UNIKLINIK RWTH AACHEN

Klinische Pharmakologie

Polypharmazie

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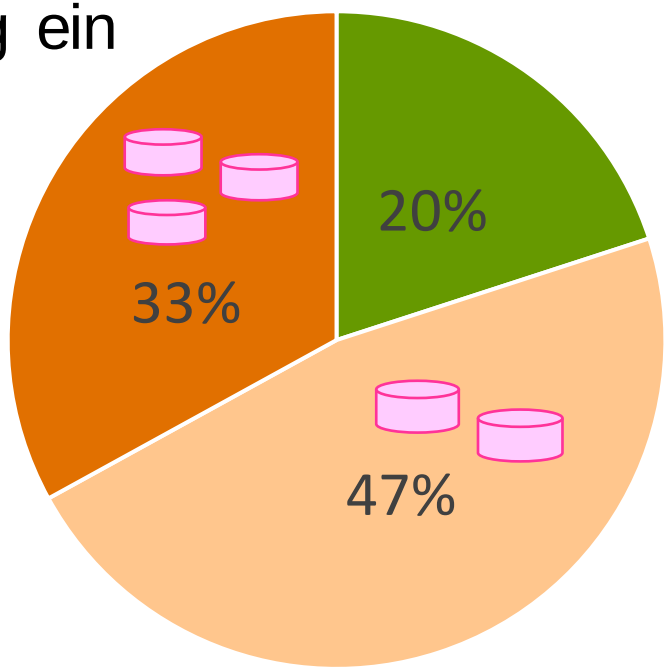
Institut für Klinische Pharmakologie, Aachen

Arzneimittel pro Patient

- Vier von fünf über 65-jährigen nehmen regelmäßig Medikamente ein
- Jeder Dritte (> 65 y) nimmt mehr als drei Medikamente regelmäßig ein



> 5 =
„Polypharmazie“

De Vries, Stingl, Breteler. Br J Clin Pharmacol. 2021;87:2732–2756

Polypharmazie

Wechselwirkungen

Multimorbidität
Gebrechlichkeit

Verschreibungs
-kaskaden

Nebenwirkungen

Polypharmazie-Sprechstunde in Aachen

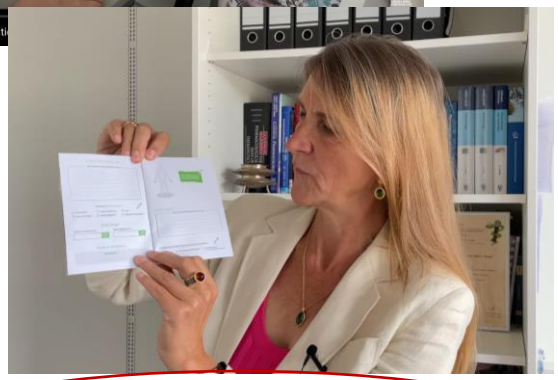
Geriatric specialists

Polypharmazie-Sprechstunde
für ältere Patientinnen und Patienten

Klinik für Altersmedizin (Medizinische Klinik VI)
Klinikdirektor: Univ.-Prof. Dr. med. Cornelius Bollheimer

Institut für Klinische Pharmakologie
Institutsdirektorin: Univ.-Prof. Dr. med. Julia Stingl

Pharmacists



Clinical pharmacologists

Polypharmazie-Sprechstunde

Patient medication assessment:

- Brown Bag Review
- Mobility/Frailty analysis
- Patient reported safety outcomes

Potential inadequate medication analysis:

- Causality assessment (WHO) for adverse drug effects
- Check for PIM: Priscus list
- Interaction database
- Monitoring/Dosing

Personalized Therapy recommendations:

- Dose adjustments
- Adequate medication (often: deprescribing)
- Safety/ADR documentation

Jan Geissler
Dr. Tamás Bereczky
Dr. Eglys González
Stefan Huber
Michi Geissler
Luba Mock

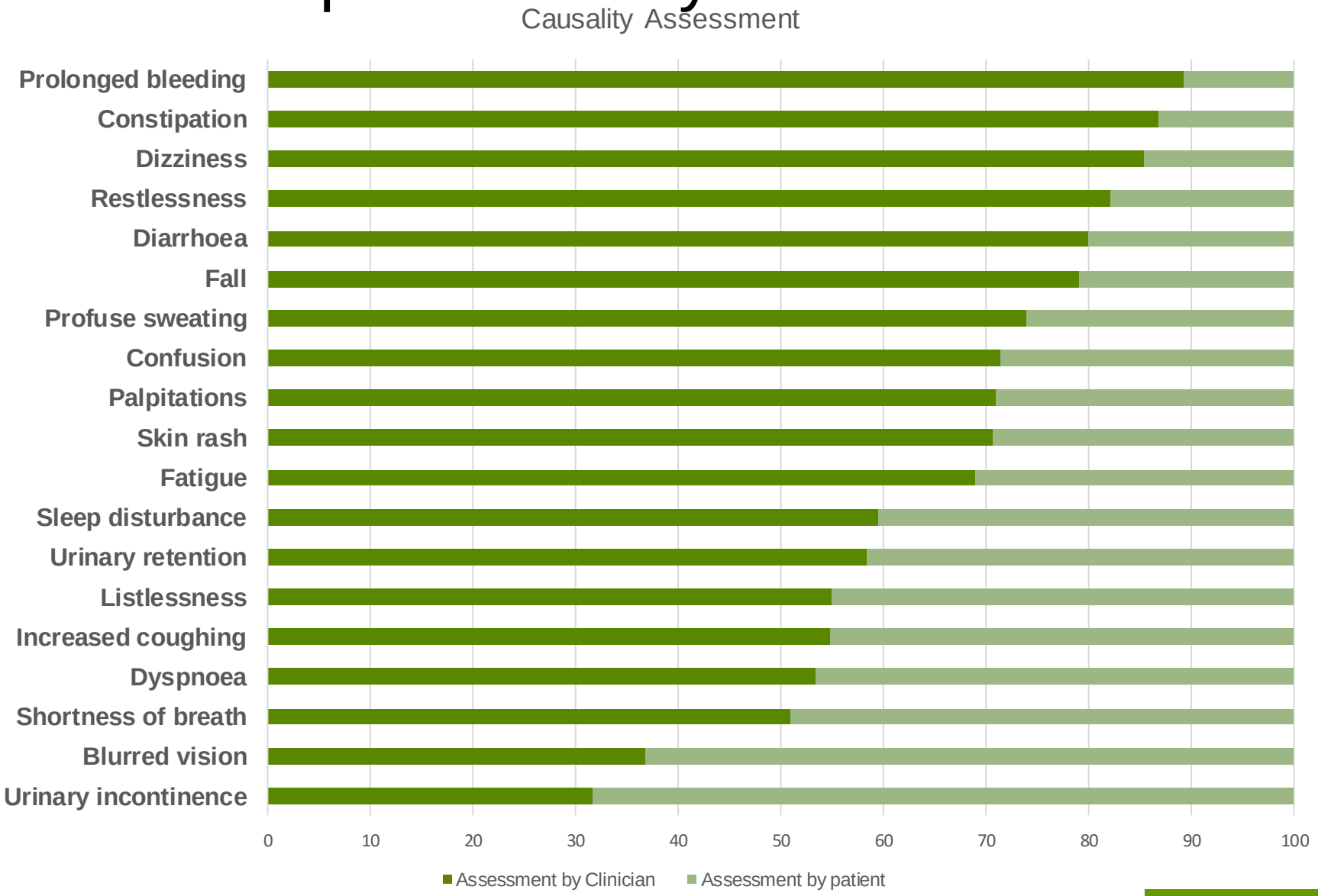
Prof. Dr. med. Julia Stingl
PD Dr. med. Katja Just
Dr. rer. nat. Justyna Wozniak
Jason-Christopher Radermacher
Klinische Pharmakologie

11th May 2023

Improving Safety in Polymedication by Managing Drug-Drug-Gene Interactions

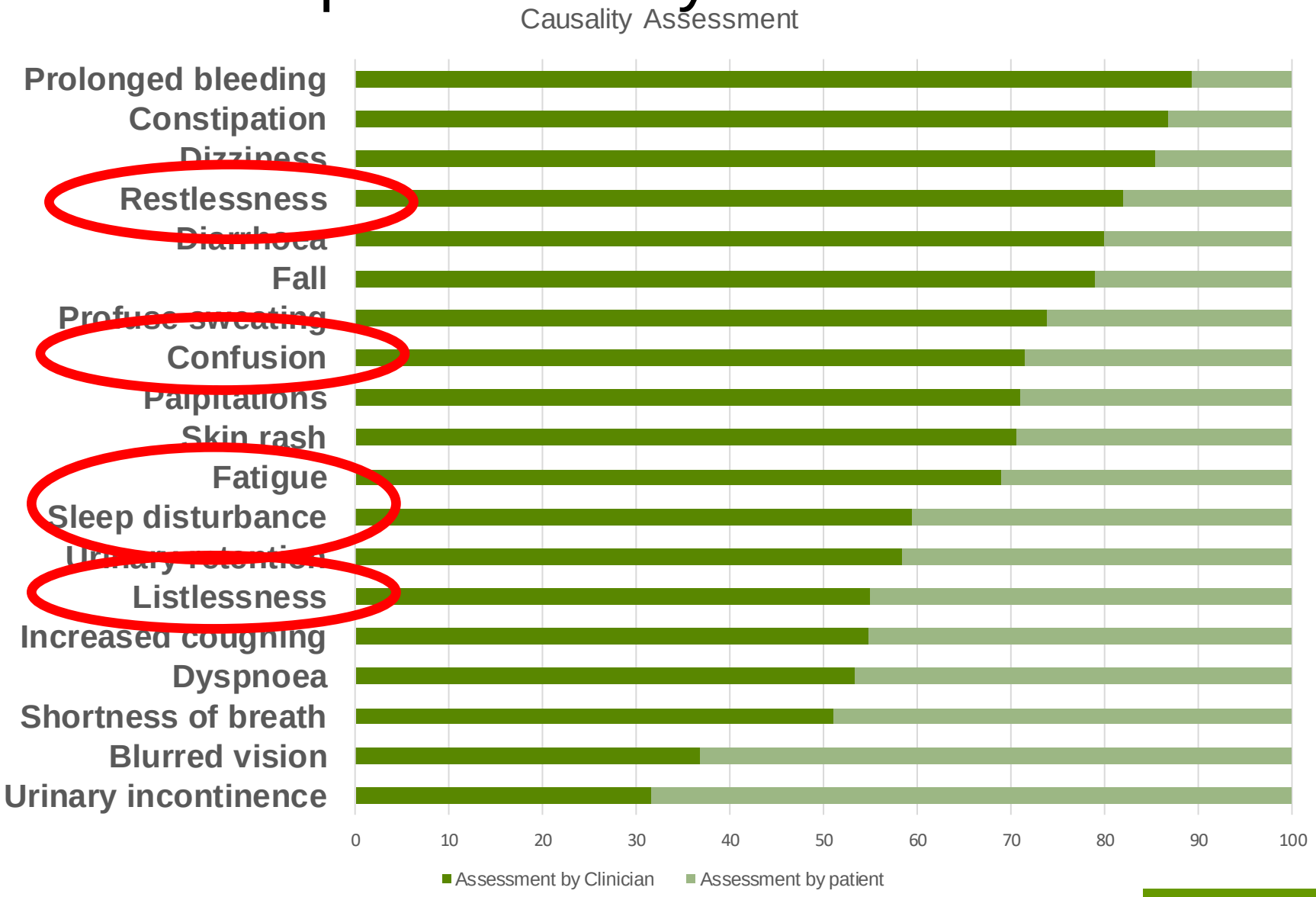
SafePolyMed.eu

Patient reported safety outcomes



Stingl J, Wozniak J, Just K, Laurentius T: Auswertung Polypharmaziesprechstunde, Data on file

Patient reported safety outcomes



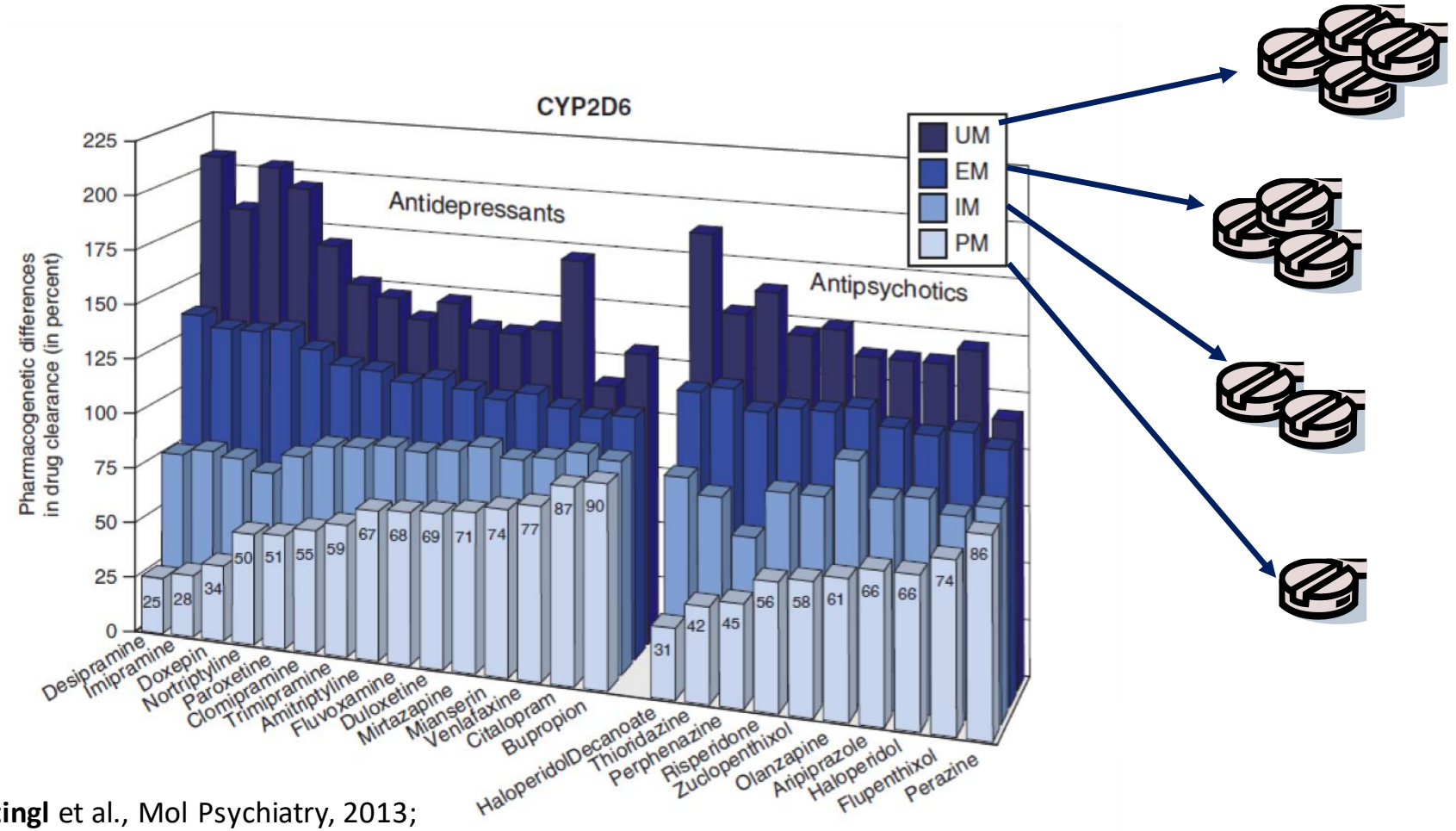
Stingl J, Wozniak J, Just K, Laurentius T: Auswertung Polypharmaziesprechstunde, Data on file

Pharmacogenetics and drug safety

Pharmacogenetic variability may lead to higher exposure to drug or metabolites

Quelle: UPGx Promotional video, EU Horizon 2020 Programme (grant agreement number 668353 [U-PGx]).

Pharmakogenetische Dosisempfehlungen: Actionable Drugs

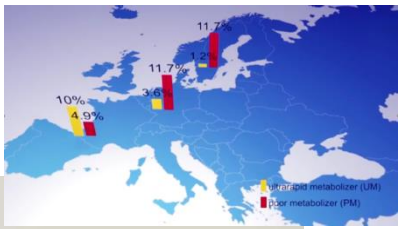


Stingl et al., Mol Psychiatry, 2013; 18:273-287

EU-Horizon2020: Implementation of **Preemptive pharmacogenomics**

Implementing Pharmacogenomics in Europe: Design and Implementation Strategy of the Ubiquitous Pharmacogenomics Consortium

CH van der Wouden[1], A Cambon-Thomsen[2], E Cecchin[3], KC Cheung[4], CL Dávila-Fajardo[5], VH Deneer[6], V Dolžan[7], M Ingelman-Sundberg[8], S Jönsson[9], MO Karlsson[9], M Kriek[10], C Mitropoulou[11], GP Patrinos[12], M Pirmohamed[13], M Samwald[14], E Schaeffeler[15], M Schwab[15,16,17], D Steinberger[18], J Stingl[19], G Sunder-Plassmann[20], G Toffoli[3], RM Turner[13], MH van Rhenen[4], JJ Swen[1], and H-J Guchelaar[1] on behalf of the Ubiquitous Pharmacogenomics Consortium



PHARMACOGENETICS

The right drug for you

Personalized prescribing is gaining momentum, but is there enough evidence for it to become standard clinical practice?

Ubiquitous Pharmacogenomics will spend 3 years studying the clinical outcomes of 8,000 patients in a large randomized controlled trial in 7 hospitals in 7 European countries.

Nature 2016; 537, S60–S62

Clin Pharmacol Ther. 2017 Mar;101(3):341-358. doi: 10.1002/cpt.602.

Study design

18 months with training and PGx testing

3342 patients

18 months therapy as usual

18 months therapy as usual

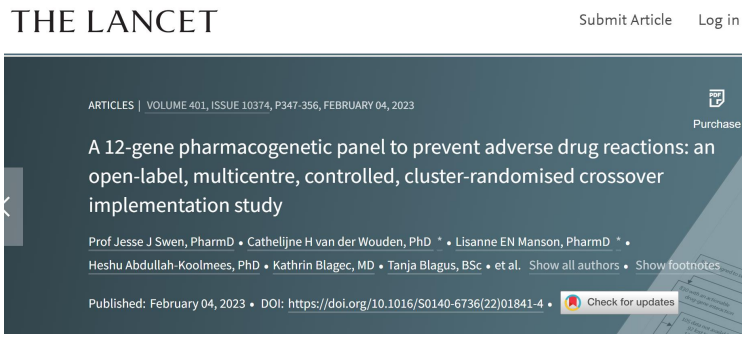
3602 patients

18 months with training and PGx testing

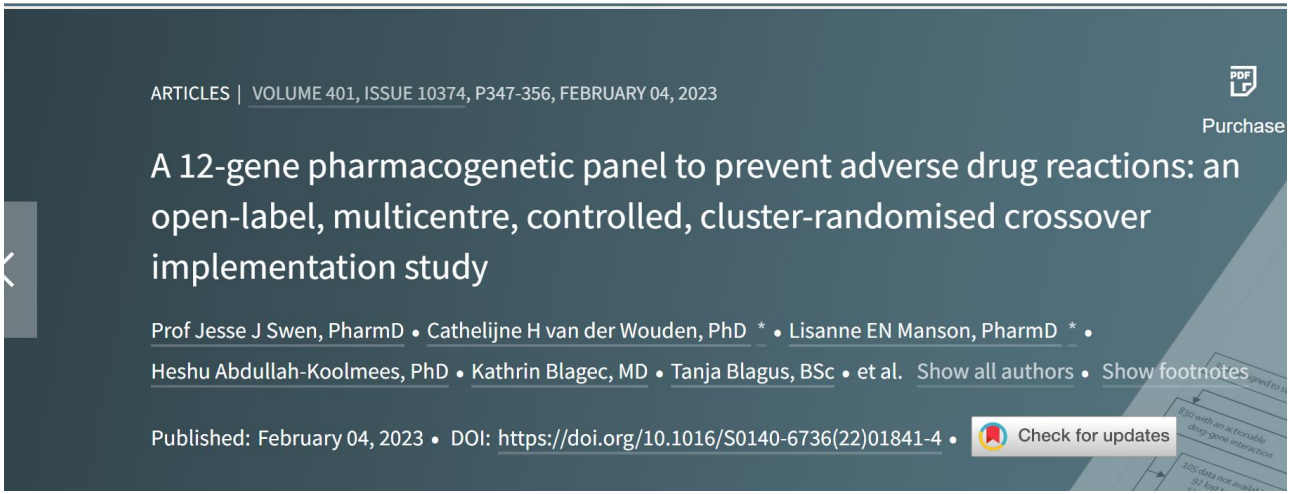
Number of ADR

Number of ADR

- Different hospitals in seven countries in Europe:
  - Psychiatry,
  - Transplantation,
  - Oncology,
  - General Practice,
  - Hospital pharmacy,
  - Internal medicine



Lancet. 2023 Feb 4;401(10374):347-356. doi: 10.1016/S0140-6736(22)01841-4.



…, the prevalence of ..a causal clinically relevant **adverse drug reaction** was

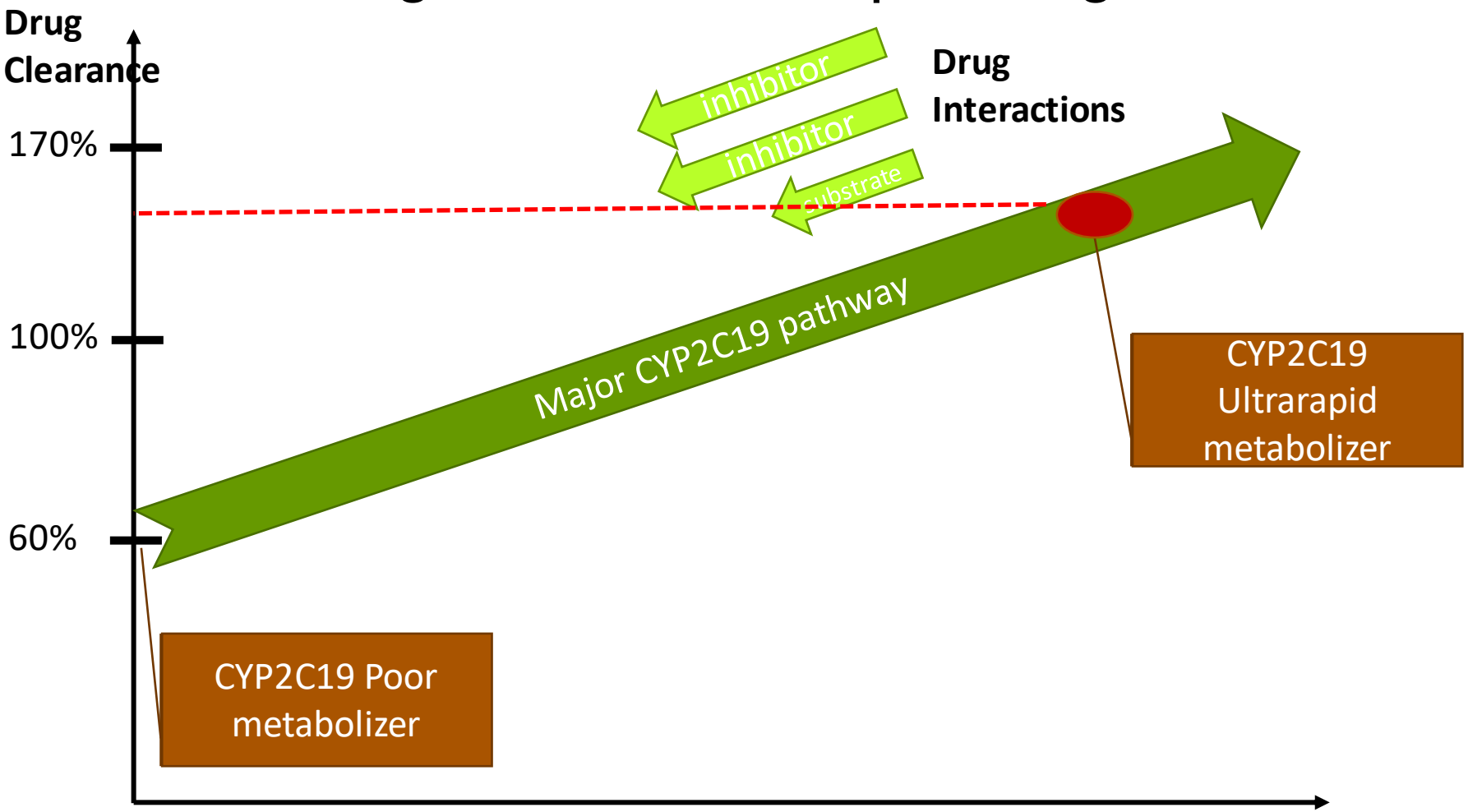
21% the study group and

29% in the control group,

reducing the risk of an adverse drug reaction by 30% (OR 0.70 [95% CI 0.61–0.79]; p <0·0001; figure 2).

Pharmakogenetik und Arzneimittelwehselwirkungen

Auswirkungen auf Dosisanpassung



Pharmakogenetik und Arzneimittelwehselwirkungen

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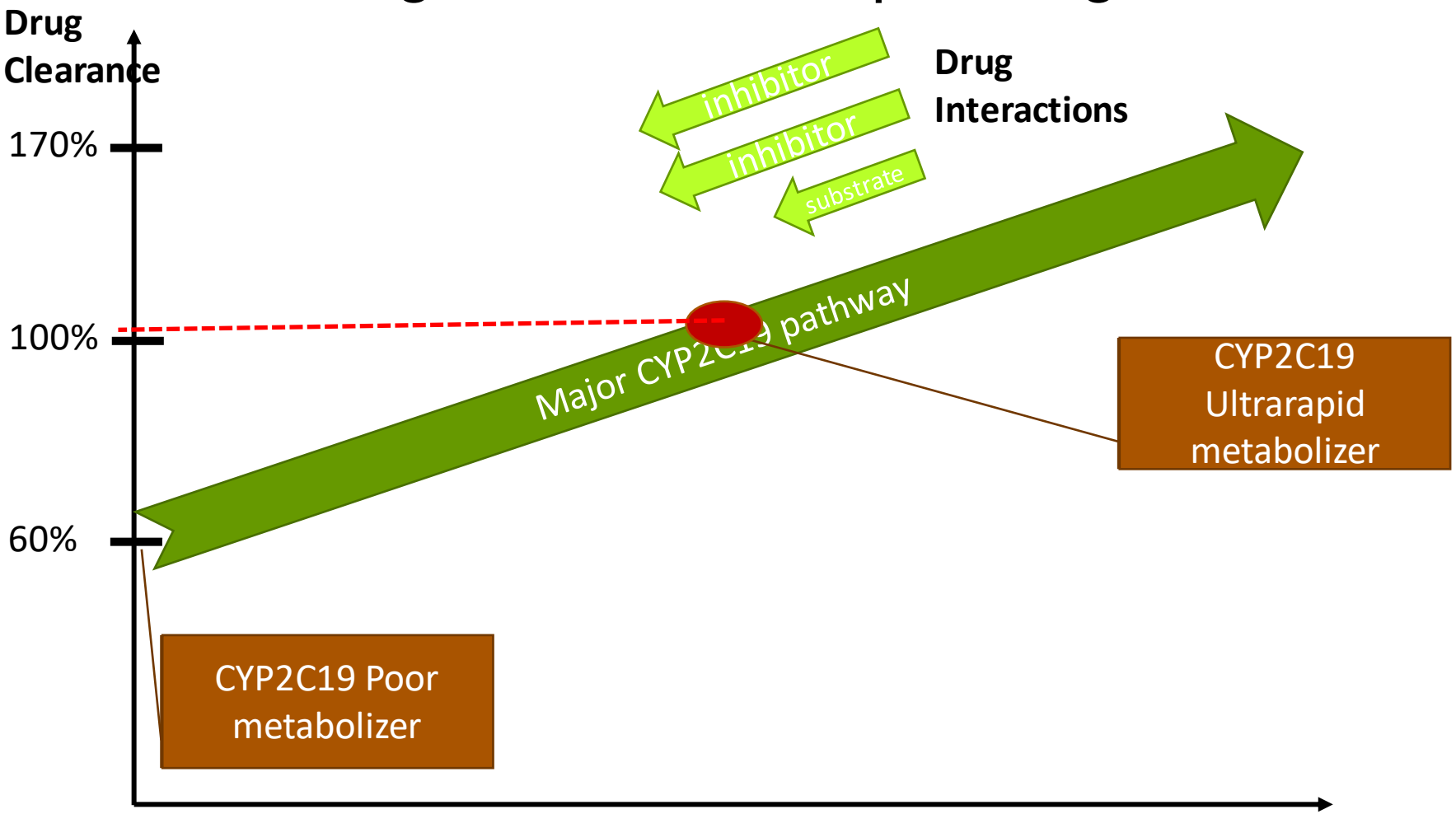
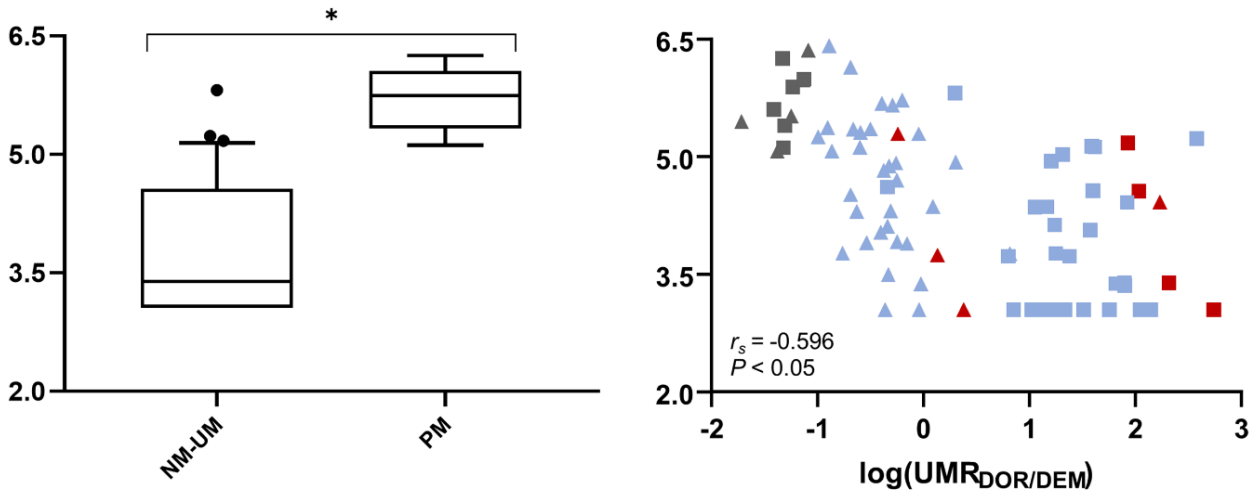


Quantitative Bestimmung der Arzneimittelclearance

- **Metabolomics** reveals biomarkers in human urine and plasma to predict cytochrome P450 2D6 (CYP2D6) activity.



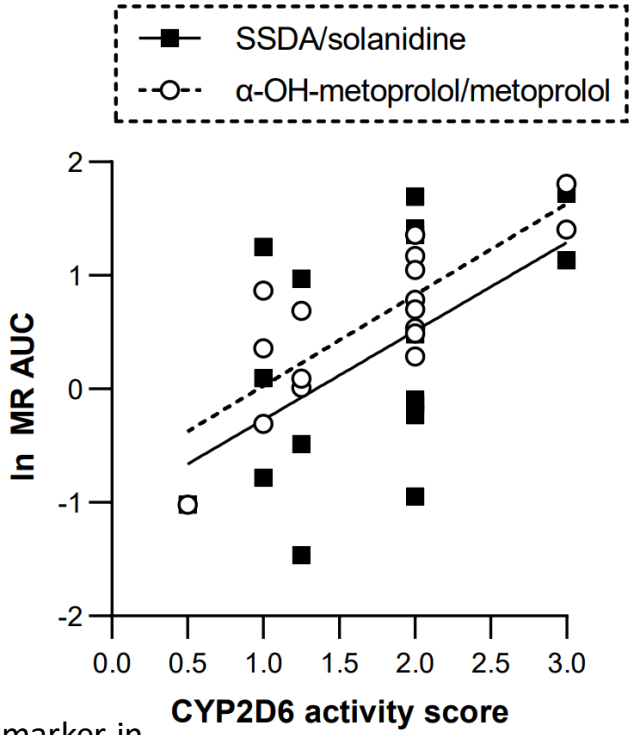
Magliocco G, Desmeules J, Matthey A, Quirós-Guerrero LM, Bararpour N, Joye T, Marcourt L, Queiroz EF, Wolfender JL, Gloor Y, Thomas A, Daali Y. Br J Pharmacol. 2021 Dec;178(23):4708-4725. doi: 10.1111/bph.15651.

CYP2D6 phenotyping

CYP2D6 activity predicted from pharmacogenetics:

CYP2D6 Activity score:

- Poor Metabolizer=0
- Intermediate Metabolizer=0.5-1.5
- Extensive Metabolizer=2
- Ultrarapid Metabolizer=3

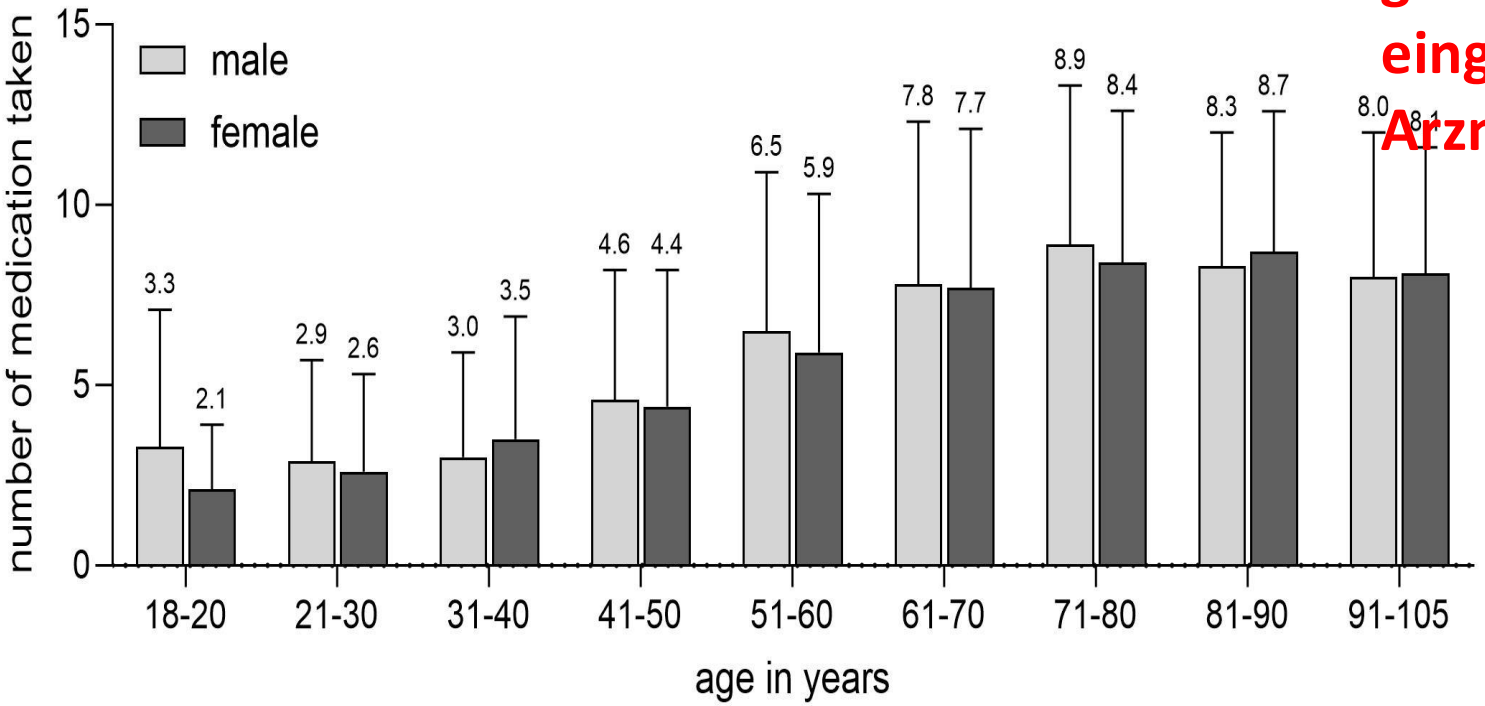


Nutrimetric validation of solanidine as dietary-derived CYP2D6 activity marker in vivo. J Müller, J Sarömba, P Ziegler, R Tremmel, J Rengelshausen, E Schaeffeler, K Just, M Schwab, T Kraus, JC Stingl, Clin Pharmacol Ther. 2023 Nov 16. doi: 10.1002/cpt.3106. Online ahead of print

	SSDA/ solanidine	α-OH-metoprolol/ metoprolol
Slope ± SE	0.78 ± 0.33	0.80 ± 0.15
r^2	0.27	0.65
p-value	0.0330, *	<0.0001, ****

Unerwünschte Arzneimittelwirkungen, die zu Krankenhausnotaufnahmen führten ADREDStudie

Mittlere Anzahl gleichzeitig eingenommener Arzneimittel: 7

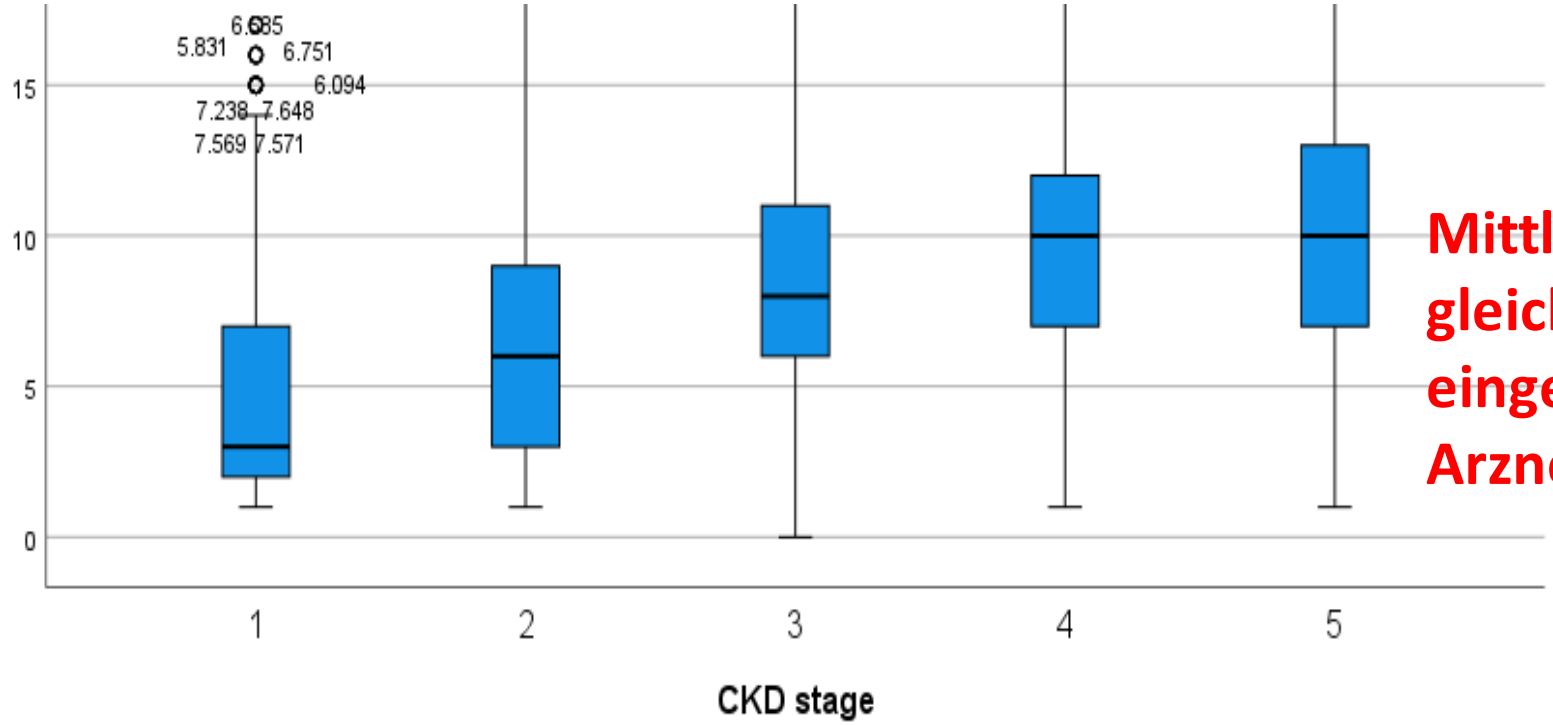


Schurig AM, …Stingl JC. Adverse Drug Reactions (ADR) and Emergencies. Dtsch Arztebl Int. 2018 Apr 13;115(15):251-258.

Anzahl der gleichzeitig eingenommenen Arzneimittel und Nierenfunktion

- Daten aus der ADRED Studie (n=7967 Fälle)

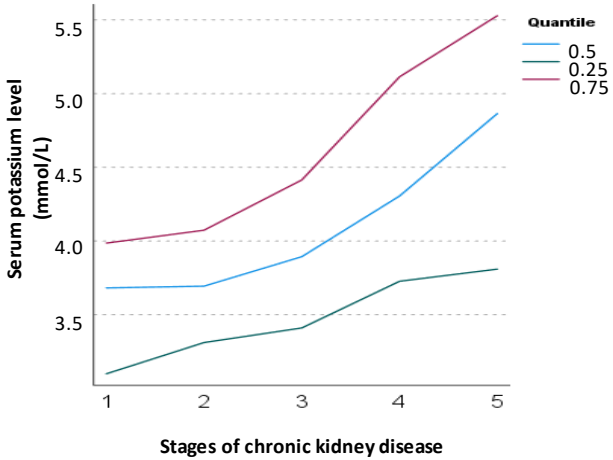
CKD stage	N
1	1383
2	2345
3	2289
4	768
5	328
Gesamt	7113



Mittlere Anzahl gleichzeitig eingenommener Arzneimittel: 10

Arzneimittelwechselwirkungen

- Interaktionen: Kalium-senkende und Kalium-sparende Arzneimittel
- N=1097 Patienten aus ADRED und Polypharmazieambulanz mit dokumentierten Kalium-Spiegeln und CKD stages



Model adjusted for sex, use of thiazides, of other low-ceiling diuretics, loop diuretics, aldosterone and potassium-sparing agents, ACE inhibitors/ ARBs, and number of other drugs.

Just K., et al. Influence of drugs on potassium levels in older, multi-medicated patients (article in submission)

Wechselwirkungen bei Polypharmazie: Arzneimitteleffekte auf Kaliumspiegel

- Kaliumsparende und Kaliumsenkende Diuretika
- Mit abnehmender Nierenfunktion kann die Kalium-Modulation von Arzneimitteln verändert sein

CKD

1
2
3
4
5

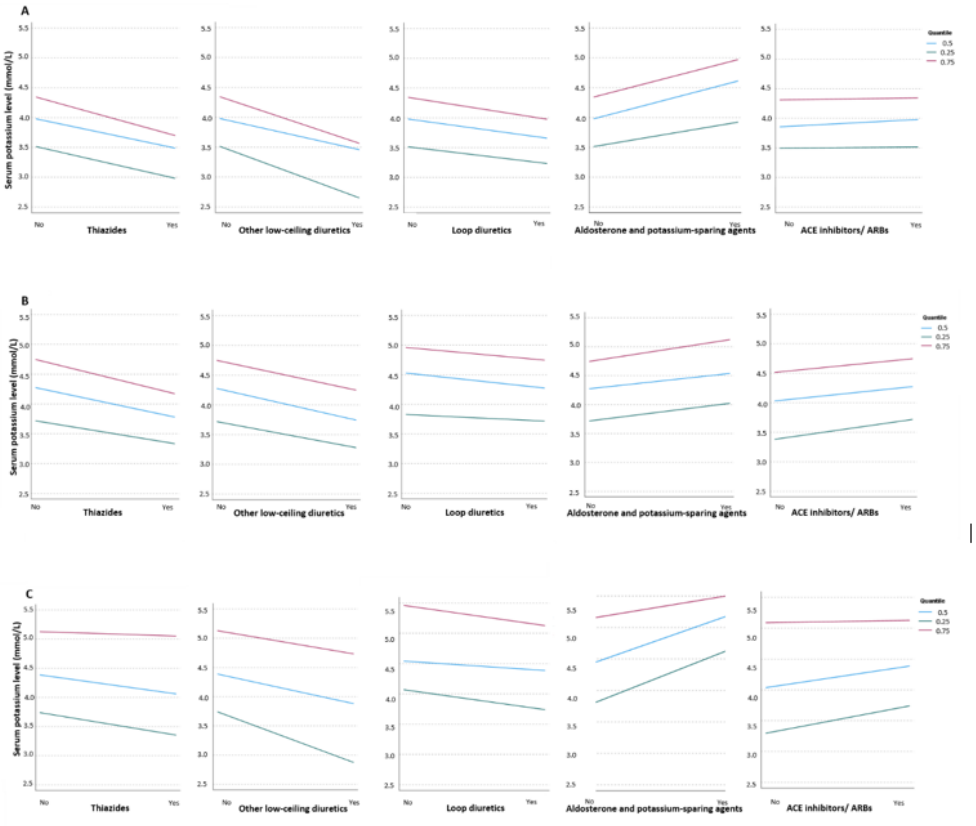


Figure 2. Estimation of drug effects on serum potassium levels according to use of drugs of interest stratified in patients with chronic kidney disease (CKD) stage 1 and 2 (A), CKD stage 3 (B), and CKD stage 4 and 5 (C)

Just K., et al. Influence of drugs on potassium levels in older, multi-medicated patients (article in submission)

Polypharmazie bei Niereninsuffizienz

- **Wechselwirkungen** zwischen Arzneimitteln verstärkt
- **Pharmakogenetik** spielt eine größere Rolle, wenn Nierenfunktion wegfällt
- **Pharmakovigilanz** nimmt an Bedeutung zu
- **Personalisierte Therapie und Dosierung**