Assistant supervisor in two PhD projects at the Department of Pharmaceutical Biosciences for Ari Brekkan (since spring 2014), Joao Abrantes (since spring 2015). Assistant supervisor in three PhD projects at the Department of Pharmacy for Maria Swartling (since spring 2018), Eman Ibrahim (since spring 2019) and (since spring 2021).
Professional	*Consultancy* Since 2012 I have been doing consultancy concerning pharmacometrics, pharmacokinetics and pharmacodynamics to academia, pharmaceutical industry and regulatory authorities. *Teaching/Supervision* In 2001, I was functioning as tutor on the NONMEM Basic Course, given by Professors Stuart Beal and Lewis Sheiner. During my stay at the Division of Pharmacokinetics and Drug Therapy, I have been involved in the planning, development and performance of three PhD-student courses. The courses were 3-4 days long and covered 1) Clinical Drug Development including Trial Simulation (1998), 2) Basic Population Modelling (2000) and, 3) NONMEM related programming in Perl and S-Plus (2001). In 2002, Dr Niclas Jonsson and I together gave the course Basic Population Modelling at Helsinki University for an audience consisting of researchers within the pharmaceutical area in Finland. In spring 2005, Dr Ulrika Simonsson and I together gave the course Basic Population Modelling at the University of Cape Town, South Africa, for a group of participants with pharmaceutical and statistical background. Since spring 2005, I was involved in a PhD project (Samuel Fanta) in collaboration with the University of Helsinki. My contribution in the project was to teach out the basics of population analysis and to supervise during the NONMEM analysis of cyclosporine A data. Samuel Fanta defended his thesis in 2009. *Research collaborations* From spring 2005 to spring 2006, I was involved in research collaboration between Uppsala University and University of Cape Town, funded by SIDA. My input to project was teaching activities (see above) and also practical supervision for Alistair Davidse during population modelling. From April 2014 to October 2016, I was involved in the European IMI project DDMoRe (http://www.ddmore.eu/) and specifically working with the qualification of models uploaded to the Model Repository. From 1 January 2016 to December 2021, I was involved in the European Horizon 2020 project Ubiquitous Pharmacogenomics (http://upgx.eu/) specifically working with developing pharmacometric models integrating PGx information with other sources of variability to predict expected effect for genetic variant groups on various outcomes.

Senior expert
Was appointed as senior expert at the Medical Products Agency in February 2011.

Expert at half-time controls
Elisabet Nielsen, 24 November 2006: Evaluation of dosing strategies for antimicrobial agents based on PK/PD principles. Department of Pharmaceutical Biosciences, Uppsala University

Ebba Bergman, 31 March 2008: Department of Pharmacy, Uppsala University

Paul Baverel, 28 May 2009: Evaluation of nonparametric estimation methods in NONMEM VI. Applications on real datasets and novel methodologies. Department of Pharmaceutical Biosciences, Uppsala University.

Helena Thörn, 9 October 2009: The importance of first-pass gut wall metabolism of drugs as a determinant of bioavailability and source for inter-individual variability. Department of Pharmacy, Uppsala University

Anna-Karin Hamberg, 21 October 2011: Development, evaluation and application of model based dose individualisation of warfarin in adults and children, Department of Medical Sciences, Uppsala University

Marina Senek, 15 April 2016: New approaches for levodopa treatments in Parkinson's disease. Department of Neurosciences and Department of Pharmaceutical Biosciences, Uppsala University.

Emma Eckernäs, 9 December 2021: Pharmacokinetic/pharmacodynamic modelling and simulation of N,N-dimethyltryptamine. Unit for Pharmacokinetics and Drug Metabolism, Department of Pharmacology, Sahlgrenska Academy at University of Gothenburg.

Betygsnämnd/Defense committee
Emma Boström, 20 April 2007: Pharmacokinetics and pharmacodynamics of oxycodone and morphine with emphasis on blood-brain barrier transport. Department of Pharmaceutical Biosciences, Uppsala University.

Helena Thörn, 24 February 2012: First-pass intestinal metabolism of drugs. Experiences from *in vitro, in vivo* and simulations studies. Department of Pharmacy, Uppsala University.

Astrid Oosten, 9 December 2017: Outcomes of treatment with opioids - the role of clinical, pharmacokinetic and genetic factors
Erasmus MC, Erasmus University Rotterdam, Netherlands

Opponent/External examiner of Doctor of Philosophy thesis
Sabariah Noor Harun, September 2016: Disease progression in paediatric cystic fibrosis patients.
School of Pharmacy, University of Queensland, Australia

	Elisabet Størset, 24 March 2017: Optimizing tacrolimus treatment in kidney transplant recipients Section of Nephrology, Department of Transplant Medicine, Oslo University Hospital Rikshospitalet, Faculty of Medicine, University of Oslo, Norway
Presentations	**Invited lectures** **Estimation of optimal dosing strategies derived from population PK/PD models** Rosenö-meeting, Stockholm, 2001 **Ny metod för optimal dosering (New method for optimal dosing)** Temadag: Individuell dosering av läkemedel (Apotekarsocieteten), Stockholm, 2005 **Dosing strategies based on PK/PD information: A rational basis for balancing efficacy and safety** Rosenö-meeting, Stockholm, 2006 **Modelling and simulation (M&S) from a regulatory point of view** Pharmacokinetics UK, Edinburgh, UK, 2007. **Regulatory vision of paediatric applications** EMEA workshop on modelling in paediatric medicines, London, UK, 2008. **A European regulatory perspective: influence of model-based drug development on regulatory decision making** The IXth World Conference on Clinical Pharmacology and Therapeutics, Quebec, Canada, 2008. **Regulatory Perspective on Modelling and Simulation of Pharmacokinetic and Pharmacodynamic Data** Translational Modelling and Simulation Forum, Marcus Evans, Stockholm, Sweden, 2008. **The Role of Modelling and Simulation in European Drug Regulatory Decisions** The 5th BioSim Conference, Copenhagen, 2009 **Approaches towards implementing modeling in drug approval procedures** BioSim one-day workshop: Benefits of biosimulation in drug development. The impact on regulatory approval, , Lund, Sweden 2010 **Exposure-response and disease modelling from a regulatory view** 16th World Congress of Basic and Clinical Pharmacology, Copenhagen, Denmark, 2010 **Modeling of time to acute rejections in paediatric renal transplant recipients** 14th International Congress of Therapeutic Drug Monitoring & Clinical Toxicology, Rotterdam, October 2015

	Population modelling in haemophilia and potential usage in the clinic 13th Congress of the European Association for Clinical Pharmacology and Therapeutics (EACPT), Prague, June 24-27, 2017
Awards	**The Rosenön Award, 2004** (https://www.apotekarsocieteten.se/stipendier-och-priser/vara-priser/the-rosenon-award/)
Boards/ Committees	**Board member**: Department of Pharmaceutical Biosciences, Uppsala University 2013-2018 **Chair for the Scientific Organising Committee for the Population Approach Group in Europe (PAGE)**: PAGE conference Crete 2015, Lisbon 2016, Budapest 2017, Montreux 2018, Stockholm 2019, Ljubljana 2020 (postponed) **Board member**: International Society of Pharmacometrics 2018-2020 **Organizing committee**: The 13th Symposium on Pharmacokinetics and Drug Metabolism: Oligonucleotide-based therapeutics–New challenges in evaluation pharmacokinetic, pharmacodynamics and safety properties; Gothenburg 2015 **Board Member**: Swedish Academy of Pharmaceutical Sciences, Section for Pharmacokinetics and Drug Metabolism 2012-2016
Publications	**Original research articles** 1. Palminger Hallén I, Jönsson S, Karlsson MO, Oskarsson A. Kinetic observations in neonatal mice exposed to lead via milk. Toxicol Appl Pharmacol. 140:13-8 (1996). 2. Palminger Hallén I, Jönsson S, Karlsson MO, Oskarsson A. Toxicokinetics of lead in lactating and nonlactating mice. Toxicology and Applied Pharmacology. 136:342-7 (1996). 3. Sundberg J, Jönsson S, Karlsson MO, Hallén IP, Oskarsson A. Kinetics of methylmercury and inorganic mercury in lactating and nonlactating mice. Toxicol Appl Pharmacol. 151:319-29 (1998). 4. Sundberg J, Jönsson S, Karlsson MO, Oskarsson A. Lactational exposure and neonatal kinetics of methylmercury and inorganic mercury in mice. Toxicol Appl Pharmacol. 154:160-9 (1999). 5. Jönsson S, Karlsson MO. A rational approach for selection of optimal covariate-based dosing strategies. Clin Pharmacol Ther. 73:7-19 (2003). 6. Kjellsson MC, Jönsson S, Karlsson MO. The Back-Step Method - Method for Obtaining Unbiased Population Parameter Estimates for Ordered Categorical Data. AAPS J. 6(3):article 19 (2004). 7. Jönsson S, Cheng Y-F, Edenius C, Lees KR, Odergren T and Karlsson

MO. Population pharmacokinetic modelling and estimation of dosing strategy for NXY-059, a nitrone being developed for stroke. Clin Pharmacokinet 44(8):863-78 (2005)

8. Jönsson S, Kjellsson MC and Karlsson MO. Estimating bias in population parameters for some models for repeated measures ordinal data using NONMEM and NLMIXED. J of Pharmacokinet Pharmacodyn. 31(4):299-320 (2004)

9. Jönsson S and Karlsson MO. Estimation of dosing strategies aiming at maximizing utility or responder probability, using oxybutynin as an example drug. Eur J Pharm Sci 25(1):123-32 (2005)

10. Fanta S, Jönsson S, Backman JT, Karlsson MO, Hoppu K. Developmental pharmacokinetics of ciclosporin--a population pharmacokinetic study in paediatric renal transplant candidates. Br J Clin Pharmacol 64(6):772-84 (2007)

11. Fanta S, Niemi M, Jönsson S, Karlsson MO, Holmberg C, Neuvonen PJ, Hoppu K, Backman JT. Pharmacogenetics of cyclosporine in children suggests an age-dependent influence of ABCB1 polymorphisms. Pharmacogenet Genomics 18(2):77-90 (2008)

12. Viberg A, Cars O, Karlsson MO, Jönsson S. Estimation of cefuroxime dosage using pharmacodynamic targets, MIC distributions, and minimization of a risk function. J Clin Pharmacol. 48(11):1270-81 (2008)

13. Björkman S, Folkesson A, Jönsson S. Pharmacokinetics and dose requirements of factor VIII over the age range 3-74 years. Eur J Clin Pharmacol. 65(10):989-98 (2009)

14. Fanta S, Jönsson S, Karlsson MO, Niemi M, Holmberg C, Hoppu K, Backman JT. Long-term changes in cyclosporine pharmacokinetics after renal transplantation in children: evidence for saturable presystemic metabolism and effect of NR1I2 polymorphism. J Clin Pharmacol. 50(5):581-97. (2010)

15. Jönsson S, Davidse A, Wilkins J, Van der Walt JS, Simonsson US, Karlsson MO, Smith P, McIlleron H. Population pharmacokinetics of ethambutol in South African tuberculosis patients. Antimicrob Agents Chemother. 55(9):4230-7. (2011)

16. Jönsson S, Henningsson A, Edholm M, Salmonson T. Role of modelling and simulation: a European regulatory perspective. Clin Pharmacokinet. 51(2):69-76 (2012)

17. Kågedal M, Cselényi Z, Nyberg S, MD, Jönsson S, Raboisson P, Stenkrona P, Hooker AC, Karlsson MO. Non linear mixed effects modelling of positron emission tomography data for simultaneous estimation of radioligand kinetics and occupancy in healthy volunteers. NeuroImage. 61:849–856 (2012)

18. Frobel AK, Karlsson MO, Backman JT, Hoppu K, Qvist E, Seikku P, , Jalanko H, Holmberg C, Keizer RJ, Fanta S, Jönsson S. A Time-to-Event Model for Acute Rejections in Paediatric Renal Transplant Recipients Treated with Ciclosporin A. Br J Clin Pharmacol. 76(4):603-15 (2013)

19. Jönsson S, Simonsson US, Miller R, Karlsson MO. Population pharmacokinetics of edoxaban and its main metabolite in a dedicated renal impairment study. J Clin Pharmacol. 55(11):1268-79 (2015)

20. Niebecker R, Jönsson S, Karlsson MO, Miller R, Nyberg J, Krekels EH, Simonsson US. Population pharmacokinetics of edoxaban in patients with symptomatic deep-vein thrombosis and/or pulmonary embolism-the Hokusai-VTE phase 3 study. Br J Clin Pharmacol. 80(6):1374-87 (2015)

21. Oosten AW, Abrantes JA, Jönsson S, de Bruijn P, Kuip EJ, Falcão A, van der Rijt CC, Mathijssen RH. Treatment with subcutaneous and transdermal fentanyl: results from a population pharmacokinetic study in cancer patients. Eur J Clin Pharmacol. 72(4):459-67 (2016)

22. Brekkan A, Berntorp E, Jensen K, Nielsen EI, Jönsson S. Population pharmacokinetics of plasma-derived factor IX: procedures for dose individualization. J Thromb Haemost. 14(4):724-732 (2016)

23. Acharya C, Hooker AC, Türkyılmaz GY, Jönsson S, Karlsson MO. A diagnostic tool for population models using non-compartmental analysis: The ncappc package for R. Comput Methods Programs Biomed. 127:83-93 (2016)

24. Krekels EH, Niebecker R, Karlsson MO, Miller R, Shimizu T, Karlsson KE, Ruff CT, Simonsson US, Jönsson S. Population Pharmacokinetics of Edoxaban in Patients with Non-Valvular Atrial Fibrillation in the ENGAGE AF-TIMI 48 Study, a Phase III Clinical Trial. Clin Pharmacokinet. 55:1079–1090 (2016)

25. Nyberg J, Karlsson KE, Jönsson S, Yin OQP, Miller R, Karlsson MO, Simonsson USH. Edoxaban Exposure-Response Analysis and Clinical Utility Index Assessment in Patients With Symptomatic Deep-Vein Thrombosis or Pulmonary Embolism. CPT Pharmacometrics Syst Pharmacol. 5:222–232 (2016)

26. Lindqvist A, Jönsson S, Hammarlund-Udenaes M. Exploring Factors Causing Low Brain Penetration of the Opioid Peptide DAMGO through Experimental Methods and Modeling. Mol Pharm. 13(4):1258-66 (2016)

27. Oosten AW, Abrantes JA, Jonsson S, Matic M, van Schaik RH, de Bruijn P, van der Rijt CC, Mathijssen RH. A prospective population pharmacokinetic study on morphine metabolism in cancer patients. Clin Pharmacokinet. 56(7):733-746. (2017)

28. van der Wouden CH, Cambon-Thomsen A, Cecchin E, Cheung KC, Dávila-Fajardo CL, Deneer VH, Dolžan V, Ingelman-Sundberg M, Jönsson S, Karlsson MO, Kriek M, Mitropoulou C, Patrinos GP, Pirmohamed M, Samwald M, Schaeffeler E, Schwab M, Steinberger D, Stingl J, Sunder-Plassmann G, Toffoli G, Turner RM, van Rhenen MH, Swen JJ, Guchelaar HJ; Ubiquitous Pharmacogenomics Consortium. Implementing Pharmacogenomics in Europe: Design and Implementation Strategy of the Ubiquitous Pharmacogenomics Consortium. Clin Pharmacol Ther. 101(3):341-358 (2017)

29. Abrantes JA, Nielsen EI, Korth-Bradley J, Harnisch L, Jönsson S. Elucidation of factor VIII activity pharmacokinetics: A pooled population analysis in patients with hemophilia A treated with moroctocog alfa. Clin Pharmacol Ther. 102(6):977-988 (2017)

30. Mangles S, Rea C, Madan B, Nielsen EI, Jönsson S, Needham J, Collins PW, Rangarajan S. Real life experiences of a PK dosing study-Challenges and lessons learned. Haemophilia. 24(3):e145-e148 (2018)

31. Novakovic AM, Thorsted A, Schindler E, Jönsson S, Munafo A, Karlsson MO. Pharmacometric analysis of the relationship between absolute lymphocyte count and expanded disability status scale and relapse rate, efficacy end points, in multiple sclerosis trials. J Clin Pharmacol. 58(10):1284-1294 (2018)

32. Brekkan A, Jönsson S, Karlsson MO, Hooker AC. Reduced and optimized trial designs for drugs described by a target mediated drug disposition model. J Pharmacokinet Pharmacodyn. 45(4):637-647 (2018)

33. Abrantes JA, Jönsson S, Karlsson MO, Nielsen EI. Handling interoccasion variability in model-based dose individualization using therapeutic drug monitoring data. Br J Clin Pharmacol. 85(6):1326-1336 (2019)

34. Brekkan A, Degerman J, Jonsson S. Model-based evaluation of low dose factor VIII prophylaxis in haemophilia A. Haemophilia. 25(3):408-415 (2019)

35. Abrantes JA, Solms A, Garmann D, Nielsen EI, Jönsson S, Karlsson MO. Relationship between factor VIII activity, bleeds and individual characteristics in severe hemophilia A patients. Haematologica. 105(5):1443-1453 (2020)

36. Abrantes JA, Solms A, Garmann D, Nielsen EI, Jönsson S, Karlsson MO. Bayesian Forecasting Utilizing Bleeding Information to Support Dose Individualization of Factor VIII. CPT Pharmacometrics Syst Pharmacol 8(12):894-903 (2019)

37. Brekkan A, Jonsson S, Karlsson MO, Plan EL. Handling Underlying Discrete Variables with Bivariate Mixed Hidden Markov Models in

NONMEM. J Pharmacokinet Pharmacodyn. 46(6):591-604 (2019)

38. van der Wouden CH, Böhringer S, Cecchin E, Cheung KC, Dávila-Fajardo CL, Deneer VHM, Dolžan V, Ingelman-Sundberg M, Jönsson S, Karlsson MO, Kriek M, Mitropoulou C, Patrinos GP, Pirmohamed M, Rial-Sebbag E, Samwald M, Schwab M, Steinberger D, Stingl J, Sunder-Plassmann G, Toffoli G, Turner RM, van Rhenen MH, van Zwet E, Swen JJ, Guchelaar HJ; Ubiquitous Pharmacogenomics Consortium. Generating evidence for precision medicine: considerations made by the Ubiquitous Pharmacogenomics Consortium when designing and operationalizing the PREPARE study. Pharmacogenet Genomics. 30(6):131-144 (2020)

39. Chen C, Jönsson S, Yang S, Plan EL, Karlsson MO. Detecting placebo and drug effects on Parkinson's disease symptoms by longitudinal item-score models. CPT Pharmacometrics Syst Pharmacol. 10(4):309-317 (2021)

40. Minichmayr IK, Karlsson MO, Jönsson S. Pharmacometrics-Based Considerations for the Design of a Pharmacogenomic Clinical Trial Assessing Irinotecan Safety. Pharm Res. 38(4):593-605 (2021)

41. Swartling M, Smekal AK, Furebring M, Lipcsey M, Jönsson S, Nielsen EI. Population pharmacokinetics of cefotaxime in intensive care patients. Eur J Clin Pharmacol. 78(2):251-258 (2022)

42. Grisic A-M, Xiong W, Tanneau L, Jönsson S, Friberg LE, Karlsson MO, Dai H, Zheng J, Girard P, Khandelwal A. Model-Based Characterization of the Bidirectional Interaction Between Pharmacokinetics and Tumor Growth Dynamics in Patients with Metastatic Merkel Cell Carcinoma Treated with Avelumab. Clin Cancer Res. 28(7):1363-1371 (2022)

43. Bukkems L, Versloot O, Cnossen M, Jonsson S, Karlsson MO, Mathôt RA, Fischer K. Association between sports participation, factor VIII levels and bleeding in hemophilia A. Thromb Haemost. (2022)

Book chapters

1. Jönsson S, Jonsson EN. Timing and efficiency in population pharmacokinetics/pharmacodynamic data analysis projects. In: Ette EI, Williams PJ, editors. *Pharmacometrics: the science of quantitative pharmacology*. Hoboken, John Wiley & Sons, Inc. 287- 302 (2007).

2. Jönsson S, Henningsson A, Edholm M, Salmonson T. Contribution of modeling and simulation studies in the regulatory review: A European regulatory perspective. In: Kimko HHC.; Peck CC, editors. *Clinical Trial Simulations. Applications and trends.* New York, Springer. 15-36 (2011).