

Table A1. Rate ratio of acute kidney injury associated with exposure to current double or triple therapy combination (matching on general practice).

Current Use*	Cases n=1642	Controls n=11 039	RR (95% CI)	
			crude	adjusted†
<i>diuretics only</i>	147 (8.95)	1459 (13.22)	Reference	Reference
<i>diuretics plus NSAIDs</i>	130 (7.92)	965 (8.74)	1.35 (1.04 to 1.77)	1.22 (0.92 to 1.63)
<i>ACEIs or ARBs only</i>	109 (6.64)	935 (8.47)	Reference	Reference
<i>ACEIs or ARBs plus NSAIDs</i>	96 (5.85)	847 (7.67)	1.06 (0.77 to 1.45)	0.88 (0.63 to 1.24)
<i>diuretics plus ACEIs or ARBs</i>	329 (20.04)	1439 (13.04)	Reference	Reference
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>	430 (26.19)	1515 (13.72)	1.14 (0.95 to 1.35)	1.05 (0.86 to 1.27)

Values are reported as n (%); RR=rate ratio; CI=confidence interval

*Within 90 days before the index date; current users of other antihypertensive drugs and past users (more than 90 days before the index date) of double and triple therapy combinations are not displayed in the table, but were considered in the regression model

†Adjusted for the covariates listed in Table 1

Table A2. Rate ratio of acute kidney injury associated with exposure to current double or triple therapy combination according to NSAIDs half-life and duration of use (matching on general practice).

Current Use*	Cases n=1642	Controls n=11 039	RR (95% CI)	
			crude	adjusted [†]
<i>diuretics only</i>	147 (8.95)	1459 (13.22)	Reference	Reference
<i>diuretics plus NSAIDs</i>				
NSAIDs half-life <12 hours	125 (7.61)	910 (8.24)	1.38 (1.05 to 1.80)	1.24 (0.93 to 1.66)
≥12 hours	5 (0.30)	55 (0.50)	0.97 (0.36 to 2.56)	0.87 (0.31 to 2.48)
duration of use [‡] ≤ 30 days	28 (1.71)	105 (0.95)	2.60 (1.59 to 4.24)	2.10 (1.23 to 3.60)
31-60 days	21 (1.28)	139 (1.26)	1.30 (0.76 to 2.21)	1.34 (0.76 to 2.36)
61-90 days	26 (1.58)	168 (1.52)	1.70 (1.04 to 2.76)	1.55 (0.92 to 2.62)
>90 days	55 (3.35)	553 (5.01)	1.02 (0.72 to 1.44)	0.89 (0.61 to 1.30)
<i>ACEIs or ARBs only</i>				
<i>ACEIs or ARBs plus NSAIDs</i>	109 (6.64)	935 (8.47)	Reference	Reference
NSAIDs half-life <12 hours	92 (5.60)	817 (7.40)	1.05 (0.77 to 1.45)	0.88 (0.62 to 1.24)
≥12 hours	4 (0.24)	30 (0.27)	1.11 (0.36 to 3.40)	0.81 (0.24 to 2.81)
duration of use [‡] ≤ 30 days	9 (0.55)	87 (0.79)	0.90 (0.42 to 1.96)	0.87 (0.38 to 1.98)
31-60 days	18 (1.10)	106 (0.96)	1.71 (0.96 to 3.03)	1.52 (0.81 to 2.84)
61-90 days	21 (1.28)	156 (1.41)	1.20 (0.70 to 2.05)	0.94 (0.53 to 1.68)
>90 days	48 (2.92)	498 (4.51)	0.90 (0.61 to 1.31)	0.72 (0.48 to 1.09)
<i>diuretics plus ACEIs or ARBs</i>				
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>	329 (20.04)	1439 (13.04)	Reference	Reference
NSAIDs half-life <12 hours	409 (24.91)	1472 (13.33)	1.11 (0.93 to 1.33)	1.02 (0.84 to 1.24)
≥12 hours	21 (1.28)	43 (0.39)	2.00 (1.10 to 3.64)	2.23 (1.17 to 4.28)
duration of use [‡] ≤ 30 days	69 (4.20)	122 (1.11)	2.10 (1.48 to 2.98)	1.58 (1.07 to 2.32)
31-60 days	73 (4.45)	178 (1.61)	1.72 (1.24 to 2.39)	1.52 (1.07 to 2.18)
61-90 days	104 (6.33)	324 (2.94)	1.23 (0.93 to 1.62)	1.11 (0.82 to 1.50)

	>90 days	184 (11.21)	891 (8.07)	0.84 (0.68 to 1.05)	0.82 (0.64 to 1.04)
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Values are reported as n (%); RR=rate ratio; CI=confidence interval

*Within 90 days before the index date; current users of other antihypertensive drugs and past users (more than 90 days before the index date) of double and triple therapy combinations are not displayed in the table, but were considered in the regression model

#Length of exposure to double or triple therapy combination

†Adjusted for the covariates listed in Table 1

Table B1. Rate ratio of acute kidney injury associated with exposure to current double or triple therapy combination stratifying by calendar period (index date).

Current Use*	Cases n=2215	Controls n=21 993	RR (95% CI)	
			crude	adjusted†
1998-2002:				
<i>diuretics only</i>	48 (15.0)	694 (21.2)	Reference	Reference
<i>diuretics plus NSAIDs</i>	40 (12.5)	399 (12.2)	1.51 (0.97 to 2.35)	1.22 (0.76 to 1.96)
<i>ACEIs or ARBs only</i>	19 (5.9)	226 (6.9)	Reference	Reference
<i>ACEIs or ARBs plus NSAIDs</i>	11 (3.4)	161 (4.9)	0.92 (0.42 to 2.01)	0.72 (0.30 to 1.70)
<i>diuretics plus ACEIs or ARBs</i>	67 (20.9)	365 (11.2)	Reference	Reference
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>	85 (26.5)	300 (9.2)	1.56 (1.09 to 2.24)	1.47 (0.98 to 2.20)
2003-2007:				
<i>diuretics only</i>	101 (10.4)	1380 (14.3)	Reference	Reference
<i>diuretics plus NSAIDs</i>	79 (8.1)	940 (9.7)	1.16 (0.85 to 1.59)	1.03 (0.74 to 1.44)
<i>ACEIs or ARBs only</i>	66 (6.8)	938 (9.7)	Reference	Reference
<i>ACEIs or ARBs plus NSAIDs</i>	73 (7.5)	1001 (10.4)	1.06 (0.74 to 1.50)	1.00 (0.69 to 1.46)
<i>diuretics plus ACEIs or ARBs</i>	229 (23.6)	1306 (13.5)	Reference	Reference
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>	300 (30.9)	1394 (14.4)	1.25 (1.03 to 1.51)	1.24 (1.00 to 1.54)
2008-2010:				
<i>diuretics only</i>	60 (6.5)	558 (6.2)	Reference	Reference
<i>diuretics plus NSAIDs</i>	37 (4.0)	400 (4.4)	0.82 (0.53 to 1.28)	0.73 (0.45 to 1.16)
<i>ACEIs or ARBs only</i>	63 (6.8)	725 (8.0)	Reference	Reference
<i>ACEIs or ARBs plus NSAIDs</i>	54 (5.9)	745 (8.2)	0.87 (0.59 to 1.27)	0.85 (0.57 to 1.27)

<i>diuretics plus ACEIs or ARBs</i>	118 (12.8)	761 (8.4)	Reference	Reference
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>	159 (17.2)	730 (8.1)	1.47 (1.13 to 1.92)	1.46 (1.10 to 1.94)

Values are reported as n (%); RR=rate ratio; CI=confidence interval

*Within 90 days before the index date; current users of other antihypertensive drugs and past users (more than 90 days before the index date) of double and triple therapy combinations are not displayed in the table, but were considered in the regression model

†Adjusted for the covariates listed in Table 1

Table B2. Rate ratio of acute kidney injury associated with exposure to current double or triple therapy combination stratifying by diabetes diagnosis.

Current Use*	Cases n=2215	Controls n=21 993	RR (95% CI)	
			crude	adjusted†
Without diabetes:				
<i>diuretics only</i>	178 (12.0)	2400 (13.3)	Reference	Reference
<i>diuretics plus NSAIDs</i>	124 (8.3)	1541 (8.5)	1.08 (0.85 to 1.38)	0.99 (0.77 to 1.28)
<i>ACEIs or ARBs only</i>	95 (6.4)	1433 (7.9)	Reference	Reference
<i>ACEIs or ARBs plus NSAIDs</i>	73 (4.9)	1352 (7.5)	0.83 (0.60 to 1.15)	0.80 (0.57 to 1.12)
<i>diuretics plus ACEIs or ARBs</i>	263 (17.7)	1957 (10.8)	Reference	Reference
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>	320 (21.5)	1735 (9.6)	1.37 (1.14 to 1.64)	1.37 (1.13 to 1.67)
With diabetes:				
<i>diuretics only</i>	31 (4.3)	232 (5.9)	Reference	Reference
<i>diuretics plus NSAIDs</i>	32 (4.4)	198 (5.1)	1.36 (0.67 to 2.77)	1.61 (0.71 to 3.65)
<i>ACEIs or ARBs only</i>	53 (7.3)	456 (11.7)	Reference	Reference
<i>ACEIs or ARBs plus NSAIDs</i>	65 (9.0)	555 (14.2)	0.75 (0.46 to 1.22)	0.84 (0.48 to 1.47)
<i>diuretics plus ACEIs or ARBs</i>	151 (20.8)	475 (12.2)	Reference	Reference
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>	224 (30.9)	689 (17.6)	1.17 (0.84 to 1.62)	1.52 (1.04 to 2.22)

Values are reported as n (%); RR=rate ratio; CI=confidence interval

*Within 90 days before the index date; current users of other antihypertensive drugs and past users (more than 90 days before the index date) of double and triple therapy combinations are not displayed in the table, but were considered in the regression model

†Adjusted for the covariates listed in Table 1

Table C1. Rate ratio of acute kidney injury associated with exposure to current double or triple therapy combination (60-day period for both current time-window and grace period).

Current Use*	Cases n=2215	Controls n=21 993	RR (95% CI)	
			crude	adjusted†
<i>diuretics only</i>	210 (9.5)	2607 (11.9)	Reference	Reference
<i>diuretics plus NSAIDs</i>	144 (6.5)	1611 (7.3)	1.15 (0.92 to 1.44)	1.00 (0.79 to 1.27)
<i>ACEIs or ARBs only</i>	133 (6.0)	1853 (8.4)	Reference	Reference
<i>ACEIs or ARBs plus NSAIDs</i>	131 (5.9)	1787 (8.1)	1.05 (0.82 to 1.35)	0.97 (0.74 to 1.26)
<i>diuretics plus ACEIs or ARBs</i>	415 (18.7)	2318 (10.5)	Reference	Reference
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>	484 (21.9)	2236 (10.2)	1.24 (1.07 to 1.43)	1.21 (1.03 to 1.41)

Values are reported as n (%); RR=rate ratio; CI=confidence interval

*Within 60 days before the index date; current users of other antihypertensive drugs and past users (more than 60 days before the index date) of double and triple therapy combinations are not displayed in the table, but were considered in the regression model

†Adjusted for the covariates listed in Table 1

Table C2. Rate ratio of acute kidney injury associated with exposure to current double or triple therapy combination according to NSAIDs half-life and duration of use (60-day period for both current time-window and grace period).

Current Use*	Cases n=2215	Controls n=21 993	RR (95% CI)	
			crude	adjusted [†]
<i>diuretics only</i>	210 (9.5)	2607 (11.9)	Reference	Reference
<i>diuretics plus NSAIDs</i>				
NSAIDs half-life <12 hours	139 (6.3)	1539 (7.0)	1.16 (0.93 to 1.46)	1.01 (0.80 to 1.28)
≥12 hours	5 (0.2)	72 (0.3)	0.85 (0.34 to 2.12)	0.81 (0.32 to 2.07)
duration of use [‡] ≤30 days	32 (1.4)	244 (1.1)	1.63 (1.10 to 2.42)	1.24 (0.81 to 1.89)
31-60 days	41 (1.9)	375 (1.7)	1.36 (0.92 to 1.94)	1.13 (0.78 to 1.64)
61-90 days	47 (2.1)	676 (3.1)	0.90 (0.65 to 1.25)	0.81 (0.57 to 1.14)
>90 days	24 (1.1)	316 (1.4)	1.00 (0.64 to 1.55)	1.01 (0.64 to 1.60)
<i>ACEIs or ARBs only</i>				
<i>ACEIs or ARBs plus NSAIDs</i>	133 (6.0)	1853 (8.4)	Reference	Reference
<i>ACEIs or ARBs plus NSAIDs</i>				
NSAIDs half-life <12 hours	127 (5.7)	1743 (7.9)	1.05 (0.81 to 1.35)	0.97 (0.75 to 1.27)
≥12 hours	4 (0.2)	44 (0.2)	1.23 (0.43 to 3.50)	0.84 (0.27 to 2.63)
duration of use [‡] ≤30 days	19 (0.9)	223 (1.0)	1.22 (0.74 to 2.02)	1.25 (0.74 to 2.11)
31-60 days	39 (1.8)	444 (2.0)	1.22 (0.84 to 1.78)	1.08 (0.73 to 1.60)
61-90 days	53 (2.4)	767 (3.5)	0.99 (0.71 to 1.38)	0.89 (0.63 to 1.26)
>90 days	20 (0.9)	353 (1.6)	0.83 (0.51 to 1.34)	0.80 (0.48 to 1.33)
<i>diuretics plus ACEIs or ARBs</i>				
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>	415 (18.7)	2318 (10.5)	Reference	Reference
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>				
NSAIDs half-life <12 hours	466 (21.0)	2175 (9.9)	1.22 (1.06 to 1.42)	1.19 (1.02 to 1.40)
≥12 hours	18 (0.8)	61 (0.3)	1.65 (0.96 to 2.83)	1.77 (0.99 to 3.17)
duration of use [‡] ≤30 days	90 (4.1)	257 (1.2)	1.94 (1.49 to 2.53)	1.77 (1.33 to 2.36)
31-60 days	136 (6.1)	549 (2.5)	1.41 (1.13 to 1.74)	1.34 (1.06 to 1.69)
61-90 days	192 (8.7)	1013 (4.6)	1.09 (0.90 to 1.31)	1.04 (0.85 to 1.27)
>90 days	66 (3.0)	417 (1.9)	0.91 (0.69 to 1.21)	1.02 (0.75 to 1.37)

Values are reported as n (%); RR=rate ratio; CI=confidence interval

*Within 60 days before the index date; current users of other antihypertensive drugs and past users (more than 60 days before the index date) of double and triple therapy combinations are not displayed in the table, but were considered in the regression model

‡Length of exposure to double or triple combination

†Adjusted for the covariates listed in Table 1

Table D1. Rate ratio of acute kidney injury associated with exposure to current double or triple therapy combination (30-day period for both current time-window and grace period).

Current Use*	Cases n=2215	Controls n=21 993	RR (95% CI)	
			crude	adjusted†
<i>diuretics only</i>	196 (8.9)	2556 (11.6)	Reference	Reference
<i>diuretics plus NSAIDs</i>	145 (6.6)	1470 (6.7)	1.32 (1.05 to 1.66)	1.15 (0.91 to 1.46)
<i>ACEIs or ARBs only</i>	136 (6.1)	1882 (8.6)	Reference	Reference
<i>ACEIs or ARBs plus NSAIDs</i>	124 (5.6)	1652 (7.5)	1.07 (0.83 to 1.38)	1.00 (0.77 to 1.31)
<i>diuretics plus ACEIs or ARBs</i>	403 (18.2)	2217 (10.1)	Reference	Reference
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>	413 (18.7)	1943 (8.8)	1.19 (1.02 to 1.38)	1.16 (0.98 to 1.36)

Values are reported as n (%); RR=rate ratio; CI=confidence interval

*Within 30 days before the index date; current users of other antihypertensive drugs and past users (more than 30 days before the index date) of double and triple combinations are not displayed in the table, but were considered in the regression model

†Adjusted for the covariates listed in Table 1

Table D2. Rate ratio of acute kidney injury associated with exposure to current double or triple therapy combination according to NSAIDs half-life and duration of use (30-day period for both current time-window and grace period).

Current Use*	Cases n=2215	Controls n=21 993	RR (95% CI)	
			crude	adjusted [†]
<i>diuretics only</i>	196 (8.9)	2556 (11.6)	Reference	Reference
<i>diuretics plus NSAIDs</i>				
NSAIDs half-life<12 hours	139 (6.3)	1414 (6.4)	1.32 (1.05 to 1.66)	1.14 (0.90 to 1.45)
≥12 hours	6 (0.3)	56 (0.3)	1.34 (0.57 to 3.17)	1.41 (0.59 to 3.38)
duration of use [‡] ≤30 days	53 (2.4)	369 (1.7)	1.90 (1.37 to 2.62)	1.48 (1.05 to 2.08)
31-60 days	68 (3.1)	812 (3.7)	1.12 (0.84 to 1.49)	0.99 (0.73 to 1.34)
61-90 days	21 (1.0)	246 (1.1)	1.15 (0.72 to 1.84)	1.11 (0.68 to 1.82)
>90 days	3 (0.1)	43 (0.2)	0.93 (0.29 to 3.04)	1.14 (0.34 to 3.77)
<i>ACEIs or ARBs only</i>				
<i>ACEIs or ARBs plus NSAIDs</i>	136 (6.1)	1882 (8.6)	Reference	Reference
NSAIDs half-life<12 hours	121 (5.5)	1617 (7.4)	1.07 (0.83 to 1.38)	1.02 (0.78 to 1.33)
≥12 hours	3 (0.1)	35 (0.2)	1.18 (0.36 to 3.89)	0.64 (0.17 to 2.39)
duration of use [‡] ≤30 days	35 (1.6)	401 (1.8)	1.25 (0.85 to 1.85)	1.16 (0.77 to 1.76)
31-60 days	68 (3.1)	864 (3.9)	1.12 (0.83 to 1.52)	1.01 (0.74 to 1.40)
61-90 days	18 (0.8)	342 (1.6)	0.76 (0.46 to 1.26)	0.78 (0.46 to 1.32)
>90 days	3 (0.1)	45 (0.2)	0.94 (0.29 to 3.08)	0.93 (0.24 to 3.62)
<i>diuretics plus ACEIs or ARBs</i>				
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>	403 (18.2)	2217 (10.1)	Reference	Reference
NSAIDs half-life<12 hours	413 (18.7)	1943 (8.8)	1.19 (1.02 to 1.38)	1.14 (0.97 to 1.35)
≥12 hours	14 (0.6)	51 (0.2)	1.51 (0.82 to 2.76)	1.63 (0.86 to 3.10)
duration of use [‡] ≤30 days	127 (5.7)	465 (2.1)	1.52 (1.21 to 1.90)	1.41 (1.11 to 1.80)
31-60 days	232 (10.5)	1137 (5.2)	1.14 (0.96 to 1.36)	1.08 (0.89 to 1.31)
61-90 days	56 (2.5)	346 (1.6)	0.92 (0.68 to 1.24)	0.93 (0.67 to 1.29)

>90 days	12 (0.5)	46 (0.2)	1.43 (0.75 to 2.74)	1.89 (0.96 to 3.73)
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Values are reported as n (%); RR=rate ratio; CI=confidence interval

*Within 30 days before the index date; current users of other antihypertensive drugs and past users (more than 30 days before the index date) of double and triple therapy combinations are not displayed in the table, but were considered in the regression model

‡Length of exposure to double or triple combination

†Adjusted for the covariates listed in Table 1

Table E1. Rate ratio of acute kidney injury associated with exposure to current double or triple therapy combination among incident users of antihypertensive drugs.

Current Use*	Cases n=618	Controls n=6105	RR (95% CI)	
			crude	adjusted [†]
<i>diuretics only</i>	65 (10.5)	732 (12.0)	Reference	Reference
<i>diuretics plus NSAIDs</i>	43 (7.0)	409 (6.7)	1.22 (0.81 to 1.83)	1.18 (0.76 to 1.81)
<i>ACEIs or ARBs only</i>	56 (9.1)	611 (10.0)	Reference	Reference
<i>ACEIs or ARBs plus NSAIDs</i>	58 (9.4)	591 (9.7)	1.13 (0.77 to 1.67)	1.09 (0.72 to 1.66)
<i>diuretics plus ACEIs or ARBs</i>	82 (13.3)	496 (8.1)	Reference	Reference
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>	117 (18.9)	444 (7.3)	1.57 (1.15 to 2.15)	1.46 (1.04 to 2.06)

Values are reported as n (%); RR=rate ratio; CI=confidence interval

*Within 90 days before the index date; current users of other antihypertensive drugs and past users (more than 90 days before the index date) of double and triple therapy combinations are not displayed in the table, but were considered in the regression model

[†]Adjusted for the covariates listed in Table 1

Table E2. Rate ratio of acute kidney injury associated with exposure to current double or triple therapy combination according to NSAIDs half- life and duration of use, among incident users of antihypertensive drugs.

Current Use*	Cases n=618	Controls n=6105	RR (95% CI)	
			crude	adjusted [†]
<i>diuretics only</i>	65 (10.5)	732 (12.0)	Reference	Reference
<i>diuretics plus NSAIDs</i>				
NSAIDs half-life<12 hours	42 (6.8)	384 (6.3)	1.26 (0.84 to 1.91)	1.22 (0.79 to 1.89)
≥12 hours	1 (0.2)	25 (0.4)	0.46 (0.06 to 3.47)	0.46 (0.06 to 3.55)
duration of use [‡] ≤30 days	11 (1.8)	65 (1.1)	1.89 (0.95 to 3.77)	1.56 (0.75 to 3.24)
31-60 days	7 (1.1)	59 (1.0)	1.22 (0.52 to 2.86)	1.23 (0.51 to 2.97)
61-90 days	10 (1.6)	96 (1.6)	1.26 (0.62 to 2.54)	1.18 (0.57 to 2.46)
>90 days	15 (2.4)	189 (3.1)	0.93 (0.52 to 1.68)	0.97 (0.52 to 1.82)
<i>ACEIs or ARBs only</i>				
56 (9.1)	611 (10.0)	Reference	Reference	
<i>ACEIs or ARBs plus NSAIDs</i>				
NSAIDs half-life<12 hours	56 (9.1)	569 (9.3)	1.14 (0.77 to 1.68)	1.10 (0.72 to 1.68)
≥12 hours	2 (0.3)	22 (0.4)	0.97 (0.22 to 4.28)	0.95 (0.21 to 4.37)
duration of use [‡] ≤30 days	9 (1.5)	56 (0.9)	1.81 (0.84 to 3.92)	1.86 (0.82 to 4.19)
31-60 days	8 (1.3)	79 (1.3)	1.13 (0.51 to 2.48)	0.96 (0.41 to 2.23)
61-90 days	12 (1.9)	136 (2.2)	0.99 (0.51 to 1.90)	1.01 (0.51 to 2.01)
>90 days	29 (4.7)	320 (5.2)	1.07 (0.67 to 1.72)	1.02 (0.61 to 1.71)
<i>diuretics plus ACEIs or ARBs</i>				
82 (13.3)	496 (8.1)	Reference	Reference	
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>				
NSAIDs half-life<12 hours	111 (18.0)	429 (7.0)	1.55 (1.13 to 2.12)	1.43 (1.01 to 2.03)
≥12 hours	6 (1.0)	15 (0.3)	2.66 (0.97 to 7.31)	2.85 (0.96 to 8.49)
duration of use [‡] ≤30 days	21 (3.4)	46 (0.8)	2.64 (1.47 to 4.73)	2.06 (1.06 to 3.99)
31-60 days	21 (3.4)	74 (1.2)	1.66 (0.97 to 2.84)	1.44 (0.80 to 2.59)
61-90 days	32 (5.2)	82 (1.3)	2.28 (1.42 to 3.66)	2.00 (1.18 to 3.37)
>90 days	43 (7.0)	242 (4.0)	1.11 (0.74 to 1.65)	1.12 (0.72 to 1.76)

Values are reported as n (%); RR=rate ratio; CI=confidence interval

*Within 90 days before the index date; current users of other antihypertensive drugs and past users (more than 90 days before the index date) of double and triple therapy combinations are not displayed in the table, but were considered in the regression model

‡Length of exposure to double or triple therapy combination

†Adjusted for the covariates listed in Table 1

Table F1. Rate ratio of acute kidney injury associated with exposure to current double or triple therapy combination among prevalent users of antihypertensive drugs.

Current Use*	Cases n=1597	Controls n=15 888	RR (95% CI)	
			crude	adjusted†
<i>diuretics only</i>	144 (9.0)	1900 (12.0)	Reference	Reference
<i>diuretics plus NSAIDs</i>	113 (7.1)	1330 (8.4)	1.14 (0.88 to 1.48)	0.99 (0.76 to 1.30)
<i>ACEIs or ARBs only</i>	92 (5.8)	1278 (8.0)	Reference	Reference
<i>ACEIs or ARBs plus NSAIDs</i>	80 (5.0)	1316 (8.3)	0.87 (0.64 to 1.18)	0.79 (0.57 to 1.09)
<i>diuretics plus ACEIs or ARBs</i>	332 (20.8)	1936 (12.2)	Reference	Reference
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>	427 (26.7)	1980 (12.5)	1.29 (1.10 to 1.50)	1.27 (1.07 to 1.51)

Values are reported as n (%); RR=rate ratio; CI=confidence interval

*Within 90 days before the index date; current users of other antihypertensive drugs and past users (more than 90 days before the index date) of double and triple therapy combinations are not displayed in the table, but were considered in the regression model

†Adjusted for the covariates listed in Table 1

Table F2. Rate ratio of acute renal failure associated with exposure to current double or triple therapy combination according to NSAIDs half- life and duration of use, among prevalent users of antihypertensive drugs.

Current Use*	Cases n=1597	Controls n=15 888	RR (95% CI)	
			crude	adjusted [†]
<i>diuretics only</i>	144 (9.0)	1900 (12.0)	Reference	Reference
<i>diuretics plus NSAIDs</i>				
NSAIDs half-life <12 hours	109 (6.8)	1272 (8.0)	1.15 (0.89 to 1.50)	1.00 (0.76 to 1.31)
≥12 hours	4 (0.3)	58 (0.4)	0.87 (0.31 to 2.43)	0.91 (0.32 to 2.58)
duration of use [‡] ≤30 days	21 (1.3)	143 (0.9)	1.86 (1.14 to 3.04)	1.44 (0.85 to 2.44)
31-60 days	19 (1.2)	187 (1.2)	1.36 (0.82 to 2.25)	1.12 (0.65 to 1.90)
61-90 days	26 (1.6)	283 (1.8)	1.18 (0.76 to 1.83)	1.02 (0.65 to 1.60)
>90 days	47 (2.9)	717 (4.5)	0.89 (0.63 to 1.26)	0.82 (0.57 to 1.16)
<i>ACEIs or ARBs only</i>				
92 (5.8)	1278 (8.0)	Reference	Reference	
<i>ACEIs or ARBs plus NSAIDs</i>				
NSAIDs half-life <12 hours	76 (4.8)	1284 (8.1)	0.84 (0.62 to 1.16)	0.77 (0.56 to 1.08)
≥12 hours	4 (0.3)	32 (0.2)	1.82 (0.63 to 5.28)	1.17 (0.36 to 3.77)
duration of use [‡] ≤30 days	8 (0.5)	139 (0.9)	0.80 (0.38 to 1.68)	0.78 (0.36 to 1.69)
31-60 days	16 (1.0)	168 (1.1)	1.33 (0.76 to 2.33)	1.16 (0.64 to 2.10)
61-90 days	18 (1.1)	254 (1.6)	1.03 (0.61 to 1.74)	0.90 (0.52 to 1.57)
>90 days	38 (2.4)	755 (4.8)	0.72 (0.49 to 1.06)	0.64 (0.43 to 0.97)
<i>diuretics plus ACEIs or ARBs</i>				
82 (13.3)	496 (8.1)	Reference	Reference	
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>				
NSAIDs half-life <12 hours	409 (25.6)	1914 (12.0)	1.28 (1.09 to 1.50)	1.26 (1.06 to 1.49)
≥12 hours	18 (1.1)	66 (0.4)	1.54 (0.90 to 2.64)	1.58 (0.90 to 2.80)
duration of use [‡] ≤30 days	62 (3.9)	188 (1.2)	1.85 (1.35 to 2.53)	1.74 (1.24 to 2.44)
31-60 days	73 (4.6)	235 (1.5)	1.81 (1.36 to 2.42)	1.69 (1.24 to 2.31)
61-90 days	108 (6.8)	418 (2.6)	1.53 (1.20 to 1.95)	1.46 (1.13 to 1.90)
>90 days	184 (11.5)	1139 (7.2)	0.98 (0.80 to 1.19)	0.99 (0.80 to 1.23)

Values are reported as n (%); RR=rate ratio; CI=confidence interval

*Within 90 days before the index date; current users of other antihypertensive drugs and past users (more than 90 days before the index date) of double and triple therapy combinations are not displayed in the table, but were considered in the regression model

‡Length of exposure to double or triple therapy combination

†Adjusted for the covariates listed in Table 1

Table G. Rate ratio of acute kidney injury associated with exposure to current double or triple therapy combination stratifying by osteoarthritis diagnosis.

Current Use*	Cases n=2215	Controls n=21 993	RR (95% CI)	
			crude	adjusted†
Without osteoarthritis:				
<i>diuretics only</i>	165 (9.4)	2175 (12.1)	Reference	Reference
<i>diuretics plus NSAIDs</i>	122 (6.9)	1361 (7.6)	1.21 (0.94 to 1.55)	1.03 (0.79 to 1.35)
<i>ACEIs or ARBs only</i>	117 (6.6)	1618 (9.0)	Reference	Reference
<i>ACEIs or ARBs plus NSAIDs</i>	115 (6.5)	1564 (8.7)	1.03 (0.78 to 1.35)	0.99 (0.74 to 1.33)
<i>diuretics plus ACEIs or ARBs</i>	327 (18.5)	1969 (11.0)	Reference	Reference
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>	418 (23.7)	1920 (10.7)	1.39 (1.18 to 1.64)	1.38 (1.15 to 1.65)
With osteoarthritis:				
<i>diuretics only</i>	44 (9.8)	457 (11.2)	Reference	Reference
<i>diuretics plus NSAIDs</i>	34 (7.6)	378 (9.3)	0.76 (0.43 to 1.36)	0.69 (0.36 to 1.33)
<i>ACEIs or ARBs only</i>	31 (6.9)	271 (6.7)	Reference	Reference
<i>ACEIs or ARBs plus NSAIDs</i>	23 (5.1)	343 (8.4)	0.64 (0.32 to 1.26)	0.61 (0.28 to 1.31)
<i>diuretics plus ACEIs or ARBs</i>	87 (19.3)	463 (11.4)	Reference	Reference
<i>diuretics plus ACEIs or ARBs plus NSAIDs</i>	126 (28.0)	504 (12.4)	1.19 (0.79 to 1.80)	1.30 (0.81 to 2.09)

Values are reported as n (%); RR=rate ratio; CI=confidence interval

*Within 90 days before the index date; current users of other antihypertensive drugs and past users (more than 90 days before the index date) of double and triple therapy combinations are not displayed in the table, but were considered in the regression model

†Adjusted for the covariates listed in Table 1