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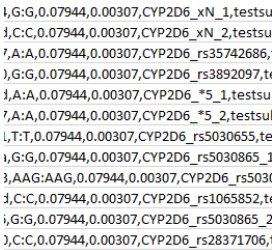
The Importance of **Gene-Drug-Drug-Interactions** in Pharmacogenomics Decision Support

Kathrin Blagec, Wolfgang Kuch, Matthias Samwald

Section for Artificial Intelligence and Decision Support
Medical University of Vienna

Pharmacogenomics (PGx) Decision Support

PGx test raw results	Genotype	Predicted phenotype	Predicted drug response	Dosing recommendation
	CYP2D6*1/*2xN	CYP2D6 Ultrarapid metabolizer	Increased risk for adverse drug reactions when prescribed standard dosage of tramadol	Reduce dosage of tramadol by 30%

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**

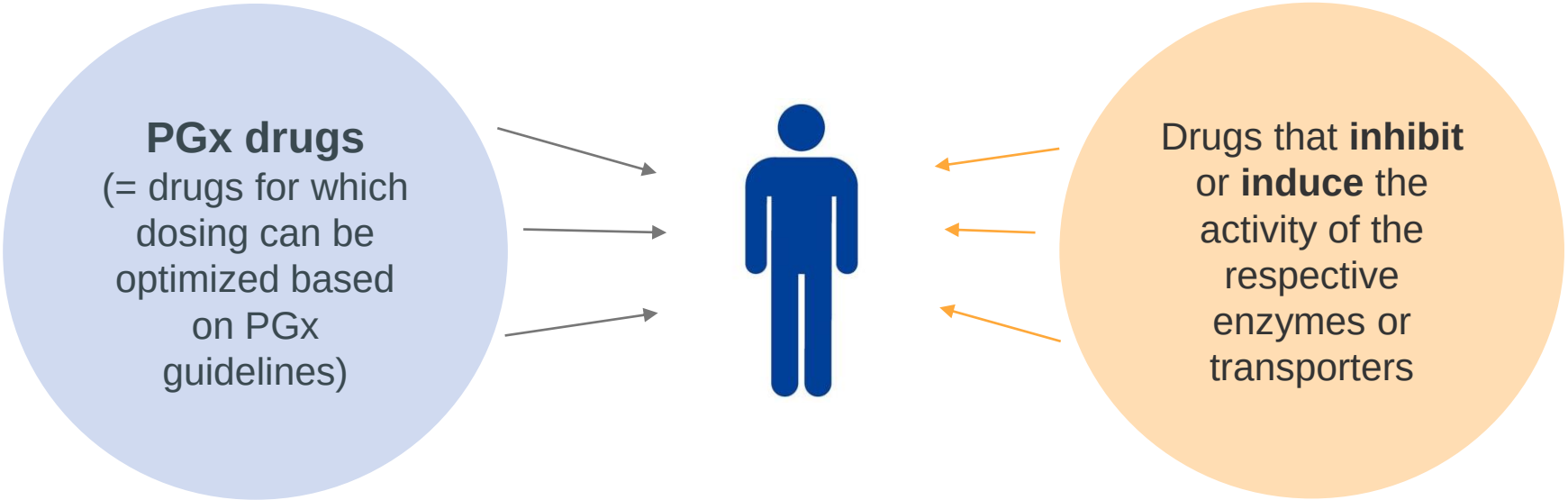
PGx recommendation: **Reduce dose by 30%**

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

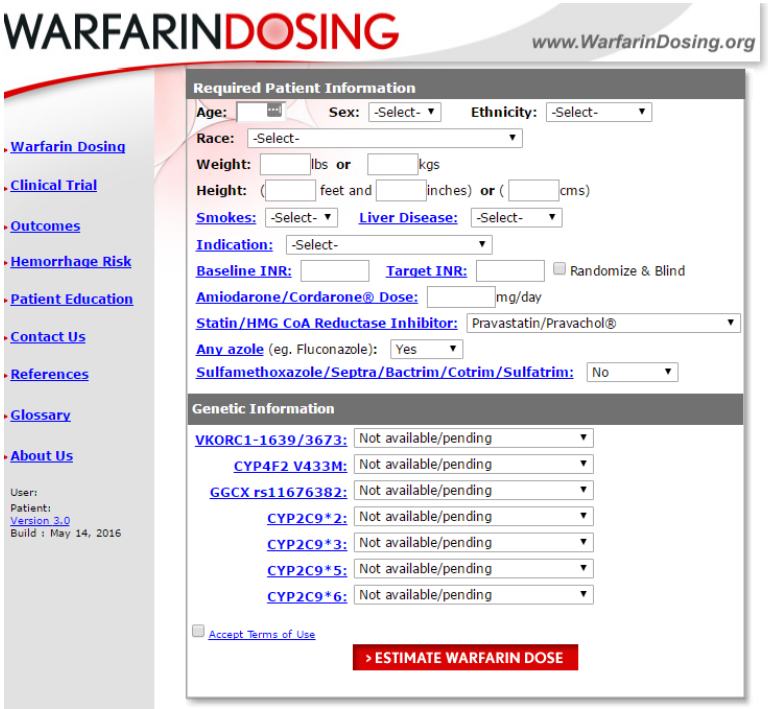
How can gene-drug-drug interactions be addressed in PGx decision support?

Future perspective:

- Development and incoporation 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



Gene-drug-drug interactions are not uncommon.

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

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