

Supplement

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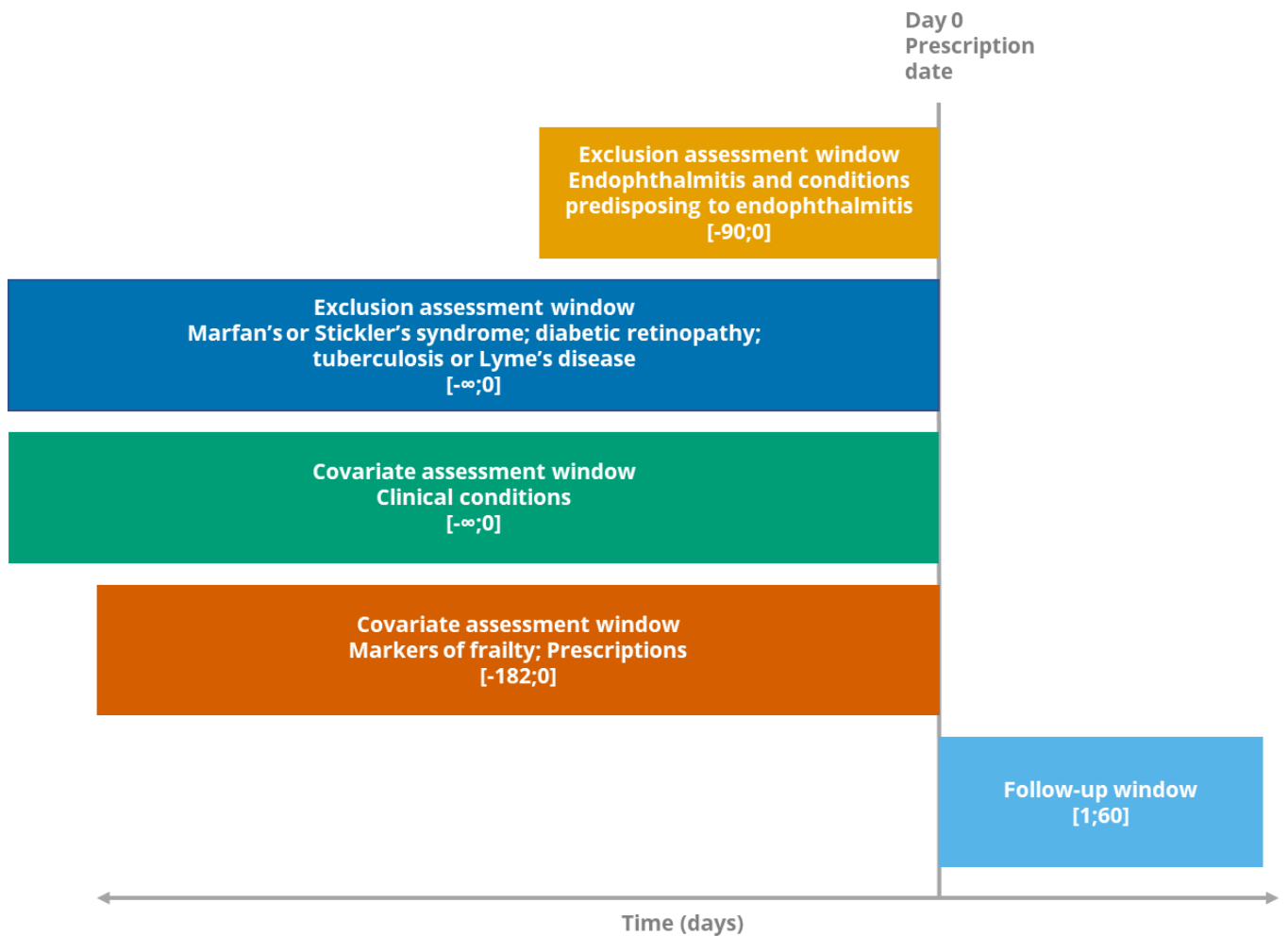
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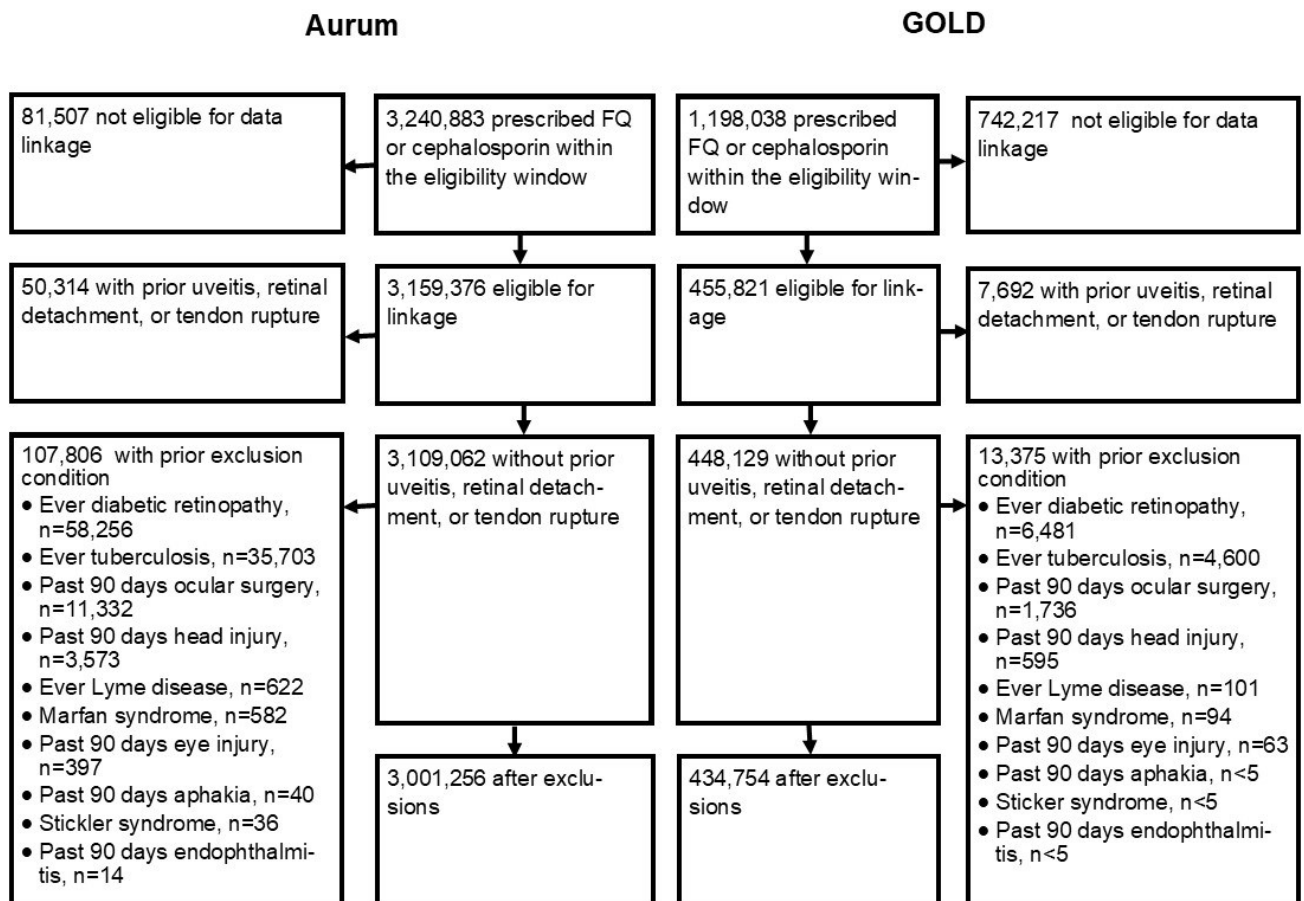
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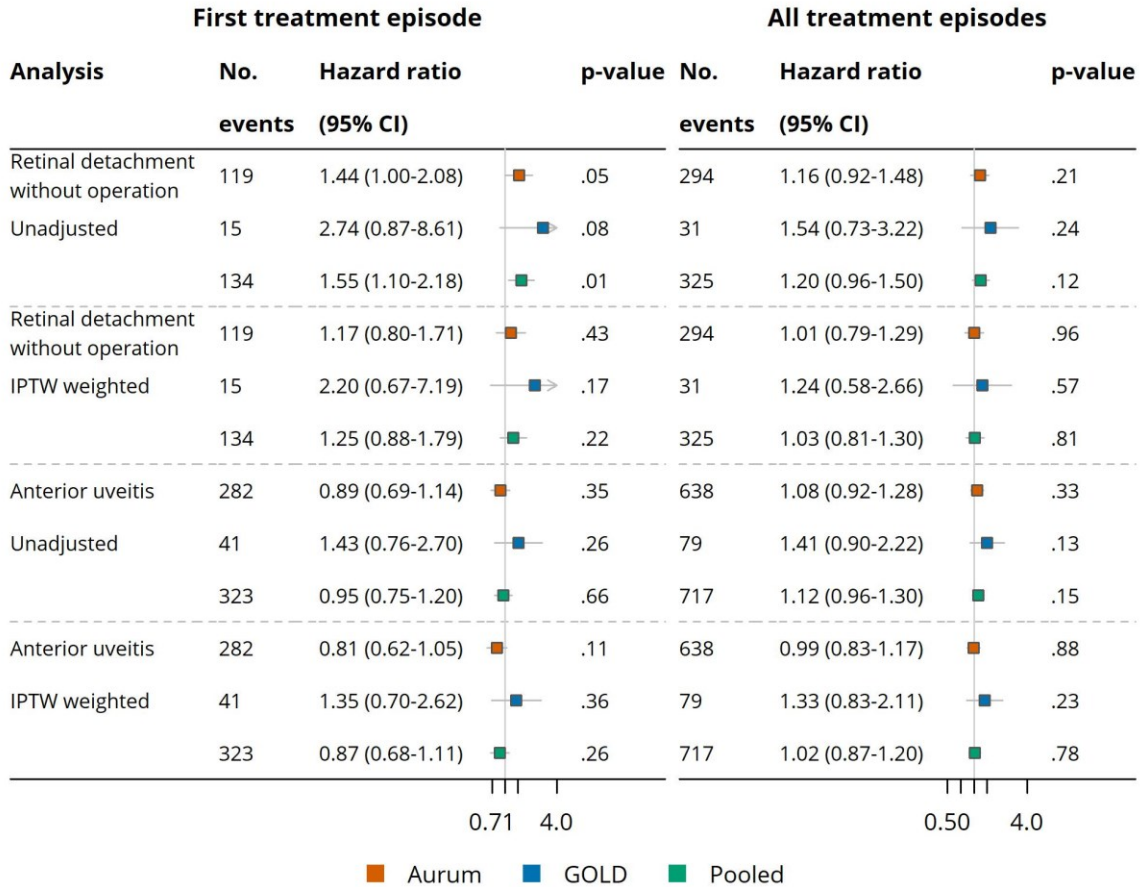


eFigure 1: Graphical depiction of cohort design

Treatment episodes within the eligibility window of fluoroquinolone or cephalosporins among adults (aged 18+ years) were included if the individual had no exclusion criteria conditions prior to prescription. Multiple treatment episodes were included per person if present.

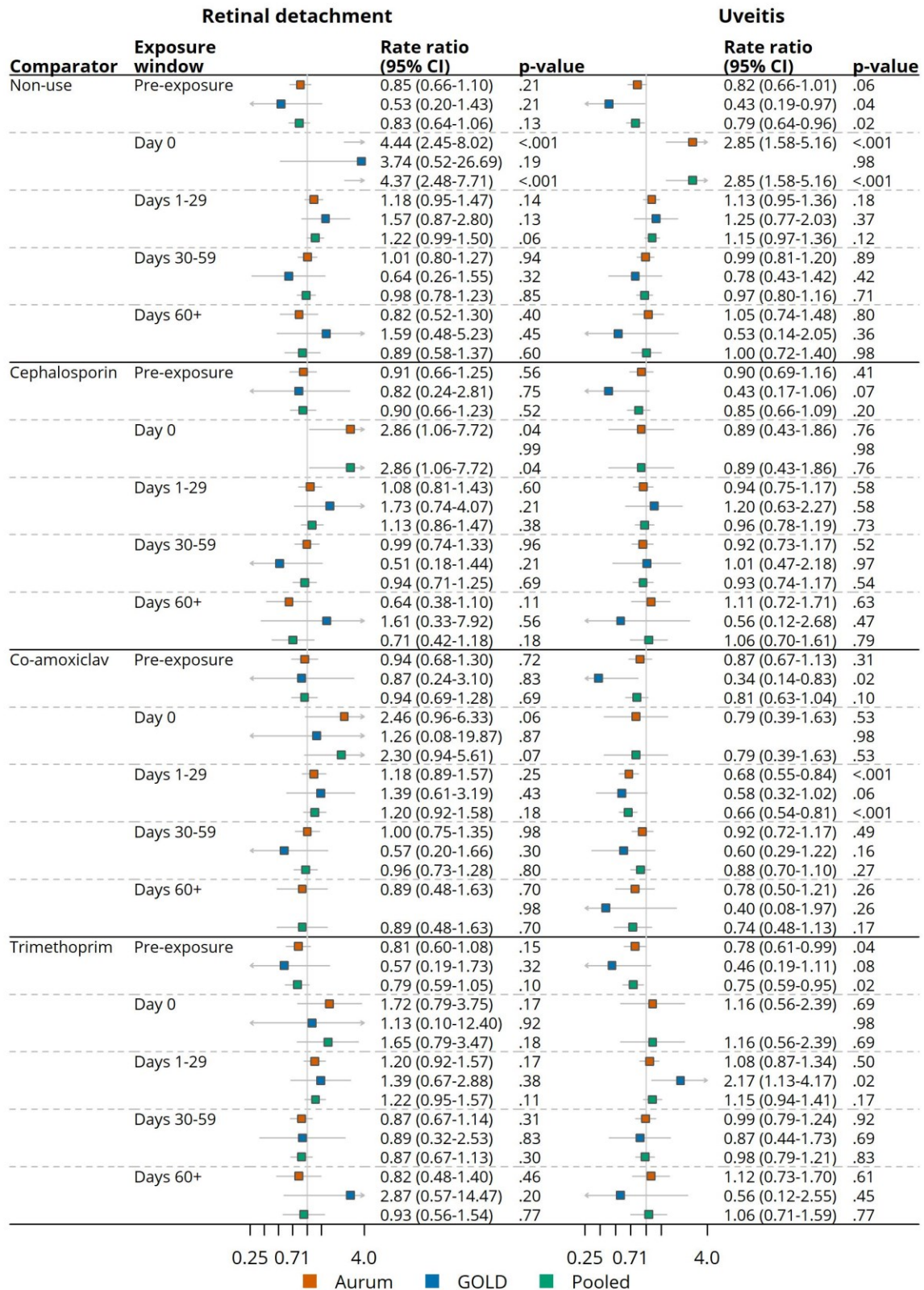


eFigure 2: Flow chart of individuals included in the cohort study



eFigure 3: Hazard ratios comparing risk of anterior uveitis and retinal detachment with or without subsequent operation, following exposure to fluoroquinolone, relative to cephalosporin prescription

Definitions: CI, confidence interval.



eFigure 4: Self-controlled case series - Rate ratios for anterior uveitis and retinal detachment, with or without subsequent operation, comparing fluoroquinolone use to non-use or to use of comparator antibiotics

Definitions: CI, confidence interval.

eTable 1: Cohort study – Calendar year and ethnicity of fluoroquinolone and cephalosporin users at first treatment episode

Characteristic	Aurum		GOLD	
	Cephalosporin, N = 1,973,915	Fluoroquinolone, N = 1,027,341	Cephalosporin, N = 280,900	Fluoroquinolone, N = 153,854
Calendar year				
1997-2001	640,472 (32.4)	237,294 (23.1)	74,556 (26.5)	29,827 (19.4)
2002-2006	668,811 (33.9)	278,322 (27.1)	113,411 (40.4)	52,750 (34.3)
2007-2011	440,157 (22.3)	243,405 (23.7)	73,001 (26.0)	44,769 (29.1)
2012-2016	172,802 (8.8)	182,231 (17.7)	17,180 (6.1)	21,217 (13.8)
2017-2019	51,673 (2.6)	86,089 (8.4)	2,752 (1.0)	5,291 (3.4)
Ethnicity				
White	1,680,597 (90.6)	883,403 (91.7)	246,015 (95.0)	135,536 (95.5)
Asian/Asian British	92,419 (5.0)	40,166 (4.2)	6,437 (2.5)	2,961 (2.1)
Black/Caribbean/African/ Black British	48,855 (2.6)	23,311 (2.4)	2,774 (1.1)	1,541 (1.1)
Other	20,076 (1.1)	9,750 (1.0)	2,619 (1.0)	1,275 (0.9)
Mixed/Multiple	13,464 (0.7)	7,064 (0.7)	1,040 (0.4)	612 (0.4)
Missing	118,504	63,647	22,015	11,929

Main value in each table cell is number of patients, and value in brackets is percentage of individuals.

eTable 2: Cohort study - Baseline characteristics of fluoroquinolone and cephalosporin users over all treatment episodes

Characteristic	Aurum		GOLD	
	Cephalosporin, N = 4,266,152	Fluoroquinolone, N = 2,131,292	Cephalosporin, N = 577,082	Fluoroquinolone, N = 309,349
Age, median (IQR)	57 (39, 73)	58 (42, 72)	58 (40, 74)	59 (44, 73)
Female	3,182,804 (74.6)	1,135,965 (53.3)	429,822 (74.5)	169,979 (54.9)
Calendar year				
1997-2001	1,009,432 (23.7)	374,260 (17.6)	113,448 (19.7)	45,902 (14.8)
2002-2006	1,472,491 (34.5)	580,988 (27.3)	227,632 (39.4)	101,946 (33.0)
2007-2011	1,164,727 (27.3)	582,142 (27.3)	183,296 (31.8)	103,335 (33.4)
2012-2016	478,286 (11.2)	413,609 (19.4)	45,565 (7.9)	47,214 (15.3)
2017-2019	141,216 (3.3)	180,293 (8.5)	7,141 (1.2)	10,952 (3.5)
Ethnicity				
White	3,753,088 (92.1)	1,892,313 (92.9)	519,390 (95.9)	280,813 (96.3)
Asian/Asian British	181,659 (4.5)	76,941 (3.8)	11,545 (2.1)	5,182 (1.8)
Black/African/Caribbean/ Black British	82,033 (2.0)	38,649 (1.9)	4,383 (0.8)	2,435 (0.8)
Other	35,505 (0.9)	16,423 (0.8)	4,569 (0.8)	2,103 (0.7)
Mixed/Multiple	23,761 (0.6)	11,741 (0.6)	1,807 (0.3)	1,013 (0.3)
Missing	190,106	95,225	35,388	17,803
Below 10th percentile Carstairs Index	210,437 (4.9)	116,645 (5.5)	21,076 (3.7)	13,713 (4.4)
BMI, median (IQR)	28 (25, 32)	28 (25, 32)	25.8 (22.7, 29.6)	26.1 (23.1, 29.7)
Missing	742,807	375,798	53,017	27,716
Current smoker	1,424,863 (33.4)	682,830 (32.0)	190,556 (33.0)	96,139 (31.1)
Heavy drinker	86,878 (2.0)	61,506 (2.9)	10,091 (1.7)	7,724 (2.5)
Prior 6 months				
Number of GP appointments, median (IQR)	2.0 (0.0, 6.0)	2.0 (0.0, 6.0)	5 (2, 10)	6 (3, 11)
Hospitalised	870,638 (20.4)	491,496 (23.1)	118,130 (20.5)	72,020 (23.3)
Corticosteroid use	471,352 (11.0)	299,635 (14.1)	73,432 (12.7)	51,753 (16.7)
Ever prior				
Coronary heart disease	482,062 (11.3)	245,766 (11.5)	66,494 (11.5)	36,987 (12.0)
Hypertension	1,143,084 (26.8)	593,768 (27.9)	153,282 (26.6)	86,005 (27.8)

Characteristic	Aurum		GOLD	
	Cephalosporin, N = 4,266,152	Fluoroquinolone, N = 2,131,292	Cephalosporin, N = 577,082	Fluoroquinolone, N = 309,349
Diabetes	342,900 (8.0)	181,923 (8.5)	79,699 (13.8)	44,872 (14.5)
Uncontrolled diabetes	197,924 (4.6)	106,313 (5.0)	27,628 (4.8)	16,581 (5.4)
Cerebrovascular disease	288,365 (6.8)	138,888 (6.5)	39,459 (6.8)	19,672 (6.4)
Dementia	94,991 (2.2)	33,081 (1.6)	12,571 (2.2)	4,133 (1.3)
HIV	2,903 (0.1)	3,157 (0.1)	267 (0.0)	236 (0.1)
Chronic liver disease	18,807 (0.4)	15,378 (0.7)	2,076 (0.4)	1,749 (0.6)
Chronic kidney disease	778,880 (18.3)	374,983 (17.6)	114,249 (19.8)	60,829 (19.7)
Peripheral vascular disease	112,341 (2.6)	65,858 (3.1)	17,210 (3.0)	10,225 (3.3)
Myocardial infarction	158,518 (3.7)	85,180 (4.0)	22,411 (3.9)	13,077 (4.2)
Carotid artery disease	14,524 (0.3)	8,080 (0.4)	2,199 (0.4)	1,320 (0.4)
Multiple sclerosis	36,580 (0.9)	21,111 (1.0)	5,318 (0.9)	3,038 (1.0)
Cataract	408,553 (9.6)	205,683 (9.7)	56,266 (9.8)	30,082 (9.7)
Glaucoma	105,300 (2.5)	53,687 (2.5)	15,148 (2.6)	8,363 (2.7)
Posterior vitreous detachment	40,157 (0.9)	24,059 (1.1)	5,382 (0.9)	3,550 (1.1)
HSV1 infection	85,048 (2.0)	40,102 (1.9)	18,724 (3.2)	9,187 (3.0)
Rheumatoid arthritis	86,197 (2.0)	38,712 (1.8)	17,454 (3.0)	8,326 (2.7)

Main value in each table cell is number of patients, and value in brackets is percentage of individuals, except for age and BMI where median and interquartile range are presented.

Definitions: BMI, body mass index; GP, general practitioner; HSV1, herpes simplex virus 1; HIV, human immunodeficiency virus; IQR, interquartile range.

eTable 3: Cohort study - Maximum across imputed datasets of absolute standardised mean differences before and after weighting at first treatment episode

Characteristic	Aurum		GOLD	
	Unweighted	Weighted	Unweighted	Weighted
Age	0.047	0.018	0.039	0.015
Female	0.497	0.001	0.458	<0.001
Below 10th percentile Carstairs Index	0.031	0.001	0.042	0.001
BMI	0.019	0.005	0.048	0.004
Current smoker	0.026	0.001	0.047	0.001
Heavy drinker	0.067	<0.001	0.059	<0.001
Corticosteroid in prior 6 months	0.052	0.007	0.070	0.005
Coronary heart disease	0.003	0.009	0.003	0.009
Hypertension	0.024	0.008	0.024	0.007
Diabetes	0.017	0.006	0.015	0.006
Uncontrolled diabetes	0.019	0.004	0.025	0.002
Cerebrovascular disease	0.016	0.007	0.025	0.009
Dementia	0.050	0.005	0.061	0.005
HIV	0.028	<0.001	0.013	<0.001
Chronic liver disease	0.031	<0.001	0.029	<0.001
Chronic kidney disease	0.014	0.008	0.010	0.007
Peripheral vascular disease	0.021	0.004	0.016	0.005
Myocardial infarction	0.010	0.006	0.009	0.005
Carotid artery disease	0.006	0.001	0.006	0.002
Multiple sclerosis	0.004	0.001	0.001	<0.001
Cataract	0.010	0.006	0.012	0.006
Glaucoma	0.003	0.003	0.004	0.002
Posterior vitreous detachment	0.022	<0.001	0.019	<0.001
HSV1 infection	0.007	0.001	0.017	<0.001
Rheumatoid arthritis	0.019	0.003	0.021	0.002

eTable 4: Cohort study - Maximum across imputed datasets of absolute standardised mean differences before and after weighting over all treatment episodes

Characteristic	Aurum		GOLD	
	Unweighted	Weighted	Unweighted	Weighted
Age	0.061	0.016	0.055	0.013
Female	0.466	0.001	0.426	0.001
Below 10th percentile Carstairs Index	0.025	0.001	0.040	0.001
BMI	0.025	0.004	0.039	0.007
Current smoker	0.029	0.001	0.042	0.001
Heavy drinker	0.056	<0.001	0.053	<0.001
Corticosteroid in prior 6 months	0.093	0.006	0.115	0.004
Coronary heart disease	0.007	0.009	0.014	0.008
Hypertension	0.024	0.008	0.028	0.006
Diabetes	0.021	0.006	0.027	0.005
Uncontrolled diabetes	0.016	0.004	0.026	0.004
Cerebrovascular disease	0.010	0.007	0.019	0.007
Dementia	0.048	0.004	0.062	0.003
HIV	0.026	<0.001	0.013	<0.001
Chronic liver disease	0.039	<0.001	0.031	<0.001
Chronic kidney disease	0.017	0.008	0.003	0.007
Peripheral vascular disease	0.028	0.004	0.019	0.005
Myocardial infarction	0.015	0.006	0.018	0.005
Carotid artery disease	0.007	0.001	0.007	0.002
Multiple sclerosis	0.014	0.001	0.006	0.002
Cataract	0.003	0.005	0.001	0.004
Glaucoma	0.003	0.003	0.005	0.003
Posterior vitreous detachment	0.019	<0.001	0.022	<0.001
HSV1 infection	0.008	0.001	0.016	<0.001
Rheumatoid arthritis	0.015	0.003	0.020	0.002

eTable 5: Fluoroquinolones and cephalosporins prescribed at first treatment episode

Prescribed medication	Aurum		GOLD	
	Cephalosporin, N = 1,642,125	Fluoroquinolone, N = 839,647	Cephalosporin, N = 234,158	Fluoroquinolone, N = 126,772
Cefaclor	221,848 (13.5)	0 (0.0)	36,659 (15.7)	0 (0.0)
Cefadroxil	59,256 (3.6)	0 (0.0)	5,265 (2.2)	0 (0.0)
Cefalexin	1,189,763 (72.5)	0 (0.0)	166,337 (71.0)	0 (0.0)
Cefamandole	1 (<0.1)	0 (0.0)		
Cefixime	10,988 (0.7)	0 (0.0)	1,111 (0.5)	0 (0.0)
Cefotaxime	156 (<0.1)	0 (0.0)	11 (<0.1)	0 (0.0)
Cefpodoxime	732 (<0.1)	0 (0.0)	41 (<0.1)	0 (0.0)
Cefradine	134,824 (8.2)	0 (0.0)	21,900 (9.4)	0 (0.0)
Ceftazidime	107 (<0.1)	0 (0.0)	11 (<0.1)	0 (0.0)
Ceftibuten	28 (<0.1)	0 (0.0)	4 (<0.1)	0 (0.0)
Ceftriaxone	1,807 (0.1)	0 (0.0)	136 (<0.1)	0 (0.0)
Cefuroxime	22,615 (1.4)	0 (0.0)	2,683 (1.1)	0 (0.0)
Ciprofloxacin	0 (0.0)	733,842 (87.4)	0 (0.0)	110,438 (87.1)
Levofloxacin	0 (0.0)	18,092 (2.2)	0 (0.0)	2,543 (2.0)
Moxifloxacin	0 (0.0)	3,332 (0.4)	0 (0.0)	432 (0.3)
Norfloxacin	0 (0.0)	31,827 (3.8)	0 (0.0)	7,398 (5.8)
Ofloxacin	0 (0.0)	52,554 (6.3)	0 (0.0)	5,961 (4.7)

Main value in each table cell is number of patients, and value in brackets is percentage of individuals, except for age and BMI where median and interquartile range are presented.

eTable 6: Fluoroquinolones and cephalosporins prescribed at all treatment episodes

Prescribed medication	Aurum		GOLD	
	Cephalosporin, N = 1,973,915	Fluoroquinolone, N = 1,027,341	Cephalosporin, N = 280,900	Fluoroquinolone, N = 153,854
Drug				
Cefaclor	264,608 (13.4)	0 (0.0)	42,586 (15.2)	0 (0.0)
Cefadroxil	74,286 (3.8)	0 (0.0)	6,318 (2.2)	0 (0.0)
Cefalexin	1,432,104 (72.6)	0 (0.0)	202,058 (71.9)	0 (0.0)
Cefamandole	2 (<0.1)	0 (0.0)	0 (0.0)	0 (0.0)
Cefixime	13,309 (0.7)	0 (0.0)	1,285 (0.5)	0 (0.0)
Cefotaxime	175 (<0.1)	0 (0.0)	14 (<0.1)	0 (0.0)
Cefpodoxime	877 (<0.1)	0 (0.0)	43 (<0.1)	0 (0.0)
Cefradine	160,078 (8.1)	0 (0.0)	25,376 (9.0)	0 (0.0)
Ceftazidime	113 (<0.1)	0 (0.0)	11 (<0.1)	0 (0.0)
Ceftibuten	33 (<0.1)	0 (0.0)	4 (<0.1)	0 (0.0)
Ceftriaxone	2,069 (0.1)	0 (0.0)	162 (<0.1)	0 (0.0)
Cefuroxime	26,261 (1.3)	0 (0.0)	3,043 (1.1)	0 (0.0)
Ciprofloxacin	0 (0.0)	903,584 (88.0)	0 (0.0)	134,984 (87.7)
Levofloxacin	0 (0.0)	20,363 (2.0)	0 (0.0)	2,835 (1.8)
Moxifloxacin	0 (0.0)	3,646 (0.4)	0 (0.0)	473 (0.3)
Norfloxacin	0 (0.0)	37,448 (3.6)	0 (0.0)	8,656 (5.6)
Ofloxacin	0 (0.0)	62,300 (6.1)	0 (0.0)	6,906 (4.5)

Main value in each table cell is number of patients, and value in brackets is percentage of individuals, except for age and BMI where median and interquartile range are presented.

eTable 7: Cohort study - Hazard ratios comparing risk of uveitis, retinal detachment and tendon rupture after fluoroquinolone prescription, relative to cephalosporin prescription, at first treatment episode – excluding cases with cataract surgery within 30 days

Outcome	Analysis	Aurum			GOLD			Pooled		
		HR	95% CI	p-value	HR	95% CI	P-value	HR	95% CI	p-value
Uveitis	Unadjusted	0.99	0.77-1.26	.92	1.51	0.81-2.83	.19	1.05	0.83-1.31	.69
	IPTW weighted	0.89	0.69-1.15	.37	1.38	0.72-2.65	.32	0.95	0.75-1.20	.65
Retinal detachment	Unadjusted	1.50	0.83-2.69	.17	4.57	0.51-41.14	.13	1.69	0.98-2.89	.06
	IPTW weighted	1.22	0.66-2.25	.52	4.52	0.48-43.00	.14	1.41	0.80-2.47	.23
Tendon rupture	Unadjusted	2.37	1.85-3.05	<.001	3.49	1.63-7.47	.002	2.47	1.95-3.13	<.001
	IPTW weighted	1.94	1.50-2.52	<.001	3.07	1.40-6.74	.007	2.04	1.60-2.61	<.001

Definitions: HR, hazard ratio; IPTW, inverse probability of treatment weighting; CI, confidence interval.

eTable 8: Cohort study - Hazard ratios comparing risk of uveitis, retinal detachment and tendon rupture after fluoroquinolone prescription, relative to cephalosporin prescription, at all treatment episodes – excluding cases with cataract surgery within 30 days

Outcome	Analysis	Aurum			GOLD			Pooled		
		HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
Uveitis	Unadjusted	1.18	1.00-1.39	.05	1.41	0.90-2.22	.13	1.20	1.03-1.40	.02
	IPTW weighted	1.08	0.91-1.28	.37	1.31	0.82-2.10	.25	1.10	0.94-1.29	.22
Retinal detachment	Unadjusted	1.28	0.89-1.83	.19	1.63	0.53-5.03	.36	1.31	0.94-1.84	.12
	IPTW weighted	1.09	0.75-1.59	.66	1.39	0.43-4.44	.56	1.12	0.79-1.59	.53
Tendon rupture	Unadjusted	2.21	1.90-2.56	<.001	3.24	2.05-5.11	<.001	2.29	1.99-2.64	<.001
	IPTW weighted	1.85	1.59-2.16	<.001	2.66	1.66-4.27	<.001	1.92	1.66-2.23	<.001

Definitions: HR, hazard ratio; IPTW, inverse probability of treatment weighting; CI, confidence interval.

eTable 9: Cohort study - Hazard ratios comparing risk of uveitis, retinal detachment and tendon rupture after fluoroquinolone prescription, relative to cephalosporin prescription, at first treatment episode – among individuals with a urinary tract infection within two weeks prior

Outcome	Analysis	Aurum			GOLD			Pooled		
		HR	95% CI	p-value	HR	95% CI	P-value	HR	95% CI	p-value
Uveitis	Unadjusted	0.73	0.33-1.62	.43	1.56	0.13-18.39	.64	0.83	0.41-1.68	.61
	IPTW weighted	0.61	0.27-1.41	.24	1.66	0.14-19.83	.59	0.74	0.36-1.52	.41
Retinal detachment	Unadjusted	2.33	0.31-17.34	.32	DNC	DNC	DNC			
	IPTW weighted	1.73	0.23-13.28	.51	DNC	DNC	DNC			
Tendon rupture	Unadjusted	1.99	1.04-3.81	.04	9.34	0.06-1343.87	.19	2.22	1.21-4.07	.01
	IPTW weighted	1.46	0.75-2.85	.26	7.54	0.05-1160.57	.23	1.65	0.88-3.08	.12

Definitions: HR, hazard ratio; IPTW, inverse probability of treatment weighting; CI, confidence interval. DNC, model did not converge.

eTable 10: Cohort study - Hazard ratios comparing risk of uveitis, retinal detachment and tendon rupture after fluoroquinolone prescription, relative to cephalosporin prescription, at all treatment episodes – among individuals with a urinary tract infection within two weeks prior

Outcome	Analysis	Aurum			GOLD			Pooled		
		HR	95% CI	p-value	HR	95% CI	P-value	HR	95% CI	p-value
Uveitis	Unadjusted	0.99	0.64-1.53	.97	1.30	0.34-4.91	.68	1.02	0.69-1.53	.91
	IPTW weighted	0.88	0.56-1.39	.59	1.32	0.34-5.11	.66	0.93	0.61-1.41	.72
Retinal detachment	Unadjusted	1.49	0.56-3.93	.40	DNC	DNC	DNC			
	IPTW weighted	1.19	0.43-3.26	.73	DNC	DNC	DNC			
Tendon rupture	Unadjusted	1.97	1.33-2.91	<.001	2.92	0.67-12.75	.13	2.04	1.41-2.95	<.001
	IPTW weighted	1.53	1.03-2.29	.04	2.12	0.46-9.76	.29	1.58	1.08-2.30	.02

Definitions: HR, hazard ratio; IPTW, inverse probability of treatment weighting; CI, confidence interval; DNC, model did not converge.

eTable 11: Cohort study - Hazard ratios comparing risk of uveitis, retinal detachment and tendon rupture after fluoroquinolone prescription, relative to cephalosporin prescription, at first treatment episode – limited to first prescriptions only

Outcome	Analysis	Aurum			GOLD			Pooled		
		HR	95% CI	p-value	HR	95% CI	P-value	HR	95% CI	p-value
Uveitis	Unadjusted	0.99	0.76-1.28	.93	1.49	0.76-2.94	.24	1.05	0.82-1.33	.72
	IPTW weighted	0.90	0.68-1.18	.44	1.28	0.64-2.58	.48	0.94	0.73-1.22	.66
Retinal detachment	Unadjusted	1.48	0.82-2.67	.19	4.16	0.46-37.49	.15	1.65	0.96-2.85	.07
	IPTW weighted	1.19	0.64-2.21	.58	4.35	0.46-41.47	.15	1.38	0.78-2.43	.27
Tendon rupture	Unadjusted	2.29	1.75-3.00	<.001	3.54	1.45-8.60	.007	2.39	1.85-3.08	<.001
	IPTW weighted	1.88	1.42-2.49	<.001	3.18	1.27-7.98	.02	1.97	1.51-2.58	<.001

Definitions: HR, hazard ratio; IPTW, inverse probability of treatment weighting; CI, confidence interval.

eTable 12: Cohort study - Hazard ratios comparing risk of uveitis, retinal detachment and tendon rupture after fluoroquinolone prescription, relative to cephalosporin prescription, at first treatment episode – excluding individuals with diabetes

Outcome	Analysis	Aurum			GOLD			Pooled		
		HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
Uveitis	Unadjusted	0.95	0.74-1.23	.69	1.57	0.82-3.02	.17	1.02	0.81-1.29	.88
	IPTW weighted	0.86	0.66-1.12	.27	1.49	0.76-2.92	.24	0.93	0.73-1.19	.56
Retinal detachment	Unadjusted	1.62	0.89-2.95	.11	5.51	0.04-792.19	.28	1.75	1.00-3.07	.05
	IPTW weighted	1.26	0.68-2.36	.46	4.33	0.03-624.59	.33	1.37	0.76-2.46	.29
Tendon rupture	Unadjusted	2.54	1.95-3.31	<.001	4.28	1.89-9.70	.001	2.68	2.09-3.44	<.001
	IPTW weighted	2.13	1.62-2.81	<.001	3.70	1.59-8.62	.004	2.26	1.74-2.92	<.001

Definitions: HR, hazard ratio; IPTW, inverse probability of treatment weighting; CI, confidence interval.

eTable 13: Cohort study - Hazard ratios comparing risk of uveitis, retinal detachment and tendon rupture after fluoroquinolone prescription, relative to cephalosporin prescription, at all treatment episodes– excluding individuals with diabetes

Outcome	Analysis	Aurum			GOLD			Pooled		
		HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
Uveitis	Unadjusted	1.15	0.97-1.36	.11	1.33	0.82-2.16	.24	1.16	0.99-1.36	.06
	IPTW weighted	1.04	0.88-1.24	.64	1.26	0.76-2.08	.36	1.07	0.90-1.26	.45
Retinal detachment	Unadjusted	1.52	1.04-2.21	.03	2.26	0.57-9.02	.21	1.57	1.11-2.24	.01
	IPTW weighted	1.29	0.87-1.91	.20	1.63	0.40-6.66	.45	1.32	0.91-1.91	.14
Tendon rupture	Unadjusted	2.27	1.93-2.65	<.001	3.47	2.11-5.70	<.001	2.36	2.03-2.74	<.001
	IPTW weighted	1.89	1.60-2.22	<.001	2.69	1.61-4.50	<.001	1.95	1.67-2.28	<.001

Definitions: HR, hazard ratio; IPTW, inverse probability of treatment weighting; CI, confidence interval.

eTable 14: Cohort study - Hazard ratios comparing risk of uveitis, retinal detachment and tendon rupture after fluoroquinolone prescription, relative to cephalosporin prescription, at first treatment episode– complete case analysis

Outcome	Analysis	Aurum			GOLD			Pooled		
		HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
Uveitis	Unadjusted	1.01	0.79-1.30	.92	1.50	0.80-2.79	.20	1.07	0.85-1.35	.57
	IPTW weighted	0.92	0.71-1.20	.53	1.39	0.73-2.65	.32	0.98	0.77-1.24	.84
Retinal detachment	Unadjusted	1.70	0.96-3.01	.07	4.58	0.89-23.58	.07	1.89	1.10-3.24	.02
	IPTW weighted	1.22	0.67-2.21	.51	4.54	0.84-24.38	.08	1.39	0.79-2.44	.25
Tendon rupture	Unadjusted	2.46	1.89-3.20	<.001	3.33	1.59-6.94	.001	2.54	1.98-3.26	<.001
	IPTW weighted	1.97	1.50-2.59	<.001	2.80	1.31-5.98	.008	2.04	1.59-2.63	<.001

Definitions: HR, hazard ratio; IPTW, inverse probability of treatment weighting; CI, confidence interval.

eTable 15: Cohort study - Hazard ratios comparing risk of uveitis, retinal detachment and tendon rupture after fluoroquinolone prescription, relative to cephalosporin prescription, at all treatment episodes– complete case analysis

Outcome	Analysis	Aurum			GOLD			Pooled		
		HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
Uveitis	Unadjusted	1.17	1.00-1.38	.06	1.40	0.90-2.19	.14	1.20	1.03-1.40	.02
	IPTW weighted	1.07	0.90-1.27	.45	1.32	0.83-2.09	.24	1.10	0.94-1.28	.25
Retinal detachment	Unadjusted	1.41	0.99-1.99	.06	1.86	0.70-4.95	.22	1.45	1.05-2.01	.03
	IPTW weighted	1.18	0.82-1.69	.38	1.55	0.56-4.29	.40	1.21	0.86-1.69	.27
Tendon rupture	Unadjusted	2.22	1.90-2.60	<.001	3.37	2.11-5.40	<.001	2.32	2.00-2.68	<.001
	IPTW weighted	1.85	1.57-2.17	<.001	2.73	1.68-4.44	<.001	1.92	1.65-2.23	<.001

Definitions: HR, hazard ratio; IPTW, inverse probability of treatment weighting; CI, confidence interval.

eTable 16: Cohort study - Hazard ratios comparing risk of uveitis, retinal detachment and tendon rupture after fluoroquinolone prescription, relative to cephalosporin prescription, at first treatment episode with a propensity score stratified by calendar period

Outcome	Analysis	Aurum			GOLD			Pooled		
		HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
Uveitis	Unadjusted	0.95	0.75-1.21	.69	1.45	0.78-2.69	.24	1.01	0.81-1.26	.94
	IPTW weighted	0.87	0.67-1.12	.28	1.34	0.70-2.56	.38	0.92	0.72-1.17	.50
Retinal detachment	Unadjusted	1.53	0.87-2.67	.14	4.57	0.51-41.15	.13	1.70	1.01-2.86	.04
	IPTW weighted	1.21	0.67-2.19	.52	4.41	0.44-44.12	.16	1.38	0.80-2.39	.25
Tendon rupture	Unadjusted	2.37	1.84-3.04	<.001	3.49	1.63-7.47	.002	2.46	1.95-3.12	<.001
	IPTW weighted	1.73	1.31-2.27	<.001	2.96	1.33-6.57	.009	1.83	1.42-2.37	<.001

Definitions: HR, hazard ratio; IPTW, inverse probability of treatment weighting; CI, confidence interval.

eTable 17: Cohort study - Hazard ratios comparing risk of uveitis, retinal detachment and tendon rupture after fluoroquinolone prescription, relative to cephalosporin prescription, at all treatment episodes with a propensity score stratified by calendar period

Outcome	Analysis	Aurum			GOLD			Pooled		
		HR	95% CI	p-value	HR	95% CI	p-value	HR	95% CI	p-value
Uveitis	Unadjusted	1.15	0.98-1.34	.08	1.43	0.92-2.22	.11	1.18	1.02-1.36	.03
	IPTW weighted	1.08	0.92-1.28	.34	1.37	0.87-2.17	.18	1.12	0.95-1.30	.17
Retinal detachment	Unadjusted	1.33	0.94-1.87	.11	1.87	0.64-5.49	.23	1.38	1.00-1.90	.05
	IPTW weighted	1.09	0.76-1.58	.63	1.57	0.50-4.89	.41	1.14	0.81-1.60	.46
Tendon rupture	Unadjusted	2.22	1.91-2.57	<.001	3.24	2.05-5.11	<.001	2.30	2.00-2.65	<.001
	IPTW weighted	1.69	1.44-1.98	<.001	2.74	1.70-4.41	<.001	1.77	1.52-2.06	<.001

Definitions: HR, hazard ratio; IPTW, inverse probability of treatment weighting; CI, confidence interval.