



## Newsletter Issue #3



### Editorial

**Dear Readers,**

As our project enters its **final phase**, we look back on another remarkable year of collaboration. The year 2025 has been especially significant for SafePolyMed, and I am deeply grateful for the hard work and dedication the entire team has invested in driving our results forward. With the **launch of our clinical study *EmPaSafe***, we are now putting years of research on drug interactions into practice and testing it in real-world settings.

As our results begin to move beyond academic publications and are now used in a practical setting, it becomes clear how they **can shape future practices in drug safety**.

But this is not all. 2025 has also been a year of meaningful public engagement and awareness-raising. In addition to presenting our work at academic and scientific conferences, we actively participated in broad societal events such as the **German Unity Day in Saarbrücken**. It was a pleasure to meet local communities, spark conversations, and introduce them to the importance of understanding drug interactions. We are equally proud to have launched the **third edition of our free training course on safety in polypharmacy**—an initiative that empowers patients with knowledge and helps increase their confidence and safety in managing medicines.

Below, you will find more information about our recent achievements. We invite you to explore our activities and stay tuned as we prepare to share the final results of the project.

**Thank you for being part of our journey,**  
Thorsten Lehr

## Project meeting 2025

Ljubljana, Slovenia, set the stage for the consortium's **5th Progress Meeting**, where partners met from 14 to 15 May 2025 to drive the project forward. Read more about the meeting [here](#).



## New consortium partner in SafePolyMed

As of **1 January 2025**, SafePolyMed has a new consortium partner: **Universitätsklinikum Heidelberg** has joined the project as a second clinical site in **Germany**. With this addition, the clinical study **EmPaSafe** is now being conducted across **five clinical sites**: Leiden (Netherlands), Ljubljana (Slovenia), Patras (Greece), Aachen and Heidelberg (Germany).



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## Recruitment for EmPaSafe started

This summer, recruitment for the SafePolyMed **clinical study EmPaSafe** has begun! With partner LUMC coordinating the efforts, all five clinical sites are now actively **enrolling patients interested in learning more about how medicines and genes interact**.



**More info on EmPaSafe**

## SafePolyMed training course

Under the lead of project partner Patvocates GmbH, SafePolyMed organised the third iteration of their free **online training course on safety in polypharmacy in October**. Read more about it [here](#).



### WHY JOIN THIS COURSE?

Managing multiple medications can be complex and risky. This expert-led online course will help you understand the key safety principles of polypharmacy and empower you to take an active role in medication management.

### WHO CAN PARTICIPATE?

This course is designed for:

- ✓ Patients & caregivers who want to ensure safe medication use.
- ✓ Patient advocates aiming to support their communities.
- ✓ Anyone interested in learning about polypharmacy and its safety considerations.



All materials are in English, so a good proficiency is required.

### COURSE STRUCTURE

- 7 interactive live online sessions (up to 120 min each, including Q&A, quizzes, and surveys)
- Meeting Platform: Zoom
- Learning Platform: LearnWorlds
- Certificate of Attendance (for participants attending 75% or more)

### HOW TO REGISTER?

- Click the link below and fill out the registration form:

**Register for free!**

For updates, connect with us on social media:



[www.safepolymed.eu](http://www.safepolymed.eu)



Funded by the European Union



### SCHEDULE

**October 14<sup>th</sup> Tuesday, 15:00 CEST**

**Session 1:** Introduction to Polypharmacy

**October 16<sup>th</sup> Thursday, 15:00 CEST**

**Session 2:** Drug-Drug Interactions (DDIs)

**October 21<sup>st</sup> Tuesday, 15:00 CEST**

**Session 3:** Drug-Gene- (DGIs) & Drug-Drug-Gene Interactions (DDGIs)

**October 23<sup>rd</sup> Thursday, 15:00 CEST**

**Session 4:** Vulnerability Factors

**October 28<sup>th</sup> Tuesday, 15:00 CET**

**Session 5:** Patient Reporting & PROMs

**October 30<sup>th</sup> Thursday, 15:00 CET**

**Session 6:** Safety Signal Reporting & Digital Tools

**November 4<sup>th</sup> Tuesday, 15:00 CET**

**Session 7:** Data Safety, Privacy and GDPR

## Communication and dissemination activities

On the occasion of the **German Unity Day**, SafePolyMed invited the interested public to interact and learn more at a booth in the centre of **Saarbrücken, Germany**: read about it [here](#).

Throughout the year, partners engaged key stakeholders such as **clinicians, pharmacists and doctors** in diverse formats and locations, including **Amsterdam, Netherlands** and **Victoria, Canada**.

Other presentations to **disseminate results** include:

- Lili Milani on "Long read sequencing and return of results to biobank participants" at 8th ESPT Congress in Rotterdam, Netherlands
- Laura Fuhr on "Physiologically-based pharmacokinetic modeling for individualized drug therapy" at Pharm-Tox Summit Hannover, Germany
- Dage Särg et al. on "Text-based approach for detecting cases of ADEs from EHRs of participants of the Estonian Bioban" at GeneForum
- Several partners' contributions at ESHG Pharmacogenomics Course in Portorož, Slovenia

**Featured on social media**



Our inspiring time at #ESPT2025 continues with a #SafePolyMed poster co-authored by Kristi Krebs (University of Tartu)!

🔥 *Pharmacokinetic recall study of Estonian Biobank participants carrying novel genetic variants in CYP2C19 and CYP2D6.*

Big thanks to everyone contributing to such a great event! ⭐

#DrugSafety #Polypharmacy #EURResearch #PatientSafety

**Evaluating the functional consequences of rare single nucleotide and structurally complex variants in CYP2C19 and CYP2D6**

- Offering *in vivo* confirmation that the partial gene deletion CYP2C19\*37, enriched in Estonians and Finns, is associated with a CYP2C19 poor metaboliser phenotype
- Highlighting the importance of monitoring drug-drug interactions in combination with pharmacogenetic testing

**Pharmacokinetic recall study of Estonian Biobank participants carrying novel genetic variants in CYP2C19 and CYP2D6**

Kristi Krebs<sup>1</sup>, Laura Birgit Luitva<sup>1,2</sup>, Anette Caroline Käse<sup>3</sup>, Raul Kokkasaar<sup>4</sup>, Maarja Jõele<sup>5</sup>, Georgi Hadjashov<sup>1</sup>, Kadri Mäe<sup>6</sup>, Elisabet Stersel<sup>4,5</sup>, Birgit Melane Wolmar<sup>6</sup>, Lis Karo-Astover<sup>7</sup>, Krista Fischer<sup>8</sup>, Estonian Biobank Research Team<sup>1</sup>, Volker M. Lauschke<sup>9,10,11</sup>, Magnus Ingelman-Sundberg<sup>12</sup>, Espen Molden<sup>13</sup>, Alar Iis<sup>1</sup>, Kari Oksa<sup>14</sup>, Jane Lase<sup>15,11</sup>

**1 Background**  
CYP2C19 and CYP2D6 account for the hepatic metabolism of approximately 35-40% of clinically used drugs.  
**Research Gap:** Despite identifying many rare single nucleotide and structural variants within these genes, assessing their functional impact remains challenging. The CYP2C19\*37 partial deletion allele lacks *in vivo* phenotyping data, and is therefore assigned as no function but accompanied by a limited evidence base. Non-genetic factors, such as drug-drug interactions (DDIs), can significantly influence metabolic phenotypes.

**2 Methods**  
The study was conducted in two phases: a recall phase and a clinical phase. The recall phase involved genotyping participants from the Estonian Biobank. The clinical phase involved administering a probe drug (esomeprazole) to participants and measuring its plasma concentration over time. The study was designed to evaluate the functional consequences of rare genetic variants in CYP2C19 and CYP2D6.

**3 Results**  
The study identified several novel genetic variants in CYP2C19 and CYP2D6. The CYP2C19\*37 partial deletion allele was found to be associated with a poor metaboliser phenotype. The study also identified several other variants that were associated with altered metabolic activity. The results of the study are presented in the following figures.

**4 Discussion**  
The study provides the first *in vivo* confirmation of the functional consequences of the CYP2C19\*37 partial deletion allele. The results of the study have important implications for the clinical use of drugs that are metabolized by CYP2C19 and CYP2D6.

**5 Conclusion**  
The study highlights the importance of monitoring drug-drug interactions in combination with pharmacogenetic testing. The results of the study provide valuable information for the clinical use of drugs that are metabolized by CYP2C19 and CYP2D6.

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## Latest publications

R. Mosch, M. van der Lee, H.J. Guchelaar, and J.J. Swen: **Pharmacogenetic Panel Testing: A Review of Current Practice and Potential for Clinical Implementation.**

*Annual Review of Pharmacology and Toxicology. 2025; 65: 91-109*  
doi: 10.1146/annurev-pharmtox-061724-080935

Hanna Maria Kariis, Dage Särg, Kristi Krebs, Maarja Jõeloo, Kadri Kõiv, Kairit Sirts, The Estonian Biobank Research Team, Health Informatics Research Team, Maris Alver, Kelli Lehto & Lili Milani: **Genetic influences on antidepressant side effects: a CYP2C19 gene variation and polygenic risk study in the Estonian Biobank.** *European Journal of Human Genetics.*

doi: doi.org/10.1038/s41431-025-01894-x

Simeon Rüdesheim, Helena Leonie Hanae Loer, Denise Feick, Fatima Zahra Marok, Laura Maria Fuhr, Dominik Selzer, Donato Teutonico, Annika R. P. Schneider, Juri Solodenko, Sebastian Frechen, Maaïke van der Lee, Dirk Jan A. R. Moes, Jesse J. Swen, Matthias Schwab, Thorsten Lehr: **A Comprehensive CYP2D6 Drug–Drug–Gene Interaction Network for Application in Precision Dosing and Drug Development.** *Clinical Pharmacology & Therapeutics.*

doi: doi.org/10.1002/cpt.3604

Dage Särg, Kairit Sirts, Kristi Krebs, Markus Tamm, Alise Metsküla, Marek Oja, Sven Laur, Jaak Vilo, Lili Milani: **Text-based approach for detecting cases of ADEs from EHRs of participants of the Estonian Biobank.** *Informatics in Medicine Unlocked.*

doi: doi.org/10.1016/j.imu.2025.101701

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**Funded by  
the European Union**

Grant No. 101057639