



eHealth Summit Austria, May 24, 2017



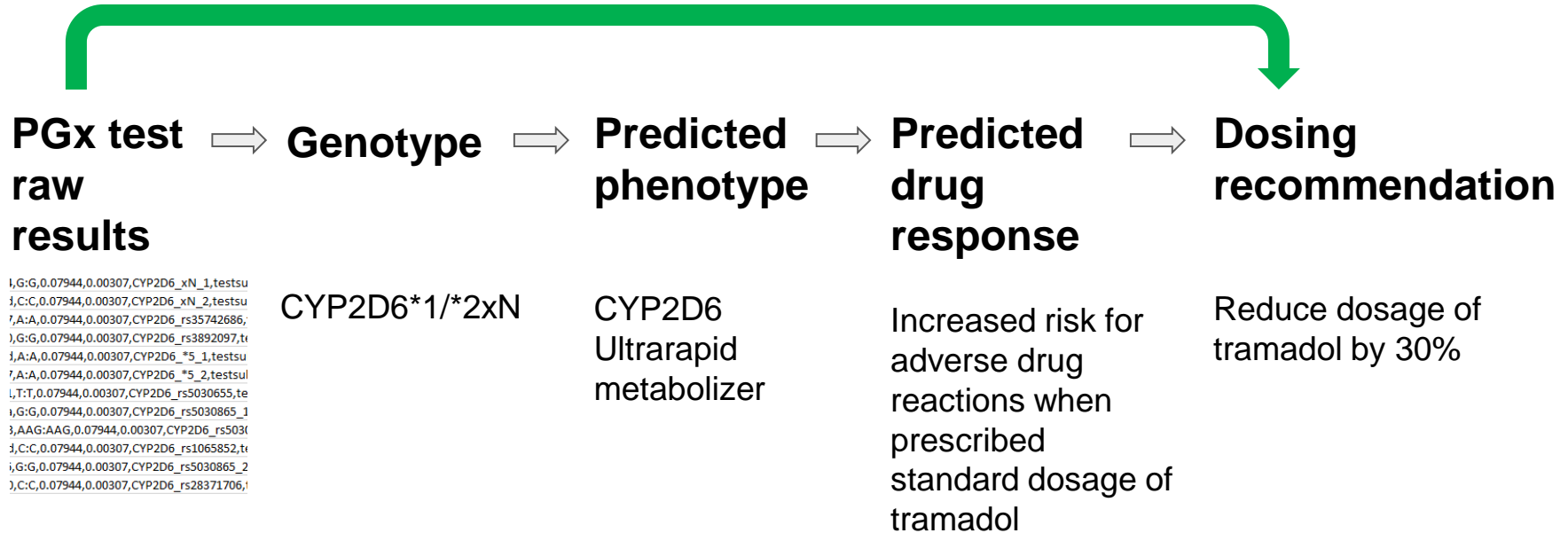
The Importance of **Gene-Drug-Drug-Interactions** in Pharmacogenomics Decision Support



Kathrin Blagec, Wolfgang Kuch, Matthias Samwald

Section for Artificial Intelligence and Decision Support
Medical University of Vienna

Pharmacogenomics (PGx) Decision Support



Genetics is not the only factor influencing drug response!

**The intake of other prescription drugs
can alter the activity of enzymes and
transporters whose function PGx tests
aim to predict!**



Example: Prescription of Tramadol



PGx result: **CYP2D6 Ultrarapid metabolizer**

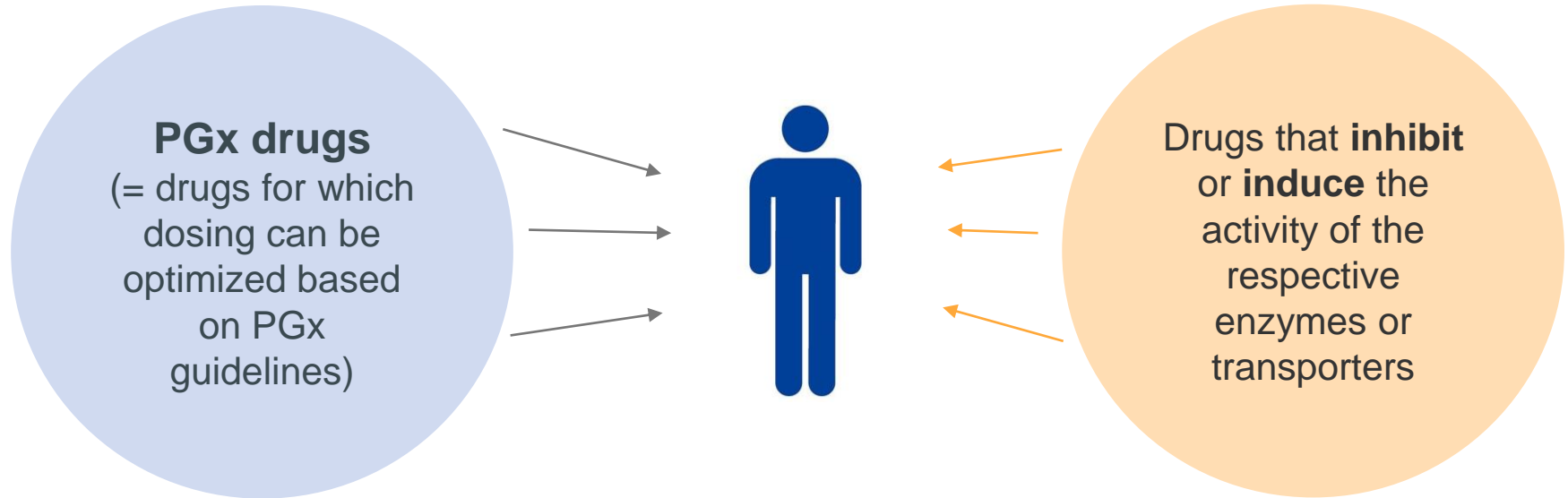
PGx recommendation: **Reduce dose by 30%**

Also receiving Fluoxetine: a **strong CYP2D6 inhibitor**

→ **Dosage??**

**Pharmacogenomic dosing guidelines consider only
SINGLE gene-drug interactions!**

How frequent are such problematic co-prescriptions?



We screened Austrian claims data for concomitant prescriptions of 4,440 distinct interaction pairs.

55 PGx drugs across 7 genes

193 inhibitor / inducer drugs

GAP-DRG database operated by the Main Association of Austrian Social Security Institutions

1,587,829 Austrian insurance holders

393,476,104 prescriptions (years 2006 and 2007)



58.8% of our study population received **at least one PGx drug**

On average, **every 4th** patient who was treated with a PGx drug concomitantly received an inhibitor or inducer of the respective enzyme or transporter!

In **half** of the cases, co-prescriptions of **moderate** (47.3%) or **strong** (7.3%) inhibitors or inducers

How can gene-drug-drug interactions be addressed in PGx decision support?

Future perspective:

- Development and incorporation of **more sophisticated dosing algorithms** based on pharmacometric data

Interim solution:

- Use a **minimum-set of high-relevance gene-drug-drug interaction** to alert healthcare providers of potential interactions

WARFARINDOSING

www.WarfarinDosing.org

The screenshot displays the WarfarinDosing.org web application interface. On the left is a navigation menu with links: Warfarin Dosing, Clinical Trial, Outcomes, Hemorrhage Risk, Patient Education, Contact Us, References, Glossary, and About Us. Below the menu, it shows 'User: Patient: Version 3.0 Build : May 14, 2016'. The main form is titled 'Required Patient Information' and includes fields for Age, Sex, Ethnicity, Race, Weight, Height, Smokes, Liver Disease, Indication, Baseline INR, Target INR, Amiodarone/Cordarone Dose, Statin/HMG CoA Reductase Inhibitor, Any azole, and Sulfamethoxazole/Septa/Bactrim/Cotrim/Sulfatrim. Below this is a 'Genetic Information' section with dropdown menus for VKORC1-1639/3673, CYP4F2 V433M, GGCX rs11676382, CYP2C9*2, CYP2C9*3, CYP2C9*5, and CYP2C9*6. At the bottom, there is a checkbox for 'Accept Terms of Use' and a red button labeled '> ESTIMATE WARFARIN DOSE'.

**Gene-drug-drug interactions are not
uncommon.**

**Addressing them in PGx decision support
helps to increase medication safety!**



This project has received funding from the European Union's Horizon 2020 research and Innovation programme under grant agreement No 668353 and by the Austrian Science Fund (FWF) [P 25608-N15].