Diagnosis, prognosis and treatment of severe falciparum malaria in African children
Hendriksen, I.C.E.

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Acknowledgements

This work was supported by grants 076908 and 082541 of The Wellcome Trust of Great Britain, and was coordinated as part of the Wellcome Trust Mahidol University-Oxford Tropical Medicine Research Programme funded by the Wellcome Trust of Great Britain. It has been an unforgettable experience to have been involved with the AQUAMAT research project. More than just a work experience, while living in Mozambique, Tanzania and Thailand, altogether for almost 7 years. During this time, many people have made their valuable contributions to the successful conduct of the studies, the writing and completion of this thesis.

Thailand

The Mahidol-Oxford Research Unit administrative, logistic and expert support has been unconditional for the research project and for me individually as a junior clinician and researcher. I would especially like to thank the following people:

Professor Arjen Dondorp: Arjen, you were a fantastic supervisor. You gave me the opportunity to become clinical trial physician for the AQUAMAT trial and conduct this PhD. It was an exciting start to prepare together the first study site, train a study team, collect the data and assist in clinical medicine in Hospital Central da Beira in Mozambique. Throughout the years, your support has been unconditional and you have visited me frequently. Your ideas and guidance for the analysis and writing have been crucial. Thanks for your warm hospitality in Bangkok, and for offering your free time to work at your house and enjoy dinners with your family. Besides work, you really took care of me. Showing me the salsa dance school could have been a potential pitfall not to complete the thesis. However, you acknowledged that entertainment is also an essential ingredient, and your encouragement has been most stimulating to finish the thesis. I am very grateful you are my promotor.

Professor Nick White: It was great that you and Joom visited me in Beira during the first year. Thank you for your confidence, hospitality, critical readings of the manuscripts and inspirational discussions. I do not know anyone else who can lecture so interestingly about malaria or other scientific topics, and also knows so much about anything else. Highlights were the Friday evening discussions over a glass of whiskey in the office. I am sorry; I still don't like whiskey!
Acknowledgements

Professor Nick Day: Thanks for your support and sharing a “Beatles birthday” in Bangkok. Dr Lisa White: you provided excellent modelling support for the PfHRP2 studies. With your in-depth understanding of the underlying biological mechanisms, you showed how mathematical modelling can be a powerful method to understand the “real” world. Dr Joel Tarning, modelling expert in the pharmacokinetics: I am very grateful for your patience to explain me some basics in your field of expertise. You conducted the POPPK analysis about quinine and artesunate. Without you, these studies would not have been possible.

Dr Sue Lee: Thank you statistical support and the never failing amount of snack food; I owe you many “stroopwafels”. Dr Charlie Woodrow: Thank you for helping with the set-up and interpretation of the ELISA assay. Sitting next to you in MORU office provided me a lot of scientific input, general support and lively discussions about all sorts of topics. Dr Pan-Ngum: Thanks for assisting in the data management, data analysis and modelling. Tharisara Sakulthaew: Thank you for logistic support. Dr Caterina Fanello: Thanks for intellectual and administrative support. Montri Rijaibun and Nuttapol Panachuenwongsakul have been very helpful with the data management. Kesinee Chotinavich, Kamolrat Silamut, Benjamas Intharabut, Ketsanee Srinamon, Forradee Nuchsongsin and Pattamon Tharaphan: Thank you all for malaria slide reading, providing hands with the ELISA assay, and the pleasant work environment in the lab. Somporn Saiwaew: I am very grateful you were my pipetting buddy, and I wish you good luck with your thesis. All other MORU staff and collaborators, there were so many: I am grateful for the interesting work environment, the pleasant collaboration, sharing nice Thai lunches, gym visits and friendships. Salsa friends and neighbours: Thanks for distraction, dances and bringing me home timely before the latin vibes would take me into the small hours.

Africa
The studies could not have been conducted without the collaboration of the parents, carers and patients in all of the 11 study sites. A large team of investigators was responsible for the local study sites. I would especially like to thank the following people:

Dr Lorenz von Seidlein: Thank you for your valuable advices and hands-on support on daily trial management in Mozambique and Tanzania. You built and maintained the networks. In both places, you helped me settle and looked after me. To focus me on data analysis and writing while working in these resource-limited settings has proven to be extremely difficult. Your cynicism in that respect was encouraging to finish this thesis after all. I appreciate you are my co-promotor.
In Mozambique, I would like to thank Dr Marcelino Lucas, Dr Alvertino Bareto, Dra Ermelinda Gomes, Dr Josefo Ferro, Dr César Jarach, Dr Olivier Wingi, Dra Estér Ivone Fernando, Dra Christina Cellarius, Dr Zacarias Raimundo Impítua, and Dr Carlos de Oliveira for their support. Dra Kajal Chagganlal, Dr Amir Seni and Dra Alínia José Pedro for taking over as trial coordinators after I moved to Tanzania. Many nurses have assisted in the project during the 5 year trial period. I would especially like to thank the following: Rosa Piedade Nicolão Fernandes, Domingos Nhamite Fernando, Alcina Cristina Guanza, Benjamim Jofrisse Nhamitambo, Ângela Félix Estefânio, Regina Francisco Dias Lapone, Domingas Santos Piripire, Elisa Muchanga, Ana Bongisse, Fernando Oliveira, Cristina Manuel Samaçalo, Faustino J.A. Parare, Matias Pechiço, Catarino Armindo, and Kátia Cristina Soares Ribeiro. I thank the lab technicians from the “Banco de Socorros” in Hospital Central da Beira and Gilberto Mujamaze for laboratory support at the CHAEM and Ponta-Gêa laboratory. Data management and logistic support (including for the best parties ever) were provided by Fidelina Cumbe, Ivan Flávio da Silva and Natércia de Jesus Grand Maison. Dr Pablo Montoya: Thanks for providing support with the HIV and malaria study and logistical support with the CD4+ testing.

Annett and Konrad: thanks for your advice in paediatrics and friendship. Lizete: You have taught me a lot about life in Africa and Portuguese language. I am glad you were there almost every day. Steven Stockhall: Thanks for showing me Africa’s wildlife and kindling an interest in photography. Nfithe band, Ernesto Ricardo and salsa group in Macurungu: I admire your positive energy, dance and African music; your surprise performance made my farewell party unforgettable.

In Tanzania, Dr Hugh Reyburn from the London School of Tropical Medicine and Hygiene, project manager of the Joint Malaria Programme. Thanks for your support and creating opportunities to collaborate and publish with different research groups.
Dr George Mtove, my Tanzanian counterpart: It was great to work with you. I have much appreciated your friendship and commitment to clinical work and research in tropical medicine. I wish you all the best with your research projects. Dr Samwel Gesase, your humble attitude, but never-failing support has been instrumental to the successful conduct of the studies in Tanzania. Dr Jacqueline Deen: Thanks for your assistance with clinical care and research at Hills ward. I am grateful to Dr Sarah Joseph for teaching me the ELISA assay to quantify PfHRP2. Dr Alison Kent: I thank you for your hard work on the ward, and your enthusiasm.
The triage, enrolment and management of more than 900 patients with severe malaria in Muheza would not have been possible without the help of the clinical trial team: Selemani Mtunguja, Walli Msuja, Emmanuel Swai, Edward Mtili, Christina Kiemi, Marwa Mongoso Mwikwabe, Hannah Wangai, Simphorosa Silaye, Stella Emmanuel, Rosalia Marwa, Michael Mngonea, Regina Malugu, Nzitu Juma Msengi, Faraja Mijombo Mtimbo and the nurses from Teule hospital. Laboratory support by Juma Kimera, Aikande Shoo, Celina Wycliffe, Weston Lemanya, and Revogatus Tarimo. Abraham Mwambuli was responsible for local data management and Veronica John Msigwa, Mwanahawa Rashidi for data entry. Thank you Lina Alex and Edna Mosha for administrative and logistic support and Lawi Sozigwa for driving. I thank also Dr Rajabu Malahiyo, hospital superintendent for the confidence and the possibility to work in Teule Hospital and Dr Steven Magesa from the National Institute of Medical Research in Amani. The quinine HPLC was conducted by Deogratias Titus Maiga, under auspices of Dr Martha Lemnge and the National Institute of Medical Research in Tanga.

I am grateful to Ben and Sally Amos, James Beard, Pam Allard and other colleagues and neighbours in Muheza and Tanga for providing housing, sharing nice dinners, and troubleshooting with electricity and water, computers, internet, insect infestations, car problems, security etc.

During my years in Africa, many new friends and colleagues have been helpful and kind, wherefore I would like to thank you all. I hope we will also meet again outside of Facebook.

The Netherlands

I thank Professor Piet Kager for acting as a second promotor, the critical reading of the final chapters, and support with the last straw. Dr Annemarie Brouwer: Thanks to your research project in Thailand I was “at the right time, at the right place”.

Diana Huis in ’t Veld: Thank you for hours of pep talk by Skype. Together we studied in Nijmegen and went to Thailand to assist in of Dr Annemarie Brouwer’s research project. Despite external circumstances causing delay of the study, we made the most of our time working in the laboratory in Bangkok, travelling and discussing about our future. You decided to start specialization in internal medicine and pursue a career in infectious diseases, and I decided to embark on the AQUAMAT project. We remained close friends and you visited me twice in Tanzania. Meanwhile, you also started a PhD research project in South-Africa. I am very grateful you are coming over to be my paranimph.
Jacobien Veenemans: Like no one else you know the ins and outs of doing research in Tanzania. We lived in the same village in Muheza, in which surroundings you conducted a micronutrient trial for the prevention of malaria. You and Hans’ Dutch sense of humour have been enlightening. Sharing your data and samples has resulted in our joint publication in chapter 6. I am glad you are my paranimph.

Friends and family in the Netherlands: Thanks for the support, by mail, visiting or otherwise during my time abroad. Although Groningen is relatively “far” away in the Netherlands, I hope to see you more often again. I would like to thank my new colleagues at the University Medical Centre in Groningen for the confidence, and the space to finish my thesis during the first few months.

Dear mom and dad, my brothers Guido en Joris, and sister-in-law: your love and support has been unconditional. Thanks for the visits and your understanding. You have helped me a lot to start up again in the Netherlands.