



Universiteit
Leiden
The Netherlands

Precision medicine using pharmacogenomic panel testing

Wouden, C.H. van der

Citation

Wouden, C. H. van der. (2020, September 2). *Precision medicine using pharmacogenomic panel testing*. Retrieved from <https://hdl.handle.net/1887/136094>

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/1887/136094>

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

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/136094> holds various files of this Leiden University dissertation.

Author: Wouden, C.H. van der

Title: Precision medicine using pharmacogenomic panel testing

Issue date: 2020-09-02

PRECISION MEDICINE USING PHARMACOGENOMIC PANEL TESTING

Cathelijne H. van der Wouden

The research presented in this thesis was performed at the department of Clinical Pharmacy and Toxicology of Leiden University Medical Center, Leiden, The Netherlands. Financial support for the publication of this thesis was provided by Afdelingsfonds Klinische Farmacie & Toxicologie and Subsidie Stichting KNMP-fondsen.

The research leading to these results has received funding from the European Community's Horizon 2020 Programme under grant agreement No.668353 (U-PGx).

Cover Design	Jetske van der Wouden www.callmejet.com
Lay Out	Jetske & Cathelijne van der Wouden
Printing	Gildeprint – Enschede www.gildeprint.nl
ISBN	978-94-6402-374-9

©2020 C.H. van der Wouden

All rights reserved. No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopy, recording, or any information storage or retrieval, without permission in writing from the author.

PRECISION MEDICINE USING PHARMACOGENOMIC PANEL TESTING

Proefschrift

ter verkrijging van
de graad van Doctor aan de Universiteit Leiden,
op gezag van Rector Magnificus prof.mr. C.J.J.M. Stolk,
volgens besluit van het College voor Promoties
te verdedigen op woensdag 2 september 2020

klokke 15:00 uur

door

Cathelijne Hendrikje van der Wouden

geboren te Chester, Verenigd Koninkrijk

in 1991

Promotor Prof. dr. H.-J. Guchelaar

Copromotor Dr. J.J. Swen

Leden promotiecommissie Prof. dr. C.J. van Asperen
Prof. dr. ir. S.M. van der Maarel
Prof. dr. B. Wilffert
University of Groningen, Groningen
University Medical Center Groningen, Groningen
Dr. M.J. Coenen
Radboud University Medical Center, Nijmegen

Aan mijn ouders

“No human is limited”

Eluid Kipchoge

After breaking the 2-hour marathon barrier in Vienna

October 12th 2019

CONTENTS

Chapter 1	General Introduction	11
-----------	----------------------	----

PART I - Generating Evidence for Pharmacogenomic Panel Testing

Chapter 2	Implementing Pharmacogenomics in Europe: Design and Implementation Strategy of the Ubiquitous Pharmacogenomics Consortium <i>Clinical Pharmacology and Therapeutics.</i> 2017;101(3):341-58	25
Chapter 3	Generating Evidence for Precision Medicine: Considerations Made by the Ubiquitous Pharmacogenomics Consortium (U-PGx) When Designing and Operationalizing the PREPARE Study <i>Pharmacogenetics and Genomics.</i> 2020; <i>in press</i>	65

PART II - Developing Tools Facilitating Implementation

Chapter 4	Dutch Pharmacogenetics Working Group (DPWG) Guideline for the Gene-Drug Interaction of DPYD and Fluoropyrimidines <i>European Journal of Human Genetics.</i> 2019;10.1038/s41431-019-0540-0	93
Chapter 5	Development of the PGx-Passport: a Panel of Actionable Germline Genetic Variants for Pre-Emptive Pharmacogenetic Testing <i>Clinical Pharmacology and Therapeutics.</i> 2019;106(4):866-73	201

PART III - Evaluating the Implementation Process

Chapter 6	Consumer Perceptions of Interactions with Primary Care Providers After Direct-To-Consumer Personal Genomic Testing <i>Annals of Internal Medicine.</i> 2016;164(8):513-22	227
Chapter 7	Pharmacist-Initiated Pre-Emptive Pharmacogenetic Panel Testing with Clinical Decision Support in Primary Care: Record of PGx Results and Real-World Impact <i>Genes.</i> 2019;10(6)	255

Chapter 8	Assessing the Implementation of Pharmacogenomic Panel Testing in Primary Care in the Netherlands Utilizing a Theoretical Framework <i>Journal of Clinical Medicine.</i> 2020;9(3)	297
-----------	--	-----

PART IV - Quantifying the Impact on Patient Outcomes and Cost-Effectiveness

Chapter 9	Cost-Effectiveness of Pharmacogenomics-Guided Prescribing to Prevent Gene-Drug-Related Deaths: A Decision-Analytic Model <i>Submitted</i>	331
-----------	---	-----

General Discussion and Summaries

Chapter 10	General Discussion and Future Perspectives <i>Adapted from Advances in Molecular Pathology.</i> 2020	395
Chapter 11	Summary	423
Chapter 12	Nederlandse Samenvatting	429

Appendix

List of Publications	439
Curriculum Vitae	441
Portfolio	443
Acknowledgments	445