UNIVERSITÄT BERN

Polypharmazie
(un) Sinn von vielen Medikamente

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Berliner DialyseSeminar

Berliner DialyseSeminar

Darlegung potentieller Interessenskonflikte

Der Inhalt des folgenden Vortrages ist Ergebnis des Bemühens um größtmögliche Objektivität und Unabhängigkeit.

Als Referent versichere ich, dass in Bezug auf den Inhalt des folgenden Vortrags **keine Interessenskonflikte** bestehen, die sich aus einem Beschäftigungsverhältnis, einer Beratertätigkeit oder Zuwendungen für Forschungsvorhaben, Vorträge oder andere Tätigkeiten ergeben.

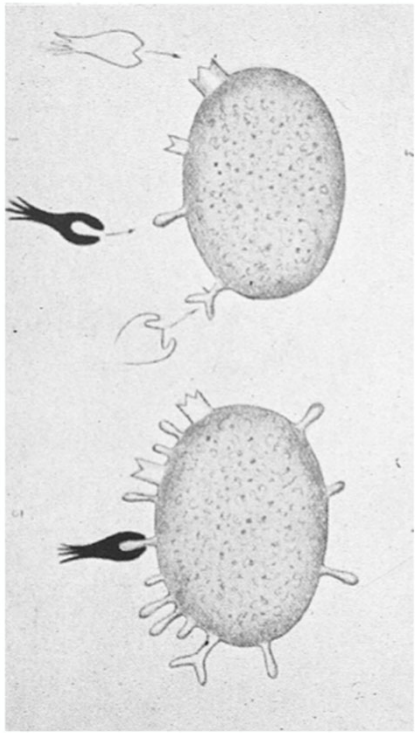
Poly-pharmazie

Viel

Circe Offering the Cup to Ulysses

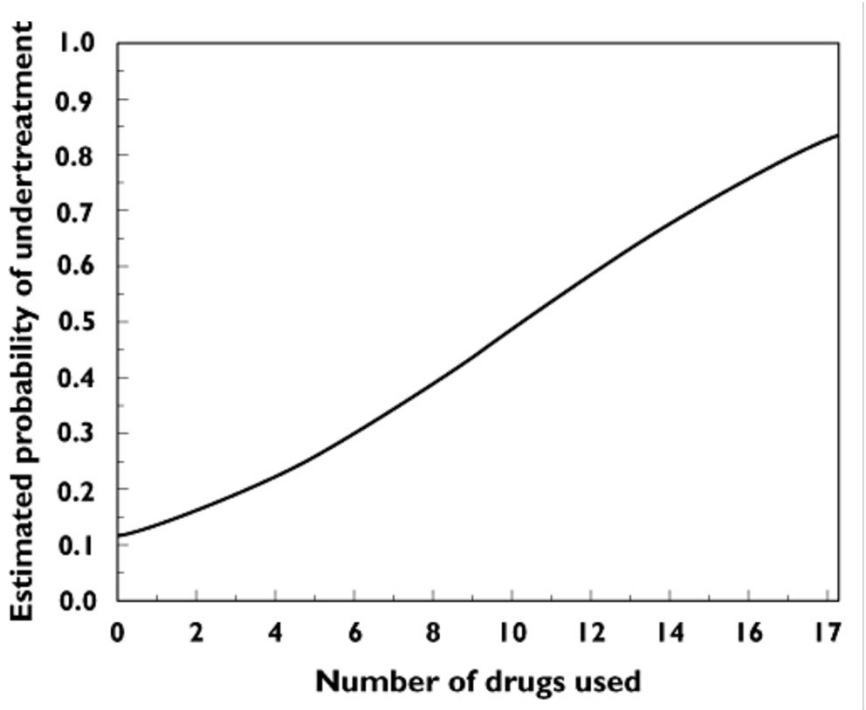
20. Jahrhundert

Zu viel



Die Zauberkugel

Polypharmazie: Ist *viel* immer *zu viel*?



Kuijpers MA et al. Br J Clin Pharmacol. 2008

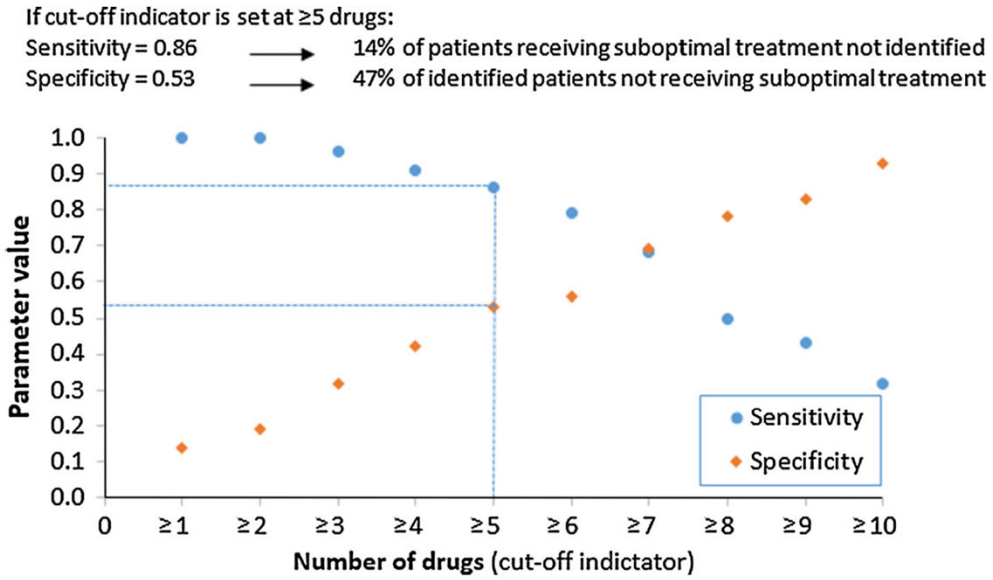
Forschung im Bereich Polypharmazie: **Herausforderungen**

Kein Definitionskonsens

Table 1 Breakdown of polypharmacy definitions according to the category of definition

Term	Numerical only	Numerical in a given duration of time or setting	Descriptive	Total number of definitions
Polypharmacy	81	9	9	99

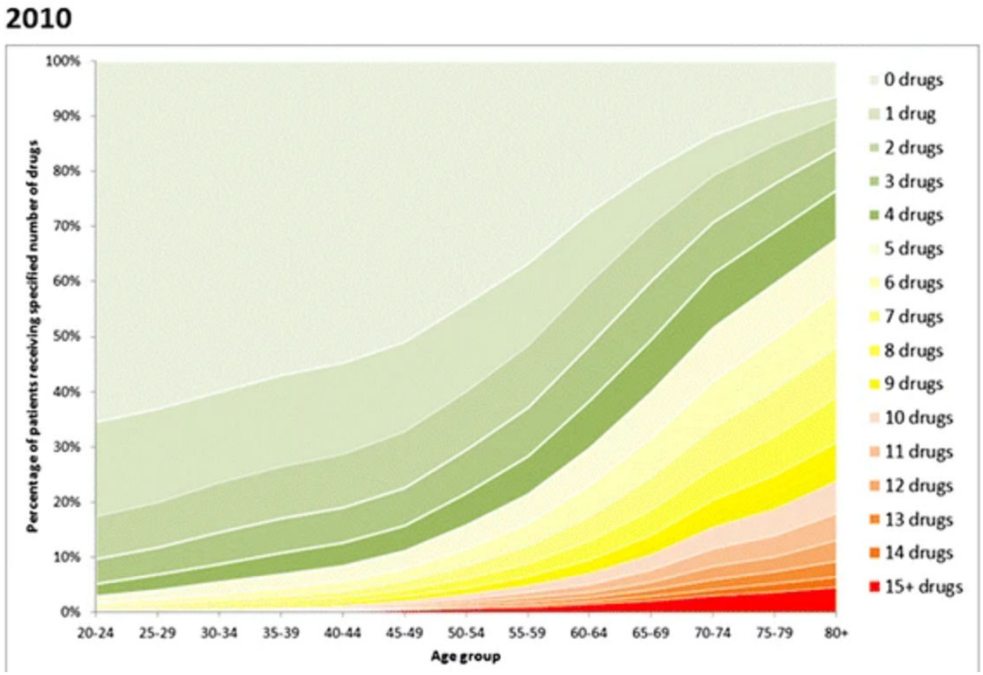
Number of medications	Number of studies
≥ 2	1
2 to 9	1
≥ 3	1
3 to 6	1
≥ 4	6
≥ 4 or ≥ 5	1
≥ 5	51
≥ 6	10
≥ 7	2
5 to 9	3
≥ 9	1
≥ 10	1



Adapted from Belfrage et al.

Forschung im Bereich Polypharmazie: **Herausforderungen**

Confounding

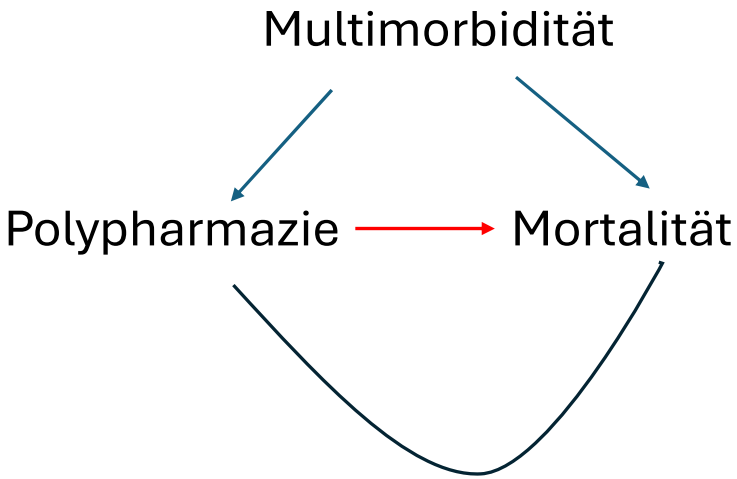


Guthrie et al. BMC Medicine (2015) 13:74

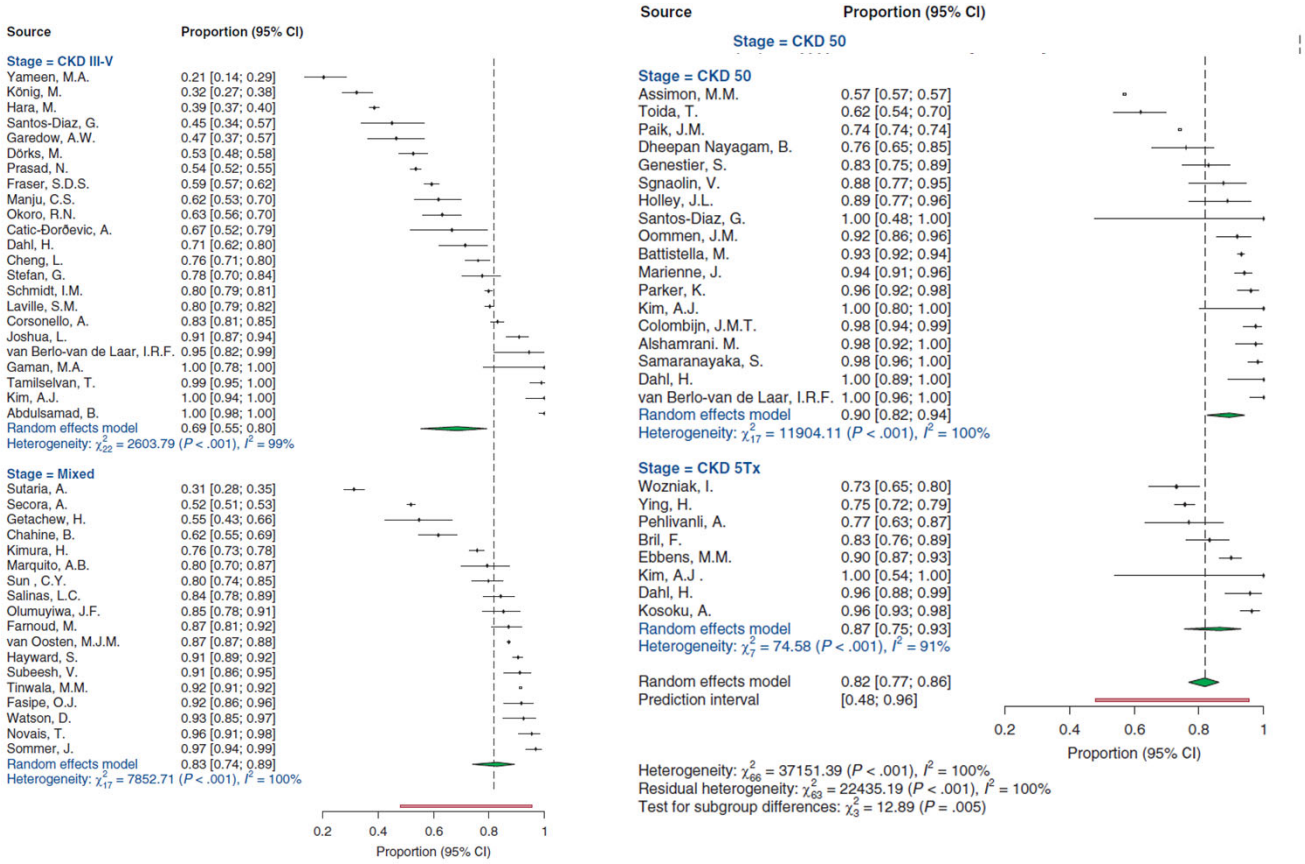
Comorbidities

62 % der Patienten über 65 Jahre mit einer häufigen chronischen Erkrankung haben mindestens eine zweite.

Salive ME et al, Epidemiol Rev. 2013



Die meisten Patienten mit CKD sind von Polypharmazie betroffen



Bei Dialysepatienten liegt die Prävalenz von Polypharmazie bei 89 %

Oosting, Ilse J. et al, Kidney360 5(6):p 841-850

Belastung durch Polypharmazie – The German chronic kidney disease study cohort

Table 1. Sample characteristics, comorbidities and medications by eGFR categories at baseline (n=5217).

Clinical characteristics	eGFR categories (ml/min/1.73²)				
	≥ 90, CKD stage G1 (n=233)	60-89, CKD stage G2 (n=883)	45-59, CKD stage G3a (n=1717)	30-44, CKD stage G3b (n=1865)	<30, CKD stage G4/5 (n=461)
Polypharmacy[d], n (%)					
Yes	144 (61.8)	649 (73.5)	1364 (79.4)	1599 (85.7)	422 (91.5)
No	89 (38.2)	234 (26.5)	353 (20.6)	266 (14.3)	39 (8.5)

Schmidt M. et al, Clinicl Kidney Journal, 2019

Prävalenz
80 %

Komorbiditäten (kardiovaskuläre Erkrankungen, Diabetes, Hypertonie und Dyslipidämie) **erhöhten signifikant die Wahrscheinlichkeit, Polypharmazie zu erhalten**

Blutdruck < 140/90 mmH ~ 50 %

Schneider MP et al, PLoS ONE 2018

Die Datenlage zu Polypharmazie und Gesundheitsoutcomes ist heterogen

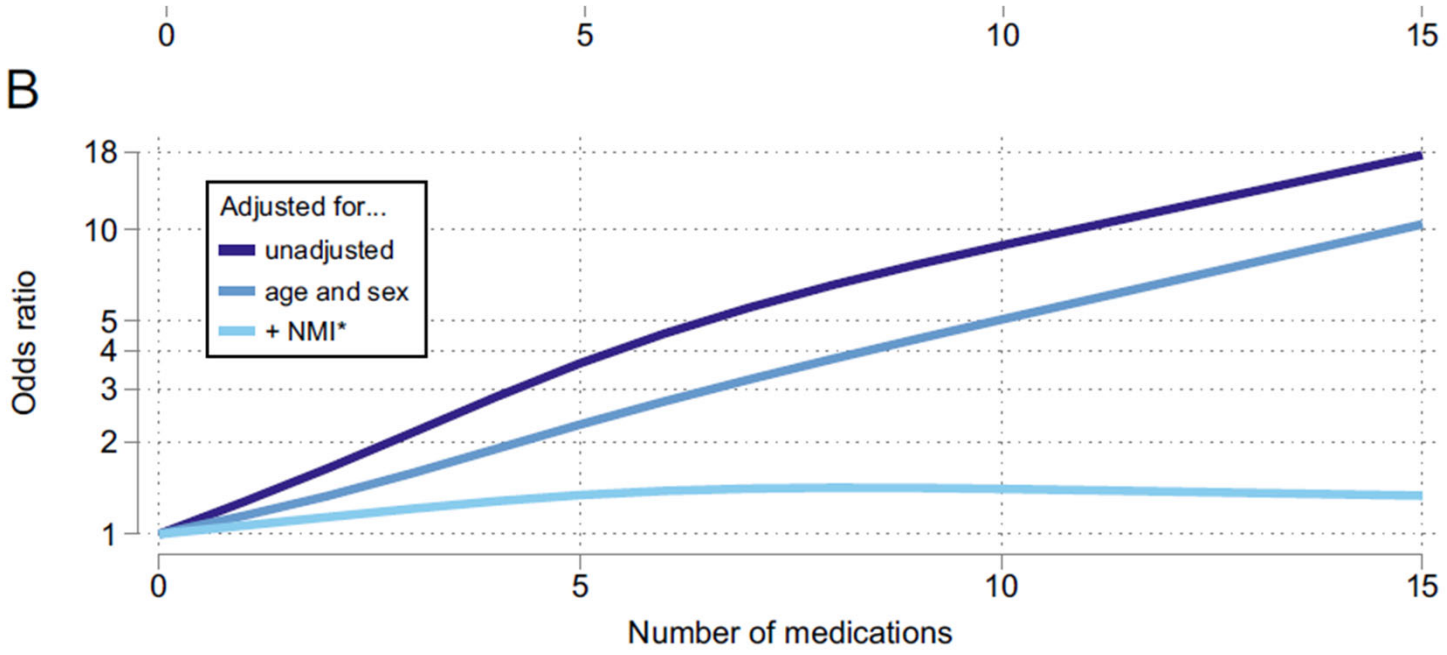
Health Outcomes Associated with Polypharmacy in Community-Dwelling Older Adults: A Systematic Review

Results—Of the total of 50 studies identified, the majority studies that were rated as "good" in terms of their adjustment for comorbidity demonstrated relationships between polypharmacy and a range of outcomes, including falls/fall outcomes/fall risk factors; adverse drug events, hospitalization, mortality, and measures of function and cognition. However, a number of these studies failed to demonstrate associations, as did a substantial proportion of those studies rated as "fair" or "poor."

Fried TR. et al., J Am Geriatr Soc. 2014

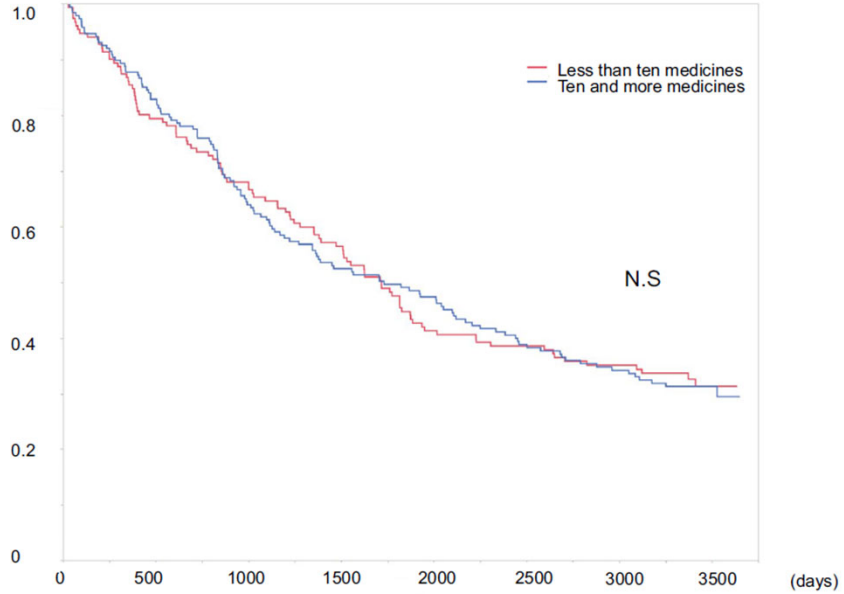
Ist Polypharmazie *per se* die Ursache für unerwünschte Wirkungen, oder ist sie ein Indikator für Komorbiditäten und/oder die Einnahme von Medikamenten, die unerwünschte Effekte verursachen?

Ergebnisse zu Polypharmazie und Mortalität mit Vorsicht betrachten



Bjørk E et al., Clin Invest. 2025

Polypharmazie korreliert sich nicht mit Gesamtmortalität bei Hämodialysepatienten



Kitamura M et al, Sci Rep 2021

Gesamtanzahl der Medikamente HR 1.01 (95% CI 0.97–1.05), p = 0.63

Polypharmacy at admission

	Drug prescrip-tions	Events *n* (%)	Adjusted HR[a] (95% CI)
All-cause mortality	≥6	15 (15.0%)	2.34 (0.52–10.60)
	<6	5 (9.6%)	Ref
All-cause hospitalization	≥6	51 (51.0%)	1.12 (0.70–2.00)
	<6	20 (38.5%)	Ref

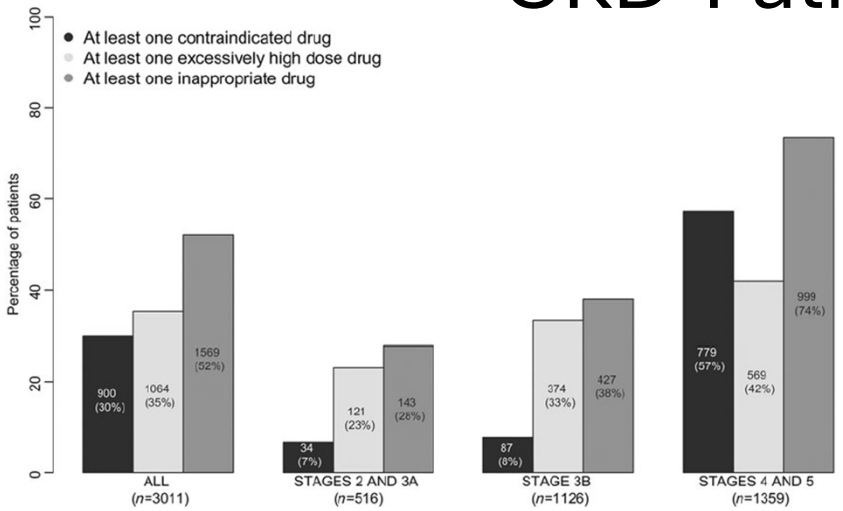
At discharge – Hospitalization HR 2.81 (1.46–5.41)

Toida T et al, Clin Exp Nephrol. 2021

Anzahl nicht-essentieller Medikamente HR: 1.06 (95% CI 1.01–1.10), p = 0.009

Die Verschreibung essenzieller Medikamente sollte Priorität haben (z. B. PPIs)

Unadequäte Medikamentenverschreibungen und unerwünschte Arzneimittelwirkungen sind bei CKD-Patienten häufig

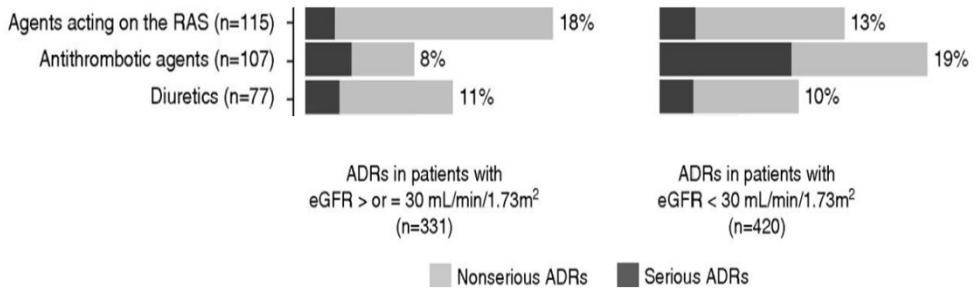


Laville SM et al., Br J Clin Pharmacol 2018

	Start of PD
Number of patients with medication claims	3760
Number of patients with PIPM exposure	1053
Percent exposed to PIPM	28.0%
95% confidence interval	26.6–29.5

HD 21.9%

Almodovar AS et al., Pharmacotherapy 2025

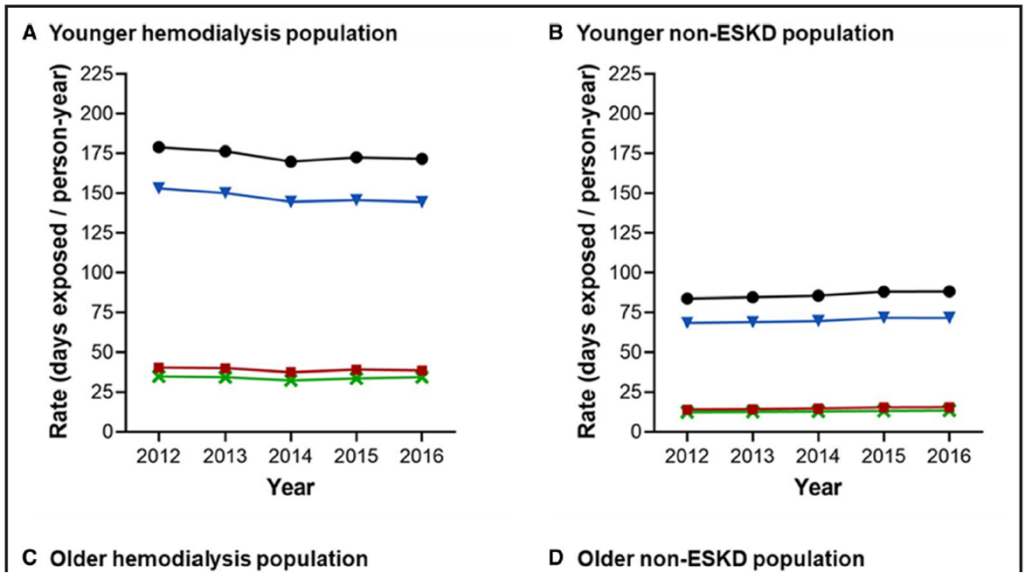


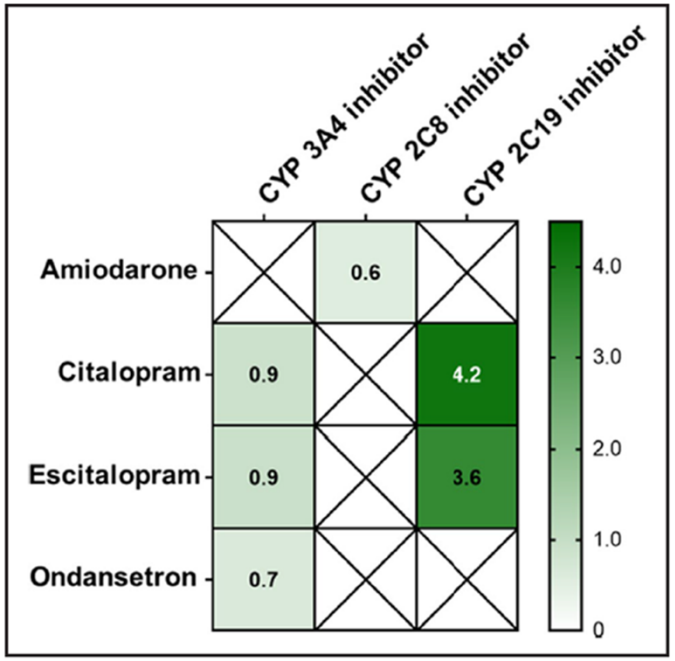
3.000 Patienten, 2 Jahre Follow-up

- 751 UAW, 150 schwerwiegende
- AKI und Blutungen – die häufigsten UAWs

Laville SM et al., CKD-REIN Study Group, CJASN 2020

HD-Patienten: höhere Nutzung von QT-verlängernden Medikamenten als Allgemeinbevölkerung

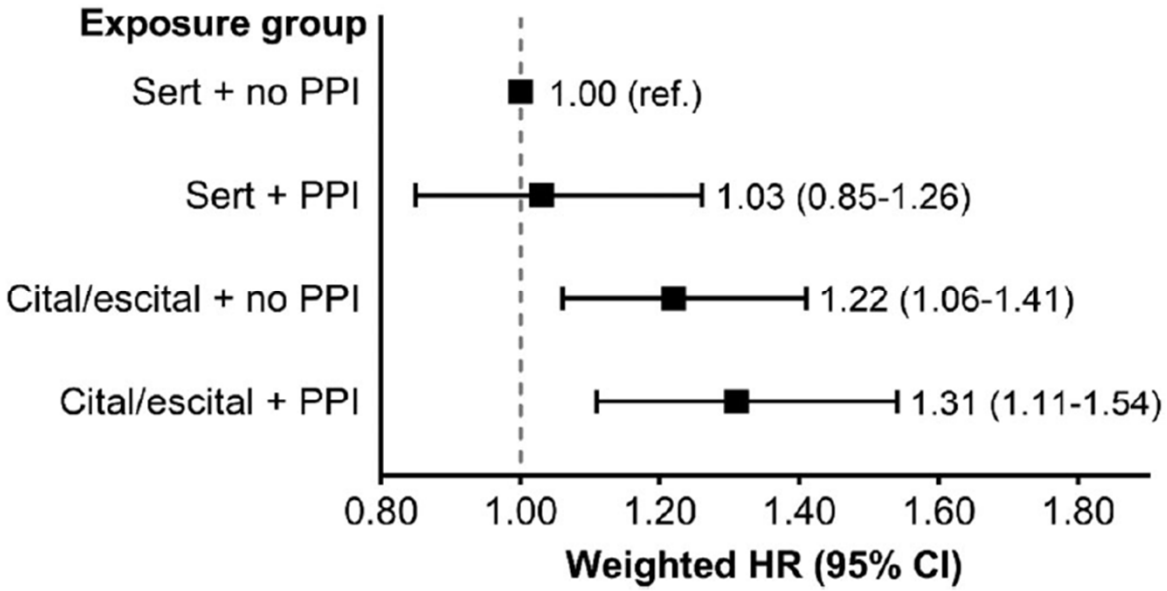




Medikamenteninduzierter plötzlicher Herztod- Vermeidbar!

Assimon MM et al., J Am Heart Assoc 2020

Protonenpumpeninhibitoren können das Risiko eines Citalopram- und Escitalopram-assoziierten plötzlichen Herztods (SCD) bei HD-Patienten erhöhen



Assimon MM et al., Pharmacoepidemiol Drug Saf. 2022

Arzneimittelinteraktion zwischen Calciumkanalblockern und Clarithromycin - akutes Nierenversagen (AKI) Risiko

Table 2. Thirty-Day Outcomes Assessed Using Hospital-Based Diagnosis Codes and All-Cause Mortality

	No. of Events (%)[a]		Absolute Risk Difference (95% CI), %	NNH (95% CI)[c]	OR (95% CI)	
	Clarithromycin (n = 96 226)	Azithromycin (n = 94 083)[b]			Unadjusted	Adjusted[d]
Acute kidney injury	420 (0.44)	208 (0.22)	0.22 (0.16-0.27)	464 (374-609)	1.98 (1.68-2.34)	2.03 (1.72-2.41)
Hypotension	111 (0.12)	68 (0.07)	0.04 (0.02-0.07)	2321 (1406-6416)	1.60 (1.18-2.16)	1.63 (1.21-2.22)
Mortality	984 (1.02)	555 (0.59)	0.43 (0.35-0.51)	231 (195-284)	1.74 (1.57-1.93)	1.74 (1.57-1.94)

Gandhi S et al., JAMA 2013

Vermeidbar!

QOL

Interaction with health care workers and social environment regarding medication
"That doctor looks at which medication is good for me… "Then that will be all right", is what I say. Doctors know better than I do." (R29, male, 60 y, 19 medications, 23 pills)
"The doctor ordered me to." (R2, female, 70 y, 16 medications, 10 pills)
"From time to time, I think 'swallow this yourself just once, so you know how it feels' because sometimes it is so difficult to explain." (R1, male, 55 y, 15 medications, 21 pills)
"I want to know what pills I am taking, and for what, and if they don't work, I sound the alarm because I do not want to swallow anything I do not need to." (R18, female, 76 y, 16 medications, 14 pills)
"I don't think I am a guinea pig, just take medication and wait and see if it works." (R23, male, 59 y, 11 medications, 12 pills)

10.1016/
j.xkme.2023.100749

Maßnahmen bei Polypharmazie → bessere Gesundheit?
Zu wenig Evidenz

JAMA Network | Open

Original Investigation | Pharmacy and Clinical Pharmacology

Cumulative Update of a Systematic Overview Evaluating Interventions Addressing Polypharmacy

Michelle S. Keller, PhD, MPH; Nabeel Qureshi, MPH; Allison M. Mays, MD, MS; Catherine A. Sarkisian, MD, MSHS; Joshua M. Pevnick, MD, MSHS

FINDINGS Fourteen SRs were identified (3 from the previous overview), 7 of which included meta-analyses, representing 179 unique published studies. Nine SRs examined medication-related process outcomes (low to very low evidence quality). Systematic reviews using pooled analyses found significant reductions in the number of PIMs, potential prescribing omissions, and total number of medications, and improvements in medication appropriateness. Twelve SRs examined clinical and functional outcomes (very low to moderate evidence quality). Five SRs examined mortality; all mortality meta-analyses were null, but studies with longer follow-up periods found greater reductions in mortality. Five SRs examined falls incidence; results were predominantly null save for a meta-analysis in which PIMs were discontinued. Of the 8 SRs examining quality of life, most (7) found predominantly null effects. Ten SRs examined hospitalizations and readmissions (very low to moderate evidence quality) and 4 examined emergency department visits (very low to low evidence quality). One SR found significant reductions in hospitalizations and readmissions among higher-intensity medication reviews with face-to-face patient components. Another meta-analysis found a null effect. Of the 7 SRs without meta-analyses for hospitalizations and readmissions, all had predominantly null results. Two of 4 SRs found reductions in emergency department visits. Two SRs examined acceptability (very low evidence quality), finding wide variation in the adoption of polypharmacy-related interventions.

Polypharmazie-bezogene Interventionen:

- Überprüfung der Medikamentenliste, Medikamentenliste + Adherence, Berücksichtigung des Krankheits kontexts, Deprescribing, Pharmakogenomik, PIMs, electronic tools etc

Outcomes: Mortalität, Gebrechlichkeit, kardiovaskuläre Ereignisse etc.

Table 3. Patient Outcomes of Deprescription.

	Intervention (n = 70)	Control (n = 70)	*P* value
Readmissions	12 (17.1%)	15 (21.4%)	.520
Active PIMs at discharge (median, IQR)	2 (2-4)	3 (2-4)	.367
Adverse event post-discharge	22 (31.4%)	23 (32.9%)	.856
Days to adverse event post-discharge (median, IQR)	10 (6.7-23.2)	9 (4-14)	.295
Patients with an ADE	3 (4.3%)	2 (2.9%)	.649
GI bleed ADE attributed to antiplatelet(s)	2 (66.7%)	1 (50%)	.559

Moryousef et al., Can J Kidney Health Dis 2022

Polypharmazie

Adäquat

Adelboden 2025, Bern

WHO : Rationales Verschreiben

oder

Inadäquat

Avalanche in the Vallée de la Sionne 1999

WHO: Irrationales Verschreiben

WHO: Adäquate Polypharmazie sollte **individuel** berücksichtigt werden bei jeder neuen Therapie und beim Übergang zwischen Versorgungseinrichtungen

Take home message

Sind viele Medikamente zu viele Medikamente?

Grundsätzlich nicht, aber das Risiko dafür besteht