SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA
68° CONGRESSO NAZIONALE SIGG
Ritorno al futuro
FIRENZE, 13-16 DICEMBRE 2023
PALAZZO DEI CONGRESSI

Prescrizioni inappropriate in pazienti anziani con IRC: studio nazionale multicentrico cross-sectional

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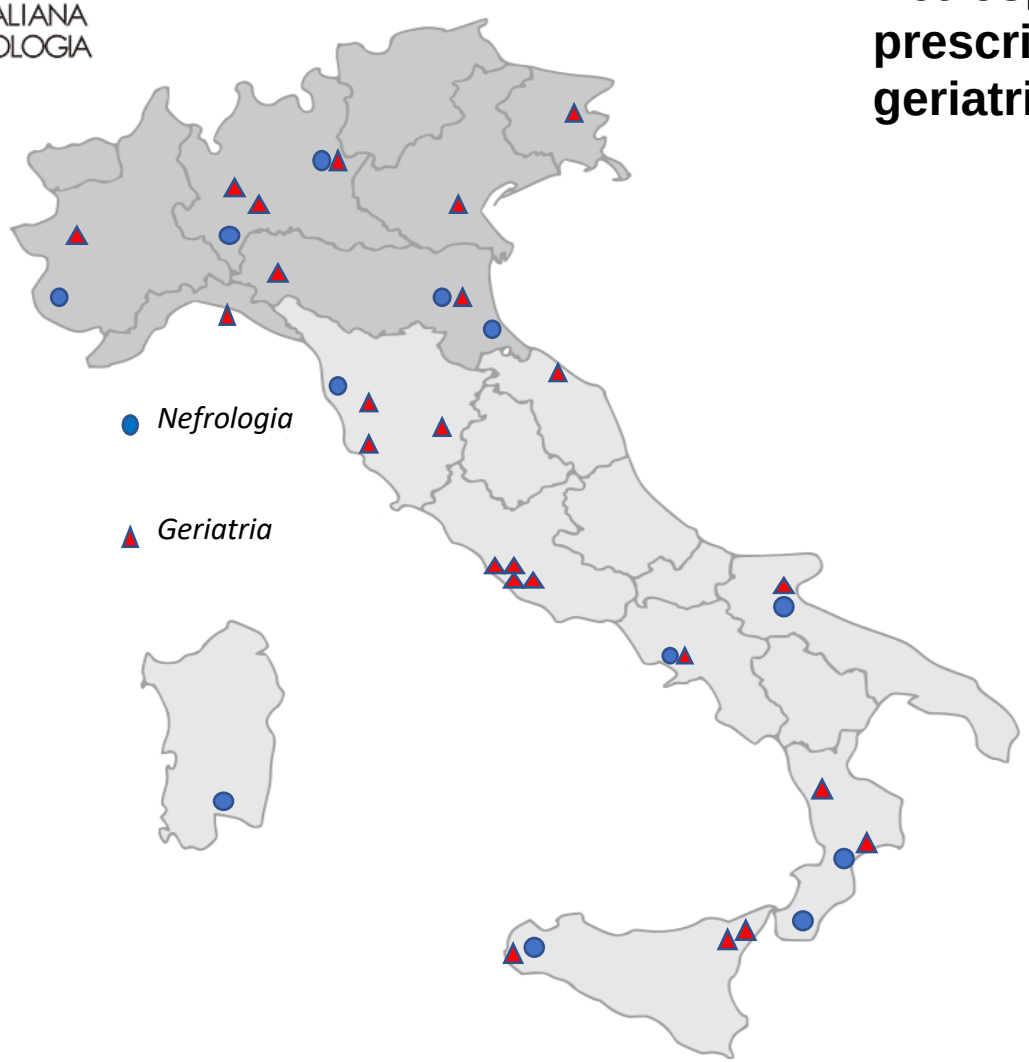
SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA

SIN-GFR Società Italiana Nefrologia

Retrospective study of CKD reporting and medication prescribing/dosing in older patients discharged from geriatric and nephrology unit in Italy



Obiettivi primari

- Prevalenza di omessa diagnosi di MRC nelle UO di Geriatria
- Prevalenza di inappropriata prescrizione/dosaggio di farmaci ad eliminazione renale al momento della dimissione in UO di Nefrologia e Geriatria
- Prevalenza di omessa prescrizione di farmaci potenzialmente appropriati al momento della dimissione in UO di Nefrologia e Geriatria

Obiettivi secondari

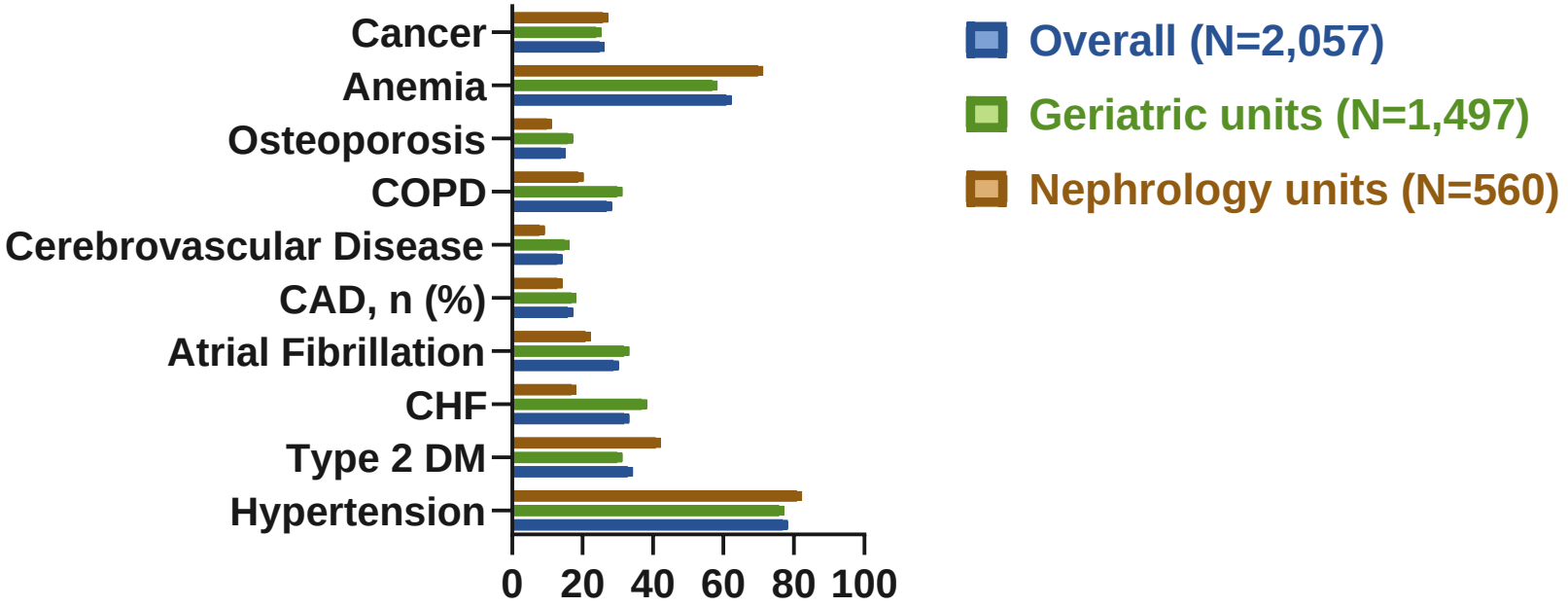
- Confronto fra diverse equazioni per la stima della eGFR nell'individuazione di inappropriata prescrizione/dosaggio di farmaci ad eliminazione renale
- Studio dei correlati di incremento dei livelli di creatinina (riduzione eGFR) tra ingresso in ospedale e dimissione
- Studio dell'impatto che l'incremento dei livelli di creatinina (riduzione eGFR) tra ingresso in ospedale e dimissione determina sull'appropriatezza prescrittiva.

frontiers | Frontiers in Pharmacology

TYPE Original Research
PUBLISHED 14 October 2022
DOI 10.3389/fphar.2022.996042

A focus on CKD reporting and inappropriate prescribing among older patients discharged from geriatric and nephrology units throughout Italy: A nationwide multicenter retrospective cross-sectional study

	Overall population (n=2,057)	Geriatric Units (n=1,497)	Nephrology Units (n=560)	p
Age, mean(SD)	82.8(7.8)	84.0(7.7)	79.4(7.3)	<0.001
Female sex, n (%)	987 (48.0)	753 (50.3)	234 (41.8)	<0.001
BMI, mean(SD)	26.6(5.6)	26.2(5.5)	27.5(5.6)	<0.001
CKD under-reporting	761 (50.8)	710 (71.1)	51 (10.2)	<0.001



Factors associated to CKD under-reporting

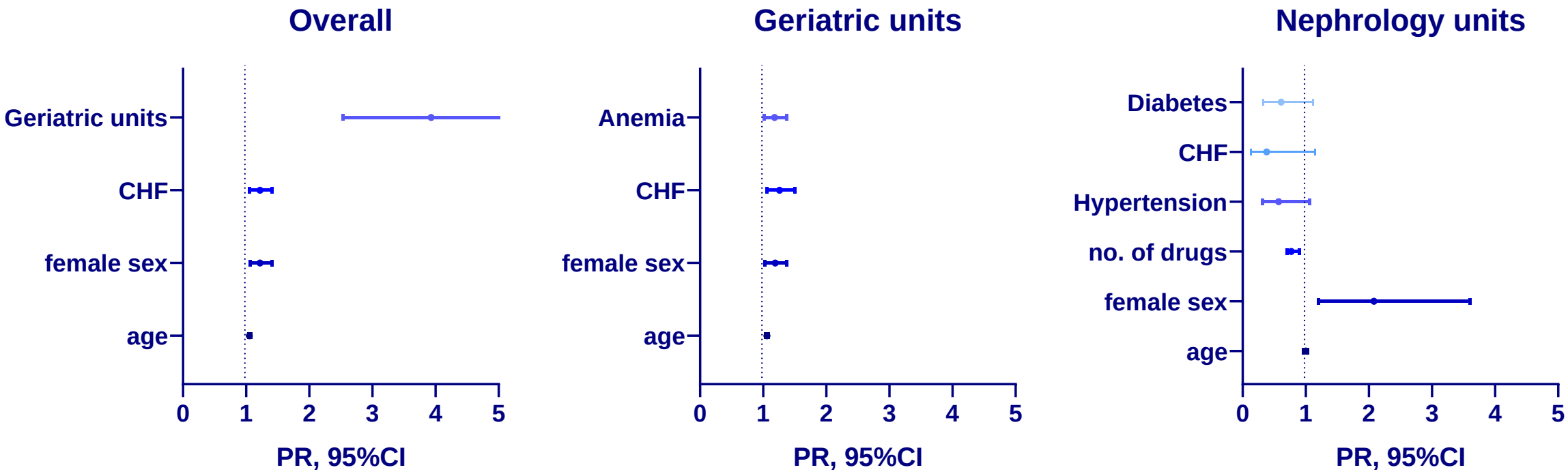
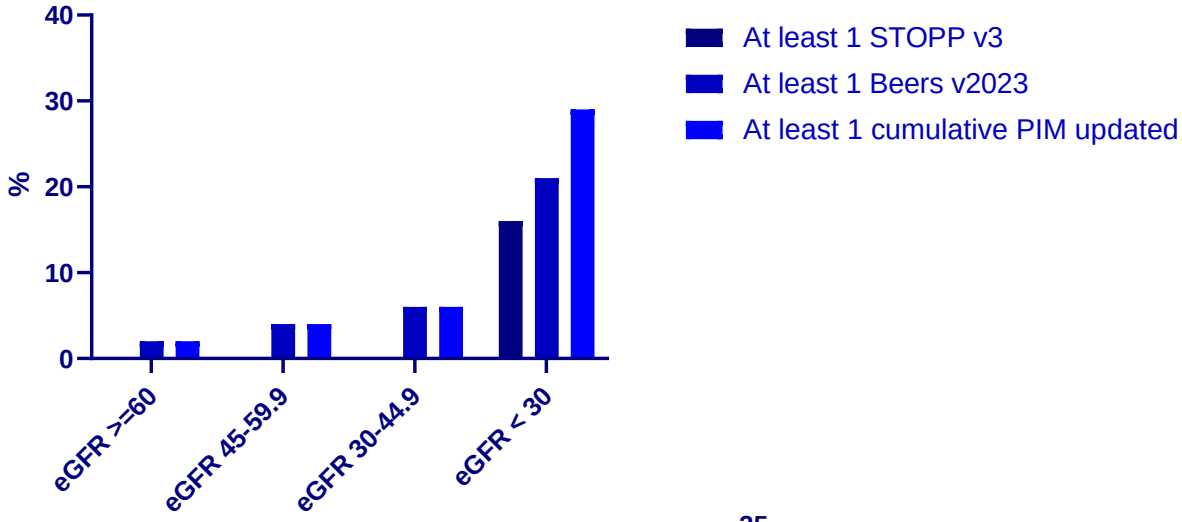


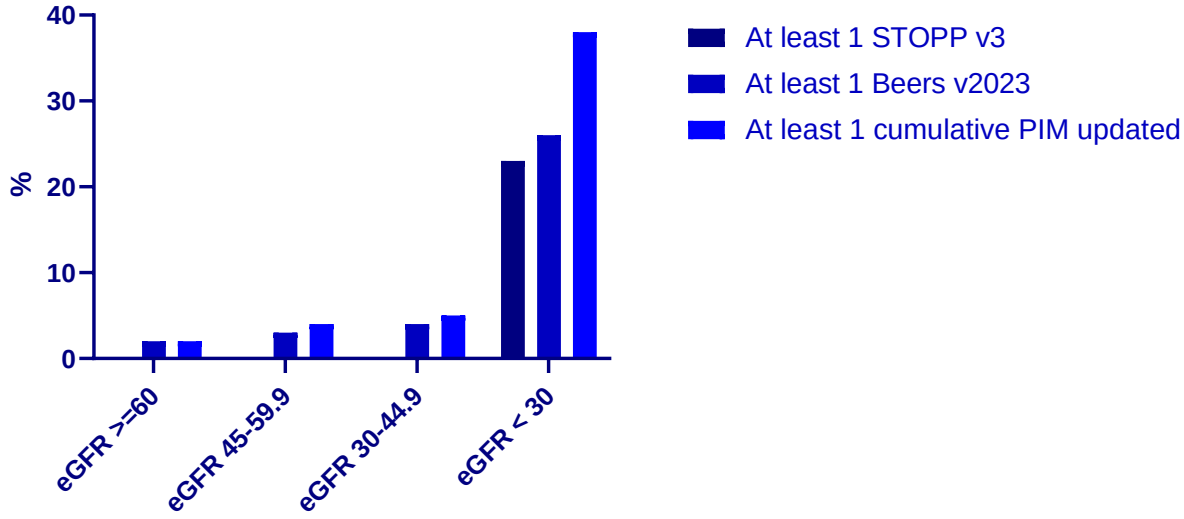
TABLE 3 Prevalence of STOPP and/or Beers PIMs and cumulative PIMs in the study population and different settings.

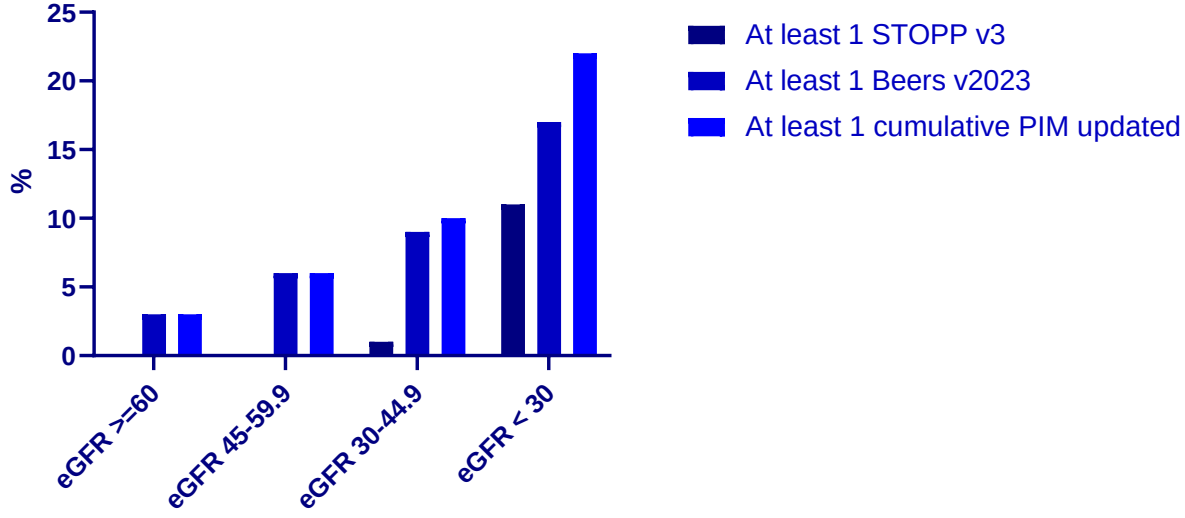
BIS eGFR, *n* (%)*	STOPP and/or Beers PIM	Geriatric STOPP and/or Beers PIMs	Nephrology STOPP and/or Beers PIMs	p^b
≥60	12 (2.5)	10 (2.4)	2 (3.7)	
45–59.9	21 (4.2)	16 (3.8)	5 (6.2)	
30–44.9	57 (9.9)	33 (7.7)	24 (16.3)	
<30	120 (24.5)	61 (28.5)	59 (21.4)	
Total, *n* (%)*	210 (10.2)	120 (8.0)	90 (16.2)	<0.001
p^a	<0.001	<0.001	<0.001	
	All PIM	Geriatric PIMs	Nephrology PIMs	
≥60	18 (3.7)	15 (3.5)	3 (5.6)	
45–59.9	33 (6.5)	22 (5.2)	11 (13.7)	
30–44.9	65 (11.3)	39 (9.1)	26 (17.7)	
<30	264 (54.0)	98 (45.8)	166 (60.4)	
Total, *n* (%)**	380 (18.5)	174 (11.7)	206 (37.0)	<0.001
p^a	<0.001	<0.001	<0.001	

*Percentages were calculated on the total number of patients belonging to each CKD stage; p^a of the comparisons among prevalence of PIM across CKD stages; p^b of the comparisons between prevalence of global PIM in nephrology and geriatric units.

Updated version of PIMs criteria







	At least one STOPP and/or Beers PIM		At least one cumulative PIM	
	Age- and sex-adj PR (95% CI)	Fully adj PR (95%CI)	Age- and sex-adj PR (95% CI)	Fully adj PR (95%CI)
Age	1.00 (0.99–1.02)	1.00 (0.97–1.02)	0.99 (0.97–1.00)	0.98 (0.96–1.00)
Female sex	0.97 (0.75–1.26)	0.97 (0.72–1.31)	0.97 (0.84–1.13)	1.00 (0.76–1.31)
BMI ≥25	1.18 (0.83–1.68)	—	1.24 (0.86–1.61)	—
Number of drugs	1.14 (1.09–1.20)	1.05 (1.01–1.10)	1.22 (1.16–1.27)	1.14 (1.09–1.19)
Hypertension	1.20 (0.86–1.68)	—	1.33 (1.05–1.69)	1.19 (0.84–1.69)
CAD	0.92 (0.64–1.31)	—	0.94 (0.77–1.15)	—
Atrial fibrillation	1.52 (1.17–1.98)	1.41 (1.03–1.44)	1.22 (1.05–1.42)	1.35 (1.01–1.81)
CHF	1.30 (1.00–1.68)	—	1.15 (1.00–1.32)	—
Diabetes	2.13 (1.56–2.91)	1.79 (1.31–2.45)	1.83 (1.40–2.40)	1.61 (1.21–2.13)
Cerebrovascular disease	0.99 (0.68–1.44)	—	0.95 (0.77–1.19)	—
Anemia	1.70 (1.26–2.30)	1.05 (0.75–1.38)	1.60 (1.22–2.08)	1.05 (0.77–1.41)
Under-reported CKD diagnosis	0.94 (0.71–1.25)	—	0.65 (0.50–0.84)	0.96 (0.68–1.35)
Nephrology setting	2.30 (1.65–3.21)	1.02 (0.71–1.45)	4.69 (3.61–6.09)	1.62 (1.14–2.31)
eGFR stage				
≥60	1	1	1	1
45.59.9	1.69 (0.86–3.31)	1.50 (0.74–3.06)	1.44 (0.98–2.11)	1.51 (0.81–2.81)
30–44.9	3.81 (2.08–6.98)	3.46 (1.85–6.47)	1.82 (1.09–3.01)	2.35 (1.34–4.13)
<30	7.92 (3.64–17.22)	8.66 (4.65–16.12)	2.41 (1.08–5.38)	14.01 (7.36–26.72)

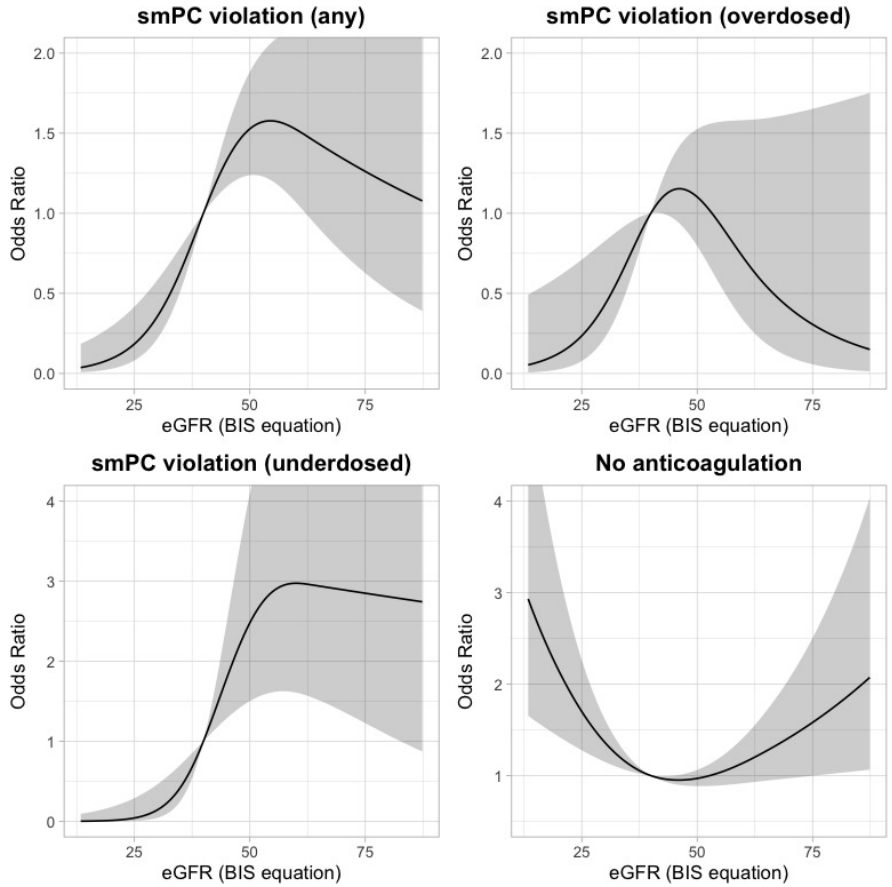
Prescriptive appropriateness of direct oral anticoagulants in older subjects with atrial fibrillation discharged from acute medical wards. N=609

submitted

Inappropriateness criteria	N	% on DOAC
smPC violations (any)	**63**	**31%**
smPC inappropriate prescriptions (prescribed even if not recommended)	3	1%
smPC overdosed (higher dose than recommended)	27	13%
smPC underdosed (lower dose than recommended)	34	17%
Explicit list of potentially inappropriate medications (any)	**98**	**48%**
STOPP C3. Direct thrombin inhibitors or factor Xa inhibitors with concurrent significant bleeding risk, i.e. bleeding diathesis or recent spontaneous bleeding	11	5%
STOPP C5. Aspirin in combination with direct thrombin inhibitor or factor Xa inhibitors in patients with chronic atrial fibrillation without a clear indication for aspirin (no added benefit from aspirin)	-	-
STOPP C6. Antiplatelet agents with direct thrombin inhibitor or factor Xa inhibitors in patients with stable coronary, cerebrovascular or peripheral arterial disease without a clear indication for anticoagulant therapy (no added benefit from dual therapy)	-	-
STOPP C10. NSAID and vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in combination (risk of gastrointestinal bleeding)	-	-
STOPP E2 and BEERS19. Direct thrombin inhibitors (e.g. dabigatran) if eGFR < 30 ml/min/1.73m2 (risk of bleeding)	2	1%
STOPP E3 and BEERS19. Factor Xa inhibitors (e.g. rivaroxaban, apixaban) if eGFR < 15 ml/min/1.73m2 (risk of bleeding)	1	0.5%
BEERS 2019. Dabigatran and Rivaroxaban: increased risk of gastrointestinal bleeding compared with warfarin and reported rates with other DOACs when used for long-term treatment of VTE or atrial fibrillation in adults ≥75y	90	44%
Pharmacokinetic drug-drug interactions (any)	**37**	**18%**
Involving Dabigatran	15	7%
Involving Apixaban	14	7%
Involving Rivaroxaban	6	3%
Involving Edoxaban	2	1%

	smPC violations			No Anticoagulation
	Any	*Overdosage*	*Underdosage*	
Univariable	**OR (95%CI), *p***			
Age, years	0.97 (0.94-1.01), 0.14	*0.93 (0.88-0.98), <.01*	1.02 (0.97-1.07), 0.50	*1.02 (1.00-1.05), 0.05*
Sex, female	0.79 (0.46-1.34), 0.38	0.99 (0.46-2.17), 0.98	0.58 (0.28-1.18), 0.14	0.86 (0.62-1.19), 0.36
BMI, kg/m^2	*1.05 (1.01-1.10), 0.02*	*1.08 (1.01-1.15), 0.02*	1.04 (0.97-1.10), 0.22	*0.94 (0.90-0.98), <.01*
Admitting ward, nephrology vs geriatrics	*0.39 (0.15-0.87), 0.03*	0.89 (0.29-2.23), 0.82	*0.12 (0.01-0.55), 0.04*	1.19 (0.79-1.77), 0.40
Arterial hypertension	0.88 (0.48-1.76), 0.71	1.39 (0.52-4.79), 0.55	0.62 (0.29-1.43), 0.23	0.72 (0.48-1.08), 0.11
Diabetes mellitus	1.10 (0.62-1.89), 0.74	0.73 (0.28-1.69), 0.49	1.61 (0.77-3.26), 0.19	1.20 (0.85-1.70), 0.30
CHF	0.84 (0.49-1.42), 0.50	0.67 (0.30-1.45), 0.31	1.16 (0.58-2.41), 0.67	*0.62 (0.45-0.86), <.01*
COPD	*1.97 (1.15-3.36), 0.01*	1.56 (0.69-3.40), 0.27	*2.50 (1.23-5.10), 0.01*	0.95 (0.67-1.34), 0.77
CAD	*0.38 (0.14-0.84), 0.03*	0.47 (0.11-1.36), 0.22	0.37 (0.09-1.06), 0.10	1.17 (0.79-1.74), 0.43
Cerebrovascular disease	0.90 (0.39-1.87), 0.80	1.08 (0.31-2.89), 0.90	0.38 (0.06-1.30), 0.19	0.87 (0.54-1.38), 0.56
Cancer	0.63 (0.31-1.20), 0.19	*0.23 (0.04-0.80), 0.05*	1.16 (0.50-2.46), 0.72	*1.79 (1.24-2.60), <.01*
Osteoporosis	0.48 (0.16-1.12), 0.12	-[£]	1.03 (0.34-2.53), 0.95	1.27 (0.81-1.99), 0.30
Anaemia	*0.34 (0.19-0.58), <.01*	*0.31 (0.14-0.68), <.01*	0.41 (0.10-1.15), 0.20	*2.28 (1.54-3.43), <.01*
Recent bleeding	1.46 (0.48-3.60), 0.45	2.08 (0.48-6.35), 0.25	1.03 (0.16-3.60), 0.97	1.50 (0.76-2.96), 0.24
eGFR, ml/min/m^2	*1.02 (1.01-1.04), <.01*	1.01 (0.99-1.03), 0.42	*1.04 (1.02-1.05), <.01*	1.00 (0.99-1.00), 0.36
Multivariable				
Age, years	1.03 (0.98-1.09), 0.19	0.98 (0.91-1.05), 0.51	*1.06 (1.00-1.12), 0.04*	0.99 (0.96-1.03), 0.69
Sex, female	0.76 (0.37-1.55), 0.46	1.33 (0.48-3.83), 0.58	0.56 (0.25-1.21), 0.15	0.98 (0.63-1.54), 0.95
BMI, kg/m^2	*1.09 (1.02-1.16), 0.01*	1.06 (0.98-1.13), 0.15	-	*0.95 (0.91-0.99), 0.01*
Admitting ward, nephrology vs geriatrics	*0.32 (0.10-0.86), 0.04*	-	0.17 (0.01-0.89), 0.009	-
COPD	1.77 (0.89-3.49), 0.10	-	2.09 (0.97-4.52), 0.06	-
CHF	-	-	-	0.82 (0.54-1.26), 0.37
CAD	0.50 (0.18-1.22), 0.16	-	-	-
Anemia	*0.50 (0.25-0.99), 0.05*	0.48 (0.17-1.31), 0.14	0.55 (0.26-1.19), 0.12	-
eGFR, ml/min/m^2	*1.02 (1.00-1.05), 0.04*	-	*1.04 (1.02-1.07), <.01*	-
Cancer	-	0.42 (0.06-1.59), 0.26	-	*1.93 (1.19-3.13), 0.01*

Prescriptive appropriateness of direct oral anticoagulants in older subjects with atrial fibrillation discharged from acute medical wards. N=609



The risk of smPC violations increases with eGFR values with a plateau starting from values of 50 ml/min/m2 and above (upper left panel).

This was mainly explained by an increasing risk of DOAC underdosage at higher eGFR (lower left panel).

The risk of overdosage peaked at eGFR values 30-50 ml/min/m2, leaning down at lower (<30 ml/min/m2) and higher (>60 ml/min/m2) ranges (upper right panel).

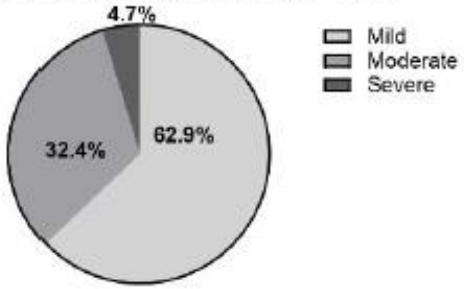
The risk of being discharged without anticoagulant therapy was U-shaped with the lower risk in intermediate eGFR values (lower right panel).

Undiagnosed and untreated anemia in older patients hospitalized in nephrology and geriatric wards: a secondary analysis of the SIN-SIGG study

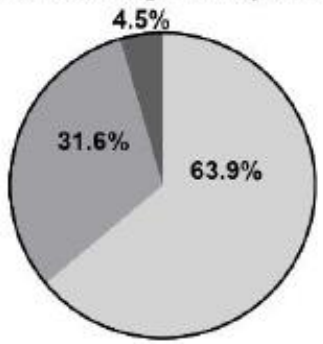
submitted

Undiagnosed and untreated anemia in older patients hospitalized in nephrology and geriatric wards: a secondary analysis of the SIN-SIGG study - *submitted*

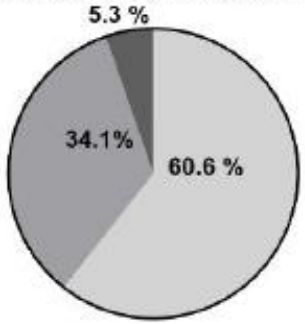
Severity of anemia in all patients (n=1269)



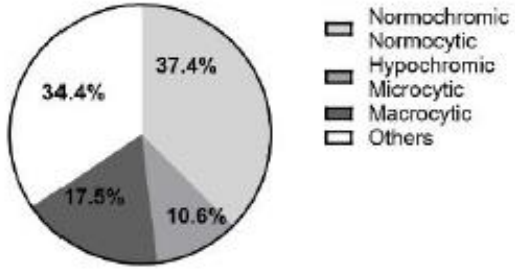
Severity of anemia in geriatric patients (n=870)



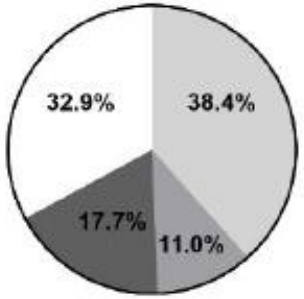
Severity of anemia in nephrology patients (n=399)



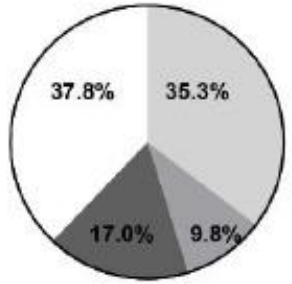
Type of anemia in all patients (n=1,269)



Type of anemia in geriatric patients (n=870)



Type of anemia in nephrology patients (n=399)



Undiagnosed and untreated anemia in older patients hospitalized in nephrology and geriatric wards: a secondary analysis of the SIN-SIGG study - *submitted*

Diagnostic inertia

	All anemic patients (n=1269)	eGFR>60 (n=235)	45-59.9 (n=269)	30-44.9 (n=380)	<30 (n=385)
Assessment of Iron status					
Present	**389 (30.6)**	**81 (31.5)**	**60 (22.3)**	**122 (32.1)**	**126 (32.7)**
Normal	166 (42.7)	43 (53.1)	24 (40.0)	46 (37.7)	53 (42.1)
Low	223 (57.3)	38 (46.9)	36 (60.0)	76 (62.3)	73 (57.9)
Not performed	880 (69.3)	154 (65.5)	209 (77.7)	258 (67.9)	259 (67.3)
Assessment of serum vitamin B12					
Performed	**297 (23.4)**	**66 (28.0)**	**51 (18.9)**	**98 (25.8)**	**82 (21.2)**
Normal	285 (96.0)	64 (97.0)	50 (98.0)	90 (91.8)	81 (98.8)
Low	12 (4.0)	2 (3.0)	1 (2.0)	8 (8.2)	1 (1.2)
Not performed	972 (76.6)	169 (71.9)	218 (81.0)	282 (74.2)	303 (78.7)
Assessment of serum folates					
Performed	**281 (22.1)**	**67 (28.5)**	**51 (18.9)**	**93 (24.5)**	**70 (18.2)**
Normal	177 (63.0)	45 (67.2)	28 (54.9)	56 (60.2)	48 (68.6)
Low	104 (37.0)	22 (32.8)	23 (45.1)	37 (39.8)	22 (31.4)
Not performed	988 (77.9)	168 (71.5)	218 (81.0)	287 (75.5)	315 (81.8)

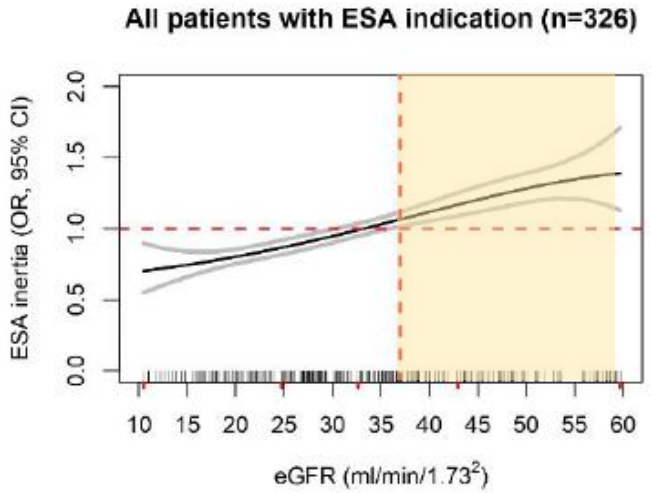
Undiagnosed and untreated anemia in older patients hospitalized in nephrology and geriatric wards: a secondary analysis of the SIN-SIGG study - *submitted*

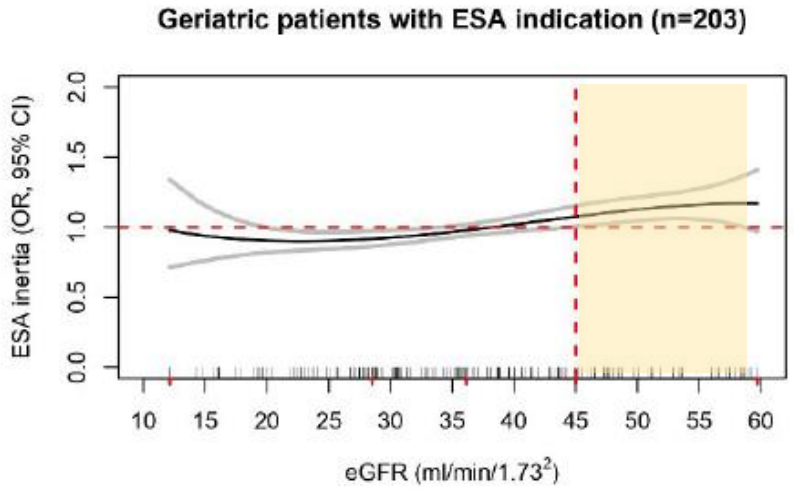
Frequency of iron status assessment among patients with hemoglobin < 10 g/dl and eGFR < 60 ml/min in the overall population and in geriatric vs nephrology units

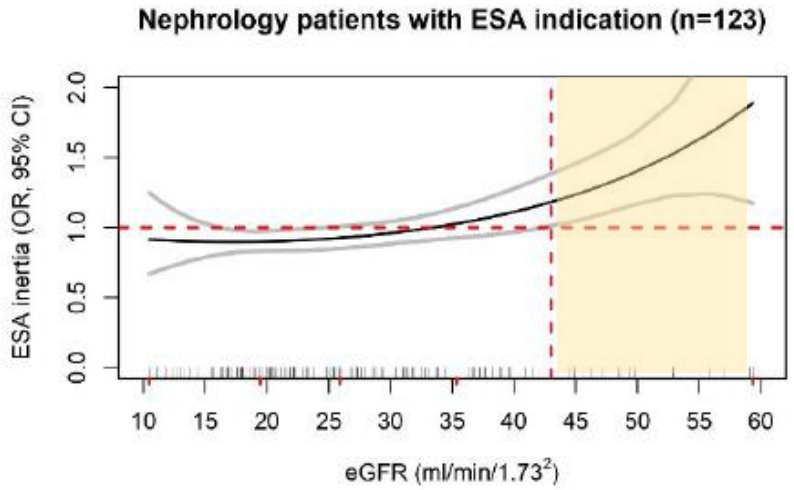
Hb < 10 g/dl and eGFR < 60 ml/min	Normal Iron tests	Low iron tests	Not performed iron tests
All (n=392)	70 (17.9)	89 (22.7)	233 (59.4)
Geriatric Units (n=242)	39 (16.1)	50 (20.7)	153 (63.2)
Nephrology units (n=150)	31 (20.7)	39 (26.0)	80 (53.3)
p			<0.001

Undiagnosed and untreated anemia in older patients hospitalized in nephrology and geriatric wards: a secondary analysis of the SIN-SIGG study - *submitted*

ESA prescriptive inertia

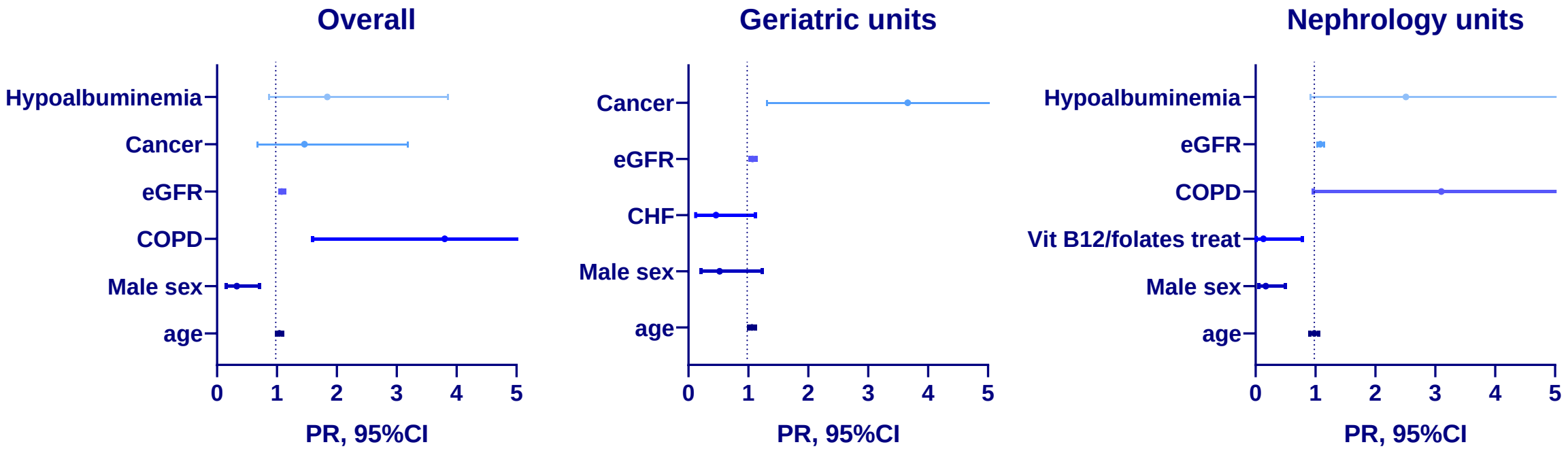






Undiagnosed and untreated anemia in older patients hospitalized in nephrology and geriatric wards: a secondary analysis of the SIN-SIGG study - *submitted*

Factors associated with ESA prescriptive inertia



Polypharmacy definitions in patients with Chronic Kidney Disease (CKD) across the literature.

Patient cohorts	Main Results	Types of medication	Definition for polypharmacy within a threshold of ≥5 medications	Definition for polypharmacy within a threshold of ≥10 medications
• Populations across 6 countries • CKD patients only excluding Dialysis patients • Cohort of CKD patients: n = 815,524 • CKD patients with polypharmacy: n = 22,413	**Two main definitions:** - "polypharmacy" → 5 ≥ Medications - "Hyperpolypharmacy" → 10 ≥ Medications ▪ Suggested	All medications	N=11 studies; [61.1%]	N=4 studies; [22.2%]
		Literature search window	**Types and number of studies**	
		2000 -> May 2022	• Five cohort studies • Five cross-sectional studies • Eight longitudinal studies	

Clinical Therapeutics
Volume 45, Issue 11, November 2023, Pages e217-e22

Polypharmacy, chronic kidney disease, and mortality among older adults: A prospective study of National Health and nutrition examination survey, 1999–2018

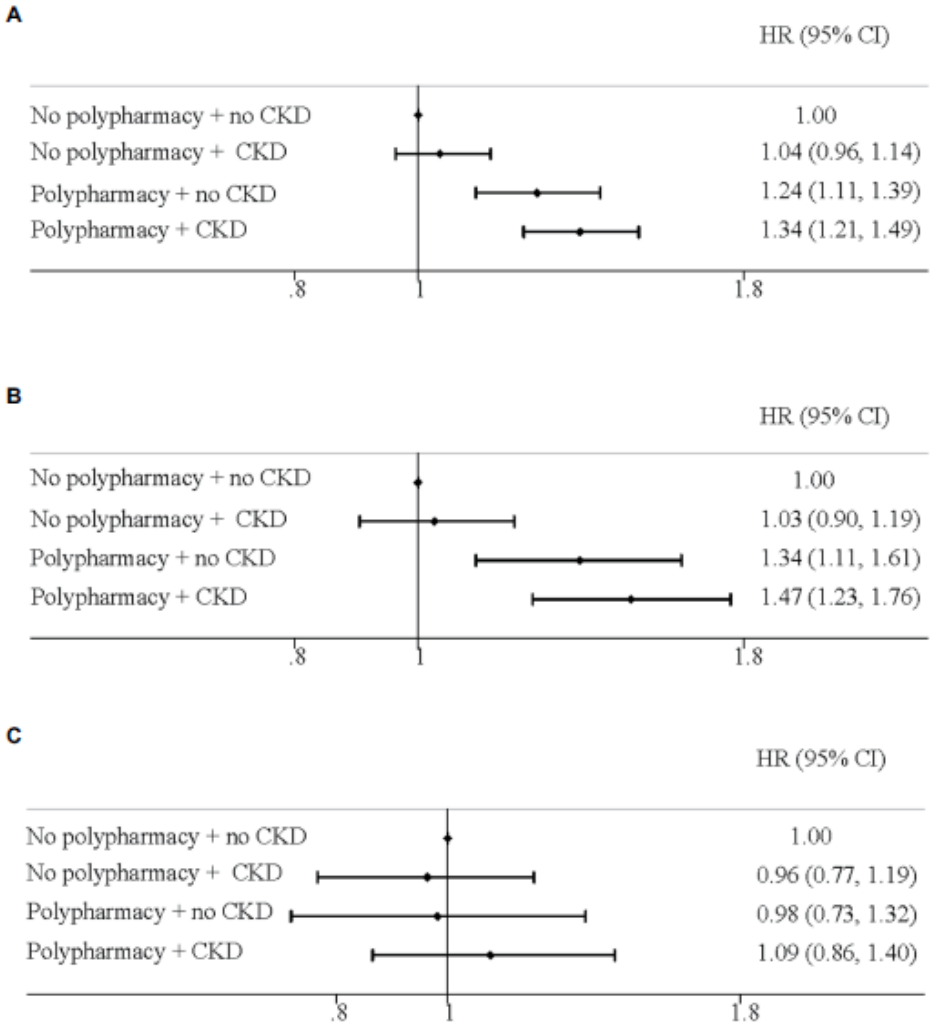


FIGURE 2
Joint effect of polypharmacy and chronic kidney disease on mortality for **(A)** all-cause; **(B)** cardiovascular disease; **(C)** cancer. Hazard ratios and 95% confidence intervals (HRs, 95% CIs) were adjusted for age, sex. Race, education, income, body mass index, drinking status, diabetes, hypertension, high cholesterol, heart disease, respiratory disease, and cancer.

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 23 March 2023
DOI 10.3389/fpubh.2023.1116583

Table 2. Logistic regression models for the association between PIMs and 30% eGFR decline

	Events, *n*	Incident rate ratio	Unadjusted	Adjusted ORs		
				Model 1	Model 2	Model 3
PIM = 0	180	0.69	Reference			
PIM = 1	117	0.99	1.45 (1.14–1.83)	1.44 (1.14–1.82)	1.38 (1.09–1.76)	1.25 (0.97–1.60)
PIM = 2	57	1.61	2.36 (1.75–3.19)	2.45 (1.81–3.30)	2.04 (1.50–2.78)	1.71 (1.24–2.37)
PIM ≥ 3	35	2.08	3.07 (2.13–4.43)	3.19 (2.21–4.60)	2.62 (1.80–3.82)	1.65 (1.08–2.52)

Model 1: adjusted for age, sex. Model 2: adjusted for model 1 covariates and BMI, smoking, hypertension, diabetes, dyslipidemia, CVD history. Model 3: adjusted for model 2 covariates and serum creatinine. eGFR, estimated glomerular filtration rate; BMI, body mass index; CVD, cardiovascular disease; CI, confidence interval; PIM, potentially inappropriate medication.

Table 3. Logistic regression models for the association between PIMs and 20% eGFR decline

	Events, *n*	Incident rate ratio	Unadjusted	Adjusted ORs		
				Model 1	Model 2	Model 3
PIM = 0	514	1.97	Reference			
PIM = 1	311	2.64	1.35 (1.17–1.56)	1.35 (1.17–1.56)	1.30 (1.12–1.50)	1.19 (1.02–1.38)
PIM = 2	148	4.19	2.18 (1.81–2.63)	2.22 (1.84–2.68)	1.94 (1.60–2.34)	1.68 (1.38–2.05)
PIM ≥ 3	91	5.42	2.86 (2.27–3.59)	2.93 (2.33–3.68)	2.51 (1.98–3.18)	1.84 (1.42–2.38)

Model 1: adjusted for age, sex. Model 2: adjusted for model 1 covariates and BMI, smoking, hypertension, diabetes, dyslipidemia, CVD history. Model 3: adjusted for model 2 covariates and serum creatinine. eGFR, estimated glomerular filtration rate; BMI, body mass index; CVD, cardiovascular disease; CI, confidence interval; PIM, potentially inappropriate medication.

Nephron

Clinical Practice: Research Article

Nephron 2023;147:177–184
DOI: 10.1159/000526326

Received: May 13, 2022
Accepted: July 14, 2022
Published online: September 16, 2022

Impact of Potentially Inappropriate Medications on Kidney Function in Chronic Kidney Disease: Retrospective Cohort Study

Table 4. Trend tests for the association between PIMs and eGFR slope

	eGFR slope, mL/min/1.73 m^2 per year	*p* value for trend
PIM = 0	−0.67±4.22	0.21
PIM = 1	−0.67±4.43	
PIM = 2	−0.77±4.80	
PIM ≥ 3	−0.72±5.03	

Differences among groups were evaluated by nonparametric trend test (Jonckheere-Terpstra trend test). eGFR, estimated glomerular filtration rate; PIM, potentially inappropriate medication.

Factors that Influence Deprescribing Potentially Inappropriate Medications in Older Adults Receiving Dialysis

CJASN
Clinical Journal of the American Society of Nephrology

Qualitative analysis

Semi-structured interviews and focus groups

N = 76 participants

53 clinicians

23 patients

Contextual factors related to deprescribing

System-level barriers to deprescribing

Limited electronic medical record interoperability

Time constraints and competing priorities

Undefined co-management among clinicians

Unclear roles delineation

Clinicians caution about prescriber boundaries

Stakeholders' limited knowledge about deprescribing

Knowledge limitations among clinicians and patients

Patients prioritize symptom control over potential harm

Clinicians expect resistance to deprescribing

Patients weigh risks and benefits

Conclusions: Challenges to integration of deprescribing into dialysis clinics include siloed health systems, time constraints, co-management behaviors, and clinician and patient knowledge and attitudes toward deprescribing.

Rasheeda K. Hall, Jeanette Rutledge, Anika Lucas, et al. ***Stakeholder Perspectives on Factors Related to Deprescribing Potentially Inappropriate Medications in Older Adults Receiving Dialysis***. CJASN doi: 10.2215/CJN.0000000000000229.
Visual Abstract by José A. Moura-Neto, MD, FASN, FRCP

Undiagnosed and untreated anemia in older patients hospitalized in nephrology and geriatric wards: a secondary analysis of the SIN-SIGG study - *submitted*