

**Table S1.** Age-adjusted association between medication-related problems and multimorbidity.

Medication-Related Problems	Age OR (95% CI) ( <i>p</i> -value)	2–4 Diseases Influence, Age Adjusted OR (95% CI) ( <i>p</i> -value)	5–9 diseases Influence, Age Adjusted OR (95% CI) ( <i>p</i> -value)	≥10 diseases Influence, Age Adjusted OR (95% CI) ( <i>p</i> -value)	Age Influence, Multimorbidity Adjusted OR (95% CI) ( <i>p</i> -value)
Duplicate therapy	1.01 (1.011–1.014) ( <i>&lt;</i> 0.001)	3.76 (3.53–4.01) ( <i>&lt;</i> 0.001)	7.49 (7.04–7.97) ( <i>&lt;</i> 0.001)	13.21 (12.40–14.09) ( <i>&lt;</i> 0.001)	1 (0.998–1) (0.76)
Drug-drug interaction	1.03 (1.022–1.030) ( <i>&lt;</i> 0.001)	3.48 (2.70–4.58) ( <i>&lt;</i> 0.001)	8.10 (6.33–10.60) ( <i>&lt;</i> 0.001)	19.85 (15.46–26.03) ( <i>&lt;</i> 0.001)	1.01 (1.006–1.014) ( <i>&lt;</i> 0.001)
Contraindicated drugs in CKD	1.08 (1.075–1.077) ( <i>&lt;</i> 0.001)	59.61 (41.76–89.23) ( <i>&lt;</i> 0.001)	269.47 (188.92–403.11) ( <i>&lt;</i> 0.001)	695.72 (487.66–1040.92) ( <i>&lt;</i> 0.001)	1.06 (1.061–1.063) ( <i>&lt;</i> 0.001)
Contraindicated drugs in liver disease	0.98 (0.980–0.983) ( <i>&lt;</i> 0.001)	7.45 (6.37–8.77) ( <i>&lt;</i> 0.001)	17.51 (15–20.59) ( <i>&lt;</i> 0.001)	35.30 (30.22–42.57) ( <i>&lt;</i> 0.001)	0.96 (0.963–0.970) ( <i>&lt;</i> 0.001)
Potentially inappropriate medication	1.04 (1.040–1.042) ( <i>&lt;</i> 0.001)	4.25 (4.15–4.36) ( <i>&lt;</i> 0.001)	12.04 (11.75–12.33) ( <i>&lt;</i> 0.001)	34.89 (33.83–36) ( <i>&lt;</i> 0.001)	1.02 (1.023–1.025) ( <i>&lt;</i> 0.001)
Anticholinergic effect-anticholinergic load score					
1	1 (1.002–1.004) ( <i>&lt;</i> 0.001)	0.94 (0.89–1) (0.04)	1.24 (1.17–1.31) ( <i>&lt;</i> 0.001)	1.91 (1.81–2.03) ( <i>&lt;</i> 0.001)	1 (0.998–1) (0.02)
2	1 (1–1.003) (0.005)	1.12 (1.03–1.21) (0.006)	1.73 (1.60–1.87) ( <i>&lt;</i> 0.001)	2.93 (2.71–3.17) ( <i>&lt;</i> 0.001)	1 (0.994–0.997) ( <i>&lt;</i> 0.001)
3 -5	1 (0.996–1) (0.28)	1.13 (0.98–1.30) (0.08)	2.38 (2.08–2.73) ( <i>&lt;</i> 0.001)	5.77 (5.04–6.61) ( <i>&lt;</i> 0.001)	0.99 (0.986–0.990) ( <i>&lt;</i> 0.001)
≥ 6	0.99 (0.986–0.988) ( <i>&lt;</i> 0.001)	1.52 (1.17–1.99) (0.002)	3.56 (2.79–4.54) ( <i>&lt;</i> 0.001)	13.04 (10.04–16.92) ( <i>&lt;</i> 0.001)	0.95 (0.943–0.964) ( <i>&lt;</i> 0.001)
Increase in fall risk	1 (1.008–1.010) ( <i>&lt;</i> 0.001)	0.95 (0.91–1) (0.03)	1.12 (1.07–1.17) ( <i>&lt;</i> 0.001)	1.65 (1.57–1.73) ( <i>&lt;</i> 0.001)	1 (1.005–1.007) ( <i>&lt;</i> 0.001)
Effect on QT interval	1.02 (1.019–1.022) ( <i>&lt;</i> 0.001)	1.07 (1–1.15) (0.03)	1.53 (1.43–1.64) ( <i>&lt;</i> 0.001)	2.43 (2.27–2.60) ( <i>&lt;</i> 0.001)	1.02 (1.014–1.017) ( <i>&lt;</i> 0.001)

Antiulcer agents without criteria for gastroprotection	1.03 (1.029–1.031) ( $<0.001$ )	1.18 (1.13–1.24) ( $<0.001$ )	1.58 (1.50–1.65) ( $<0.001$ )	1.95 (1.86–2.04) ( $<0.001$ )	1.03 (1.025–1.027) ( $<0.001$ )
Other drugs not recommended for older people	1.02 (1.017–1.019) ( $<0.001$ )	1.66 (1.57–1.75) ( $<0.001$ )	2.48 (2.35–2.62) ( $<0.001$ )	3.84 (3.64–4.06) ( $<0.001$ )	1.01 (1.011–1.013) ( $<0.001$ )
Patients needing gastroprotection	0.99 (0.978–0.996) (0.004)	1.06 (0.71–1.67) (0.79)	1.04 (0.70–1.63) (0.85)	0.81 (0.54–1.30) (0.36)	0.99 (0.980–0.997) (0.01)

CKD: chronic kidney disease.

**Table S2.** Number of contraindicated drugs in chronic kidney disease and liver disease and potentially inappropriate medications in older people by multimorbidity group at the end of the study, 2016 (N = 723,016).

Medication-Related Problems	Number of Drug†	N Comorbidities			Total N = 723,016 n (%)
		2–4 Diseases N = 137,799 n (%)	5–9 Diseases N = 393,672 n (%)	≥10 Diseases N = 191,545 n (%)	
Contraindicated drugs in CKD, n (%)	0	132,600 (96.23%)	330,864 (84.05%)	125,583 (65.56%)	589,047 (81.47%)
	1	3,988 (2.89%)	37,687 (9.57%)	32,006 (16.71%)	73,681 (10.19%)
	2	964 (0.70%)	17,557 (4.46%)	20,959 (10.94%)	39,480 (5.46%)
	3	203 (0.15%)	5,891 (1.50%)	9,282 (4.85%)	15,376 (2.13%)
	4	35 (0.03%)	1,371 (0.35%)	2,833 (1.48%)	4,239 (0.59%)
	5	6 (0.00%)	252 (0.06%)	682 (0.36%)	940 (0.13%)
	6	3 (0.00%)	44 (0.01%)	165 (0.09%)	212 (0.03%)
	7	0 (0.00%)	6 (0.00%)	29 (0.02%)	35 (0.00%)
	8	0 (0.00%)	0 (0.00%)	5 (0.00%)	5 (0.00%)
	11	0 (0.00%)	0 (0.00%)	1 (0.00%)	1 (0.00%)
Contraindicated drugs in liver disease, n (%)	0	135,304 (98.19%)	375,713 (95.44%)	173,755 (90.71%)	684,772 (94.71%)
	1	1,594 (1.16%)	8,761 (2.23%)	6,639 (3.47%)	16,994 (2.35%)
	2	701 (0.51%)	5,496 (1.40%)	5,256 (2.74%)	11,453 (1.58%)
	3	172 (0.12%)	2,695 (0.68%)	3,710 (1.94%)	6,577 (0.91%)
	4	22 (0.02%)	783 (0.20%)	1,540 (0.80%)	2,345 (0.32%)
	5	5 (0.00%)	178 (0.05%)	500 (0.26%)	683 (0.09%)
	6	1 (0.00%)	36 (0.01%)	128 (0.07%)	165 (0.02%)
	7	0 (0.00%)	8 (0.00%)	12 (0.01%)	20 (0.00%)
	8	0 (0.00%)	2 (0.00%)	5 (0.00%)	7 (0.00%)
Potentially inappropriate medication, n (%)	0	77,446 (56.20%)	111,522 (28.33%)	19,904 (10.39%)	208,872 (28.88%)
	1	31,539 (22.89%)	99,893 (25.37%)	32,684 (17.06%)	164,116 (22.69%)
	2	14,892 (10.81%)	72,962 (18.53%)	36,742 (19.18%)	124,596 (17.23%)
	3	7,114 (5.16%)	45,507 (11.56%)	31,208 (16.29%)	83,829 (11.59%)
	4	3,475 (2.52%)	27,568 (7.00%)	23,677 (12.4%)	54,720 (7.57%)
	5	1,632 (1.18%)	15,895 (4.04%)	17,204 (8.98%)	34,731 (4.80%)
	6	818 (0.59%)	9,061 (2.30%)	11,806 (6.16%)	21,685 (3.00%)
	7	404 (0.29%)	5,171 (1.31%)	7,366 (3.85%)	12,941 (1.79%)
	8	237 (0.17%)	2,888 (0.73%)	4,740 (2.47%)	7,865 (1.09%)
	9	122 (0.09%)	1,509 (0.38%)	2,736 (1.43%)	4,367 (0.60%)
	≥ 10	120 (0.09%)	1,696 (0.43%)	3,478 (1.82%)	5,294 (0.73%)

†Number of drugs according to the fifth levels of the Anatomical Therapeutic Chemical Classification System (ATC); CKD: chronic kidney disease; Note: All variables of the table showed a significant difference ( $p < 0.001$ ) between multimorbidity groups.

**Table S3.** Twenty most contraindicated drugs in chronic kidney disease in older people by multimorbidity group at the end of the study, 2016 (N = 723,016).

ATC Code (Drug), n (%)	N Comorbidities			Total N = 723,016 n (%)
	2–4 Diseases N = 137,799 n (%)	5–9 Diseases N = 393,672 n (%)	≥10 Diseases N = 191,545 n (%)	
A10BA02 (Metformin)	488 (0.35%)	12,990 (3.30%)	17,590 (9.18%)	31,068 (4.30%)
C03AA03 (Hydrochlorothiazide)	930 (0.67%)	10,304 (2.62%)	8,814 (4.60%)	20,048 (2.77%)
C09BA02 (Enalapril and diuretics)	899 (0.65%)	8,505 (2.16%)	6,024 (3.14%)	15,428 (2.13%)
N06AB04 (Citalopram)	180 (0.13%)	4,083 (1.04%)	7,054 (3.68%)	11,317 (1.57%)
C09DA01 (Losartan and diuretics)	465 (0.34%)	5,056 (1.28%)	4,812 (2.51%)	10,333 (1.43%)
A10BB09 (Gliclazide)	152 (0.11%)	3,685 (0.94%)	4,731 (2.47%)	8,568 (1.19%)
N02AX02 (Tramadol)	89 (0.06%)	2,693 (0.68%)	5,243 (2.74%)	8,025 (1.11%)
C09CA03 (Valsartan)	235 (0.17%)	3,222 (0.82%)	3,885 (2.03%)	7,342 (1.02%)
C09DA03 (Valsartan and diuretics)	290 (0.21%)	3,227 (0.82%)	2,989 (1.56%)	6,506 (0.90%)
C03DA01 (Spironolactone)	62 (0.04%)	1,804 (0.46%)	4,409 (2.30%)	6,275 (0.87%)
C08CA11 (Manidipine)	201 (0.15%)	2,740 (0.70%)	3,241 (1.69%)	6,182 (0.86%)
M05BA04 (Alendronic acid)	102 (0.07%)	1,961 (0.50%)	3,606 (1.88%)	5,669 (0.78%)
C09BA03 (Lisinopril and diuretics)	256 (0.19%)	2,605 (0.66%)	2,011 (1.05%)	4,872 (0.67%)
M01AE01 (Ibuprofen)	172 (0.12%)	1,725 (0.44%)	1,467 (0.77%)	3,364 (0.47%)
C10AB05 (Fenofibrate)	84 (0.06%)	1,434 (0.36%)	1,652 (0.86%)	3,170 (0.44%)
A10BD07 (Metformin and sitagliptin)	42 (0.03%)	1,287 (0.33%)	1,649 (0.86%)	2,978 (0.41%)
C03BA11 (Indapamide)	149 (0.11%)	1,341 (0.34%)	1,052 (0.55%)	2,542 (0.35%)
C08CA13 (Lercanidipine)	71 (0.05%)	1,163 (0.30%)	1,233 (0.64%)	2,467 (0.34%)
C03EA01 (Hydrochlorothiazide and potassium-sparing agents)	97 (0.07%)	1,279 (0.32%)	1,015 (0.53%)	2,391 (0.33%)
C09CA08 (Olmesartan medoxomil)	91 (0.07%)	1,047 (0.27%)	1,086 (0.57%)	2,224 (0.31%)

ATC: Anatomical Therapeutic Chemical Classification System.

**Table S4.** Twenty most contraindicated drugs in liver disease in older people by multimorbidity group at the end of the study, 2016 (N = 723,016).

ATC Code (Drug), n (%)	N Comorbidities			Total N = 723,016 n (%)
	2-4 Diseases N = 137,799 n (%)	5-9 Diseases N = 393,672 n (%)	≥10 Diseases N = 191,545 n (%)	
C10AA01 (Simvastatin)	915 (0.66%)	6,558 (1.67%)	6,201 (3.24%)	13,674 (1.89%)
C03CA01 (Furosemide)	114 (0.08%)	2,592 (0.66%)	6,002 (3.13%)	8,708 (1.20%)
A10BA02 (Metformin)	318 (0.23%)	3,430 (0.87%)	3,750 (1.96%)	7,498 (1.04%)
C10AA05 (Atorvastatin)	295 (0.21%)	2,741 (0.70%)	3,366 (1.76%)	6,402 (0.89%)
C03AA03 (Hydrochlorothiazide)	277 (0.20%)	1,920 (0.49%)	1,654 (0.86%)	3,851 (0.53%)
C09CA01 (Losartan)	130 (0.09%)	1,317 (0.33%)	1,736 (0.91%)	3,183 (0.44%)
N05CD06 (Lormetazepam)	107 (0.08%)	1,212 (0.31%)	1,705 (0.89%)	3,024 (0.42%)
C09BA02 (Enalapril and diuretics)	249 (0.18%)	1,572 (0.40%)	1,055 (0.55%)	2,876 (0.40%)
C09DA01 (Losartan and diuretics)	104 (0.08%)	954 (0.24%)	834 (0.44%)	1,892 (0.26%)
C10AA03 (Pravastatin)	73 (0.05%)	721 (0.18%)	1,052 (0.55%)	1,846 (0.26%)
C03CA04 (Torsemide)	59 (0.04%)	688 (0.17%)	936 (0.49%)	1,683 (0.23%)
C09CA03 (Valsartan)	57 (0.04%)	578 (0.15%)	734 (0.38%)	1,369 (0.19%)
C09DA03 (Valsartan and diuretics)	79 (0.06%)	584 (0.15%)	566 (0.30%)	1,229 (0.17%)
A10BX02 (Repaglinide)	17 (0.01%)	362 (0.09%)	670 (0.35%)	1,049 (0.15%)
C08CA11 (Manipipine)	27 (0.02%)	353 (0.09%)	471 (0.25%)	851 (0.12%)
C09BA03 (Lisinopril and diuretics)	79 (0.06%)	434 (0.11%)	311 (0.16%)	824 (0.11%)
A10BD07 (Metformin and sitagliptin)	34 (0.02%)	387 (0.10%)	375 (0.20%)	796 (0.11%)
A05AA02 (Ursodeoxycholic acid)	51 (0.04%)	367 (0.09%)	344 (0.18%)	762 (0.11%)
C10AB05 (Fenofibrate)	26 (0.02%)	313 (0.08%)	331 (0.17%)	670 (0.09%)
N05CF02 (Zolpidem)	27 (0.02%)	243 (0.06%)	312 (0.16%)	582 (0.08%)

ATC: Anatomical Therapeutic Chemical Classification System.

**Table S5.** Twenty most potentially inappropriate medications in older people by multimorbidity group at the end of the study, 2016 (N = 723,016).

ATC Code (Drug), n (%)	N Comorbidities			Total N = 723,016 n (%)
	2–4 Diseases N = 137,799 n (%)	5–9 Diseases N = 393,672 n (%)	≥10 Diseases N = 191,545 n (%)	
A02BC01 (Omeprazole)	13,838 (10.04%)	88,575 (22.50%)	66,343 (34.64%)	168,756 (23.34%)
N05BA06 (Lorazepam)	10,635 (7.72%)	55,864 (14.19%)	40,603 (21.20%)	107,102 (14.81%)
C07AB07 (Bisoprolol)	6,745 (4.89%)	41,293 (10.49%)	35,910 (18.75%)	83,948 (11.61%)
G04CA02 (Tamsulosin)	5,621 (4.08%)	26,604 (6.76%)	16,487 (8.61%)	48,712 (6.74%)
N05CD06 (Lormetazepam)	3,976 (2.89%)	23,329 (5.93%)	18,190 (9.50%)	45,495 (6.29%)
N02AX52 (Tramadol, combinations)	2,409 (1.75%)	18,022 (4.58%)	14,879 (7.77%)	35,310 (4.88%)
N06AB04 (Citalopram)	2,262 (1.64%)	17,098 (4.34%)	15,382 (8.03%)	34,742 (4.81%)
N06AB06 (Sertraline)	1,794 (1.30%)	14,811 (3.76%)	15,733 (8.21%)	32,338 (4.47%)
N05BA12 (Alprazolam)	2,678 (1.94%)	13,879 (3.53%)	9,757 (5.09%)	26,314 (3.64%)
N02AX02 (Tramadol)	1,193 (0.87%)	10,848 (2.76%)	11,461 (5.98%)	23,502 (3.25%)
C07AB03 (Atenolol)	3,014 (2.19%)	12,977 (3.30%)	6,919 (3.61%)	22,910 (3.17%)
N06AB05 (Paroxetine)	1,802 (1.31%)	11,389 (2.89%)	9,103 (4.75%)	22,294 (3.08%)
N05AH04 (Quetiapine)	1,417 (1.03%)	9,728 (2.47%)	9,275 (4.84%)	20,420 (2.82%)
N05BA01 (Diazepam)	1,800 (1.31%)	9,541 (2.42%)	7,161 (3.74%)	18,502 (2.56%)
N06AX05 (Trazodone)	1,122 (0.81%)	8,180 (2.08%)	8,591 (4.49%)	17,893 (2.47%)
C02CA04 (Doxazosin)	1,505 (1.09%)	8,938 (2.27%)	6,879 (3.59%)	17,322 (2.40%)
C03CA01 (Furosemide)	555 (0.40%)	6,594 (1.67%)	9,899 (5.17%)	17,048 (2.36%)
C07AG02 (Carvedilol)	997 (0.72%)	7,096 (1.80%)	7,399 (3.86%)	15,492 (2.14%)
N02AB03 (Fentanyl)	498 (0.36%)	5,926 (1.51%)	8,891 (4.64%)	15,315 (2.12%)
A02BA02 (Ranitidine)	1,287 (0.93%)	7,521 (1.91%)	5,566 (2.91%)	14,374 (1.99%)

ATC: Anatomical Therapeutic Chemical Classification System.