

DrugWAS: Leveraging drug-wide association studies to facilitate drug repurposing for COVID-19

Supplemental Figures

eFigure 1 Strategies for selecting severity groups for COVID-19 outcomes

eFigure 2 Spline regression analysis showing the OR trends of 49 drug associations across the COVID-19 severity scale (cumulative severity strategy)

eFigure 3 Spline regression analysis showing the OR trends of 49 drug associations across the COVID-19 severity scale (exclusive severity strategy)

Supplemental Tables

eTable 1 The number of total, potential, and significant associations conducted for primary and secondary outcomes

eTable 2 Patient counts for each severity group included in the study

eTable 3 Association between drug exposure and all-cause of death

eTable 4 Main patient characteristics by overlap weighting with propensity scores for all drug studies in the primary analysis

eTable 5 Association between drug exposure and on ventilator (cumulative severity)

eTable 6 Association between drug exposure and in ICU (cumulative severity)

eTable 7 Association between drug exposure and hospitalized-mild (cumulative severity)

eTable 8 Association between drug exposure and on ventilator (exclusive severity)

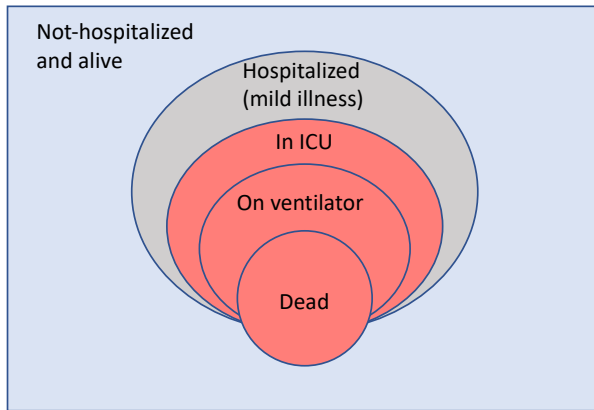
eTable 9 Association between drug exposure and in ICU (exclusive severity)

eTable 10 Association between drug exposure and hospitalized-mild (exclusive severity)

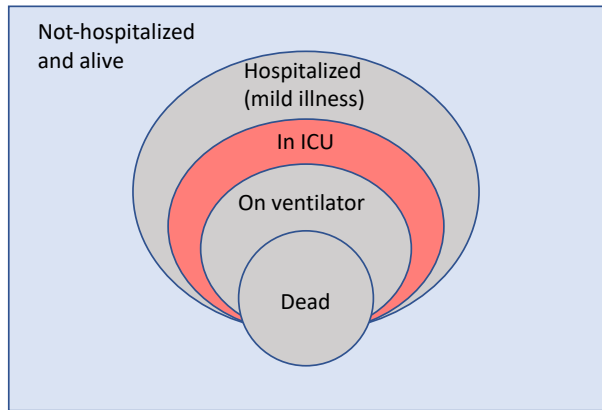
Supplemental Figures

eFigure 1 Strategies for selecting severity groups for COVID-19 outcomes. **A.** Cumulative severity strategy for the in ICU outcome includes in the severity group all the patients admitted to ICU or with a more severe outcome (ie, on ventilator or dead). **B.** Exclusive severity for the in ICU outcomes includes in the severity group only the patients admitted to ICU and exclude all the patients with any other outcome.

A Cumulative severity

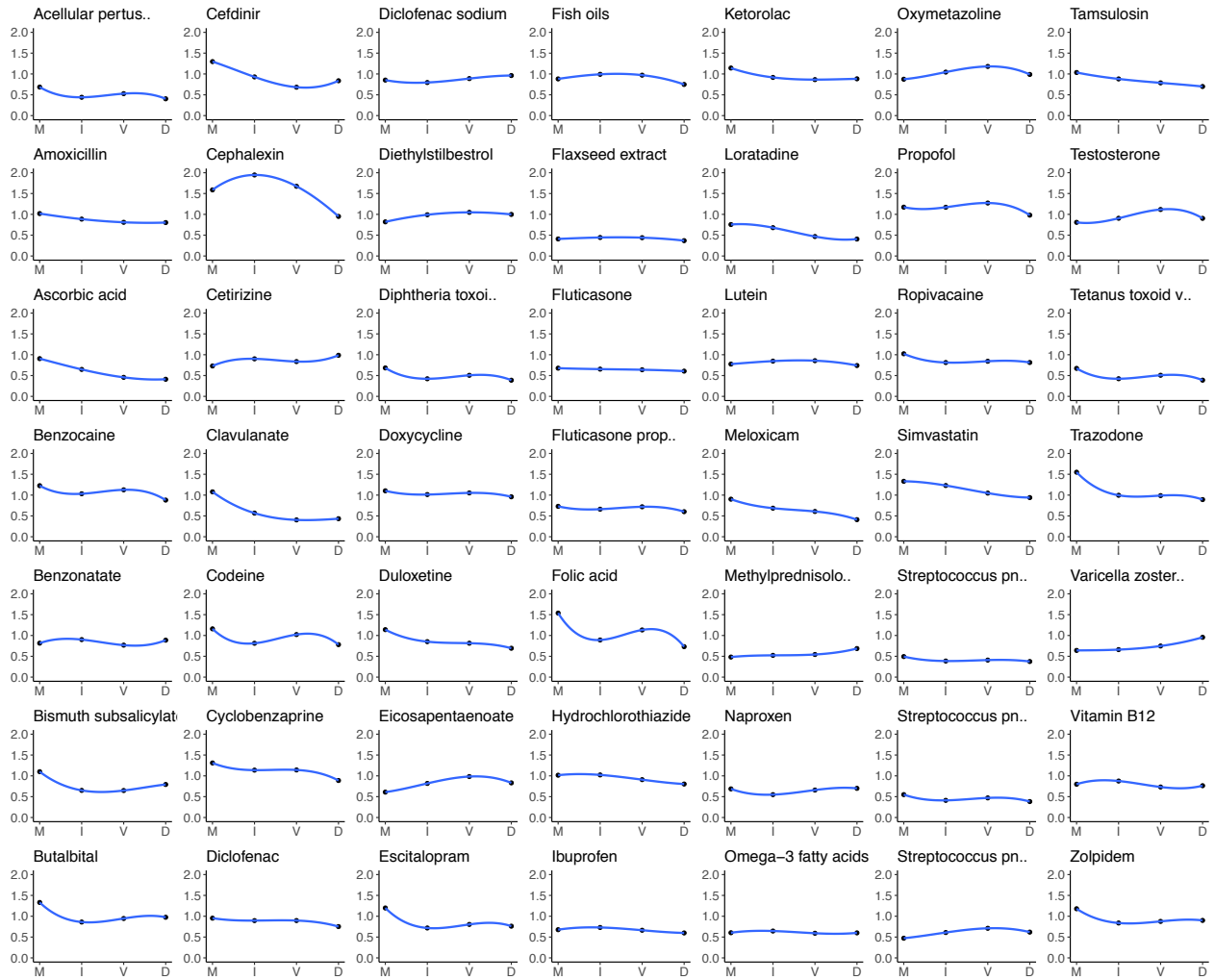


B Exclusive severity

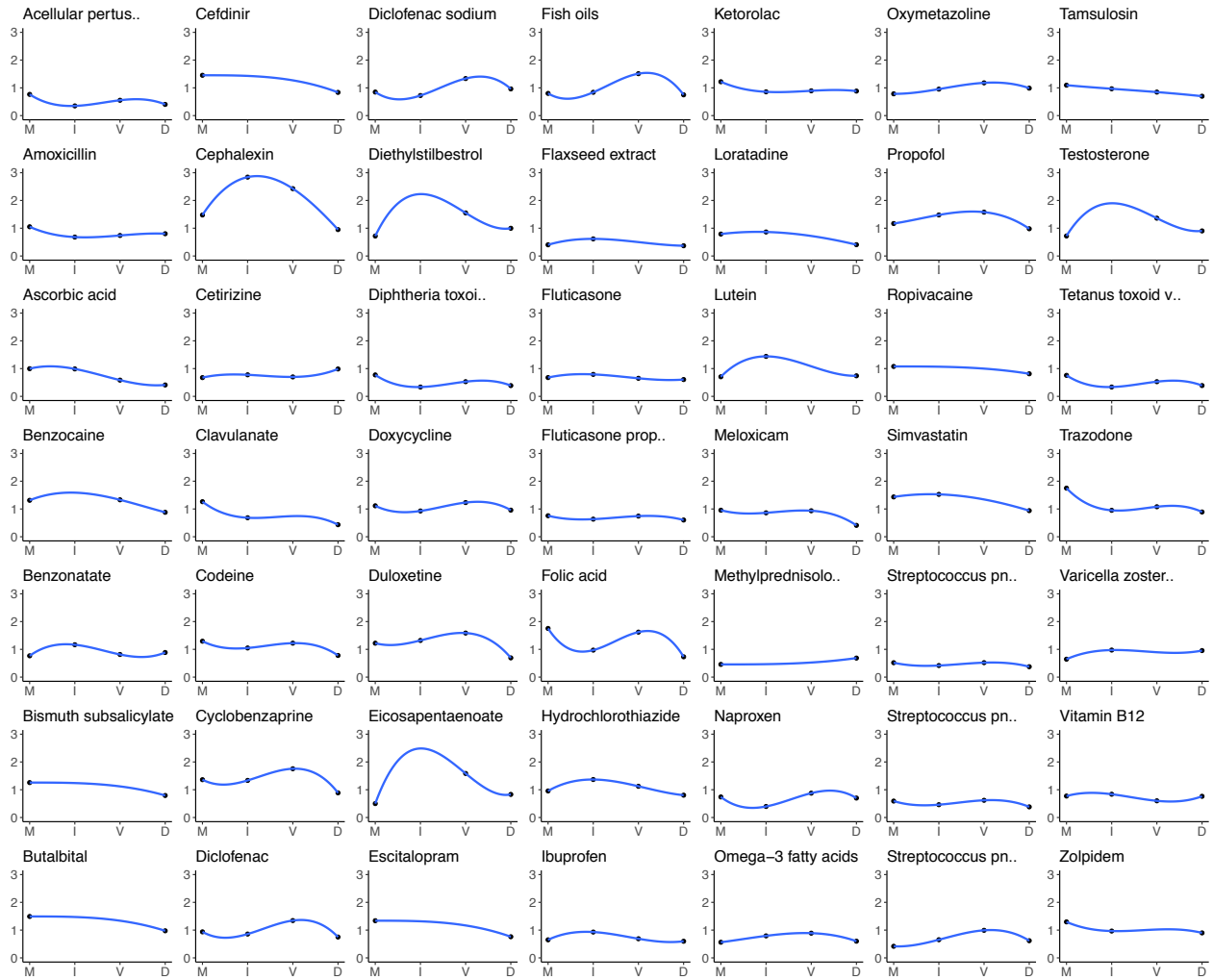


- Included in the severe COVID-19 group
- Included in the non-severe COVID-19 group
- Excluded from the study

eFigure 2 Spline regression analysis showing the OR trends of 49 drug associations across the COVID-19 severity scale: hospitalized-mild (M), ICU admission (I), on ventilation (V), and death (D). The secondary outcomes were extracted following the cumulative severity strategy.



eFigure 3 Spline regression analysis showing the OR trends of 49 drug associations across the COVID-19 severity scale: hospitalized-mild (M), ICU admission (I), on ventilation (V), and death (D). The secondary outcomes were extracted following the exclusive severity strategy.



Supplemental Tables

eTable 1 The number of total, potential, and significant associations conducted for primary and secondary outcomes.

Study	Cumulative severity			Exclusive severity		
	Significant	Potential	Total	Significant	Potential	Total
Dead	4	49	233	4	49	233
On ventilator	2	48	243	0	24	198
In ICU	5	61	261	3	45	202
Hospitalized-mild	15	77	346	10	73	331

eTable 2 Patient counts for each severity group included in the study. Notably, the hospitalized-mild cohort extracted using the cumulative severity strategy includes all hospitalized patients (N=509) and the patients who died and did not have an inpatient visit at VUMC after they were diagnosed with SARS-CoV-2 infection (N=11).

Severity group	Cumulative severity	Exclusive severity
Dead	90	90
On ventilator	114	64
In ICU	144	82
Hospitalized-mild	520	376
Not hospitalized, alive	7,248	7,248

eTable 3 Association between drug exposure and all-cause of death.

TCe/u, total count of drug exposed/unexposed patients; **SRe/u**, severity rate of drug exposed/unexposed patients computed after overlap weighting with propensity score; **OR**, odds ratio; **CI**, confidence interval. The association results are arranged in the ascending order of OR values. The statistically significant results at the 0.05 level are emphasized in bold.

Drug name	Drug class	TCe	TCu	SRe	SRu	OR	95% CI
Flaxseed extract	supplement	186	7,152	2.7	8.4	0.37	(0.11 - 1.21)
*A Streptococcus pneumoniae serotype X	vaccine	388	6,950	2.1	4.1	0.38	(0.14 - 0.98)
*B Streptococcus pneumoniae serotype X	vaccine	612	6,726	1.9	3.6	0.38	(0.17 - 0.89)
Diphtheria toxoid vaccine, inactivated	vaccine	1,166	6,172	0.7	1.7	0.39	(0.15 - 0.98)
Tetanus toxoid vaccine, inactivated	vaccine	1,169	6,169	0.7	1.7	0.39	(0.15 - 0.98)
Acellular pertussis vaccine, inactivated	vaccine	1,119	6,219	0.8	1.7	0.4	(0.16 - 1.02)
Loratadine	antihistamine	754	6,584	0.6	1.6	0.41	(0.12 - 1.34)
Meloxicam	NSAID	587	6,751	0.8	2.8	0.41	(0.13 - 1.25)
Ascorbic acid	supplement	564	6,774	1.1	2.5	0.41	(0.14 - 1.20)
Clavulanate	antibiotic	866	6,472	0.7	1.6	0.43	(0.15 - 1.25)
Ibuprofen	NSAID	3,508	3,830	0.8	1.4	0.6	(0.30 - 1.19)
Omega-3 fatty acids	supplement	434	6,904	2.8	4.4	0.6	(0.26 - 1.37)
Fluticasone propionate	corticosteroid	896	6,442	1	1.6	0.6	(0.23 - 1.55)
Fluticasone	corticosteroid	2,154	5,184	1	1.7	0.61	(0.31 - 1.18)
*C Streptococcus pneumoniae type X	vaccine	510	6,828	2.7	4.5	0.62	(0.28 - 1.36)
Methylprednisolone acetate	corticosteroid	399	6,939	1.2	2.4	0.69	(0.20 - 2.33)
Duloxetine	antidepressant	292	7,046	1.6	2.6	0.69	(0.20 - 2.40)
Tamsulosin	alpha 1 blocker	216	7,122	4	5.8	0.7	(0.25 - 1.96)
Naproxen	NSAID	982	6,356	0.9	1.6	0.7	(0.27 - 1.81)
Folic acid	supplement	417	6,921	1.9	1.9	0.73	(0.24 - 2.22)
Lutein	supplement	147	7,191	4.3	6.5	0.74	(0.23 - 2.35)
Fish oils	supplement	437	6,901	2.4	3.3	0.75	(0.31 - 1.81)
Diclofenac	NSAID	605	6,733	1.8	2.9	0.75	(0.32 - 1.77)
Escitalopram	antidepressant	499	6,839	1.2	1.1	0.76	(0.20 - 2.95)
Vitamin B12	supplement	668	6,670	2.2	2.4	0.76	(0.33 - 1.79)
Codeine	opioid	342	6,996	1.8	2.9	0.78	(0.25 - 2.43)
Bismuth subsalicylate	antidiarrheal	171	7,167	2.8	3	0.79	(0.19 - 3.25)
Amoxicillin	antibiotic	1,709	5,629	1	1.1	0.8	(0.37 - 1.75)
Hydrochlorothiazide	antihypertensive	707	6,631	2.5	4.2	0.8	(0.39 - 1.64)
Ropivacaine	anesthetic	219	7,119	2.3	3.1	0.81	(0.23 - 2.93)
Eicosapentaenoate	supplement	223	7,115	2.6	3.5	0.83	(0.26 - 2.69)
Cefdinir	antibiotic	298	7,040	1.7	1.1	0.84	(0.16 - 4.41)
Benzocaine	anesthetic	413	6,925	1.2	1.1	0.88	(0.21 - 3.65)
Ketorolac	NSAID	551	6,787	1.1	1.7	0.88	(0.28 - 2.82)

Benzonatate	antitussive	635	6,703	1.8	2.3	0.89	(0.37 - 2.14)
Cyclobenzaprine	skeletal muscle relaxant	499	6,839	1.4	2	0.89	(0.30 - 2.59)
Trazodone	antidepressant	339	6,999	2.3	2.3	0.89	(0.28 - 2.83)
Zolpidem	hypnotic	240	7,098	2	3.3	0.9	(0.25 - 3.28)
Testosterone	androgen	284	7,054	2	2.3	0.9	(0.26 - 3.12)
Simvastatin	antilipid agent	203	7,135	3.3	5.5	0.94	(0.30 - 2.97)
Cephalexin	antibiotic	416	6,922	1.6	1.5	0.95	(0.28 - 3.28)
Varicella zoster virus glycoprotein E	vaccine	222	7,116	2.9	5.4	0.96	(0.29 - 3.21)
Doxycycline	antibiotic	693	6,645	1.8	1.9	0.96	(0.40 - 2.29)
Diclofenac sodium	NSAID	341	6,997	3	3.6	0.96	(0.38 - 2.41)
Butalbital	barbituate	347	6,991	1.7	1.9	0.98	(0.29 - 3.26)
Propofol	general anesthetic	602	6,736	2	2.6	0.98	(0.42 - 2.32)
Cetirizine	antihistamine	1,388	5,950	1.1	1.2	0.99	(0.44 - 2.22)
Oxymetazoline	adrenergic agonist agent	1,143	6,195	1.5	1.3	0.99	(0.45 - 2.20)
Diethylstilbestrol	estrogen	172	7,166	4.5	5.7	1	(0.33 - 2.98)

Other abbreviations and acronyms. *A Streptococcus pneumoniae serotype X: Streptococcus pneumoniae serotype (1, 19A, 3, 5, 6A, 7F) capsular antigen diphtheria CRM197 protein conjugate vaccine; *B Streptococcus pneumoniae serotype X: Streptococcus pneumoniae serotype (14, 18C, 19F, 23F, 4, 6B, 9V) capsular antigen diphtheria CRM197 protein conjugate vaccine; *C Streptococcus pneumoniae type X: Streptococcus pneumoniae type (1, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 2, 20, 22F, 23F, 3, 33F, 4, 5, 6B, 7F, 8, 9N, 9V) capsular polysaccharide antigen; NSAID: nonsteroidal anti-inflammatory drug.

eTable 4 Main patient characteristics by overlap weighting with propensity scores for all drug studies in the primary analysis.

Drug name	Drug exposed	Patient count	Male, %	White, %	Black, %	Not Hispanic or Latino, %
Flaxseed extract	yes	186	43.6	92.1	7.9	97.5
	no	7,152	43.6	92.1	7.9	97.5
*A Streptococcus pneumoniae serotype X	yes	388	42.8	83.8	12	94.4
	no	6,950	42.8	83.8	12	94.4
*B Streptococcus pneumoniae serotype X	yes	612	44.8	81.7	14.5	95.3
	no	6,726	44.8	81.7	14.5	95.3
Diphtheria toxoid vaccine, inactivated	yes	1,166	38.1	82.2	14.1	95.6
	no	6,172	38.1	82.2	14.1	95.6
Tetanus toxoid vaccine, inactivated	yes	1,169	38.2	82.2	14.1	95.6
	no	6,169	38.2	82.2	14.1	95.6
Acellular pertussis vaccine, inactivated	yes	1,119	37.8	81.8	14.5	95.7
	no	6,219	37.8	81.8	14.5	95.7
Loratadine	yes	754	35.3	85.5	11.5	95.9
	no	6,584	35.3	85.5	11.5	95.9
Meloxicam	yes	587	33.3	86	12.4	97.2
	no	6,751	33.3	86	12.4	97.2
Ascorbic acid	yes	564	32.4	87.4	9.9	97.1
	no	6,774	32.4	87.4	9.9	97.1
Clavulanate	yes	866	33.7	86.3	12.1	96.9
	no	6,472	33.7	86.3	12.1	96.9
Ibuprofen	yes	3,508	37.6	85.1	12.3	96.6
	no	3,830	37.6	85.1	12.3	96.6
Omega-3 fatty acids	yes	434	43.1	91	6.7	97.3
	no	6,904	43.1	91	6.7	97.3
Fluticasone propionate	yes	896	36.4	83.8	14.3	96
	no	6,442	36.4	83.8	14.3	96
Fluticasone	yes	2,154	38	85.2	12.7	96.6
	no	5,184	38	85.2	12.7	96.6
*C Streptococcus pneumoniae type X	yes	510	41.9	82.4	15.7	96.9
	no	6,828	41.9	82.4	15.7	96.9
Methylprednisolone acetate	yes	399	34.3	86.4	11.8	96.3
	no	6,939	34.3	86.4	11.8	96.3
Duloxetine	yes	292	25.6	90.9	8.4	98.2
	no	7,046	25.6	90.9	8.4	98.2
Tamsulosin	yes	216	91.5	91.8	7.6	96.6
	no	7,122	91.5	91.8	7.6	96.6

Naproxen	yes	982	33	83.5	14.5	96
	no	6,356	33	83.5	14.5	96
Folic acid	yes	417	24.1	82.8	15.2	96.8
	no	6,921	24.1	82.8	15.2	96.8
Lutein	yes	147	39.2	95.7	2.9	97.8
	no	7,191	39.2	95.7	2.9	97.8
Fish oils	yes	437	40.9	90.1	7.4	98.1
	no	6,901	40.9	90.1	7.4	98.1
Diclofenac	yes	605	35.9	81.1	16.7	96.3
	no	6,733	35.9	81.1	16.7	96.3
Escitalopram	yes	499	28.9	91.1	7.9	98.5
	no	6,839	28.9	91.1	7.9	98.5
Vitamin B12	yes	668	28.8	85.4	12.1	97
	no	6,670	28.8	85.4	12.1	97
Codeine	yes	342	25.2	90.3	9.4	98.4
	no	6,996	25.2	90.3	9.4	98.4
Bismuth subsalicylate	yes	171	44.2	83.7	14.5	97.1
	no	7,167	44.2	83.7	14.5	97.1
Amoxicillin	yes	1,709	35.2	85.7	12	96.3
	no	5,629	35.2	85.7	12	96.3
Hydrochlorothiazide	yes	707	41.5	79.9	18.2	98.3
	no	6,631	41.5	79.9	18.2	98.3
Ropivacaine	yes	219	28.1	86.3	13.3	96.8
	no	7,119	28.1	86.3	13.3	96.8
Eicosapentaenoate	yes	223	39.4	87.4	10	97.3
	no	7,115	39.4	87.4	10	97.3
Cefdinir	yes	298	32.1	86.2	10.2	97.9
	no	7,040	32.1	86.2	10.2	97.9
Benzocaine	yes	413	30.2	87.9	10.3	94.4
	no	6,925	30.2	87.9	10.3	94.4
Ketorolac	yes	551	31.3	81.3	17	95.9
	no	6,787	31.3	81.3	17	95.9
Benzonatate	yes	635	32.6	85.5	12	96.1
	no	6,703	32.6	85.5	12	96.1
Cyclobenzaprine	yes	499	27.3	82.5	16.3	96.4
	no	6,839	27.3	82.5	16.3	96.4
Trazodone	yes	339	30.7	87.6	10.6	98.5
	no	6,999	30.7	87.6	10.6	98.5
Zolpidem	yes	240	33.9	94.8	4.3	98.7

	no	7,098	33.9	94.8	4.3	98.7
Testosterone	yes	284	60.3	87.9	10.6	97.1
	no	7,054	60.3	87.9	10.6	97.1
Simvastatin	yes	203	52.1	91.2	7.3	97.7
	no	7,135	52.1	91.2	7.3	97.7
Cephalexin	yes	416	33.2	88.3	10.5	97.8
	no	6,922	33.2	88.3	10.5	97.8
Varicella zoster virus glycoprotein E	yes	222	39.6	84.7	11.5	98.6
	no	7,116	39.6	84.7	11.5	98.6
Doxycycline	yes	693	36.4	87.9	10.7	97.6
	no	6,645	36.4	87.9	10.7	97.6
Diclofenac sodium	yes	341	30.6	82.1	15.6	97.3
	no	6,997	30.6	82.1	15.6	97.3
Butalbital	yes	347	28.2	81.2	15.7	97.1
	no	6,991	28.2	81.2	15.7	97.1
Propofol	yes	602	42.5	84.7	12.8	96.8
	no	6,736	42.5	84.7	12.8	96.8
Cetirizine	yes	1,388	37.5	83.6	13.6	96
	no	5,950	37.5	83.6	13.6	96
Oxymetazoline	yes	1,143	39.6	85.9	11.5	96.3
	no	6,195	39.6	85.9	11.5	96.3
Diethylstilbestrol	yes	172	43.4	91.6	6.7	97
	no	7,166	43.4	91.6	6.7	97

Other abbreviations and acronyms. *A Streptococcus pneumoniae serotype X: Streptococcus pneumoniae serotype (1, 19A, 3, 5, 6A, 7F) capsular antigen diphtheria CRM197 protein conjugate vaccine; *B Streptococcus pneumoniae serotype X: Streptococcus pneumoniae serotype (14, 18C, 19F, 23F, 4, 6B, 9V) capsular antigen diphtheria CRM197 protein conjugate vaccine; *C Streptococcus pneumoniae type X: Streptococcus pneumoniae type (1, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 2, 20, 22F, 23F, 3, 33F, 4, 5, 6B, 7F, 8, 9N, 9V) capsular polysaccharide antigen.

eTable 5 Association between drug exposure and on ventilator (cumulative severity).

TCe/u, total count of drug exposed/unexposed patients; **SRe/u**, severity rate of drug exposed/unexposed patients computed after overlap weighting with propensity score; **OR**, odds ratio; **CI**, confidence interval. The association results are arranged in the ascending order of OR values. The statistically significant results at the 0.05 level are emphasized in bold.

Drug name	Drug class	TCe	TCu	SRe	SRu	OR	95% CI
Clavulanate	antibiotic	867	6,495	0.8	2	0.4	(0.15 - 1.07)
*A Streptococcus pneumoniae serotype X	vaccine	390	6,972	2.6	4.7	0.41	(0.17 - 0.99)
Sildenafil	PDE5 inhibitor	180	7,182	2.6	6.9	0.42	(0.12 - 1.41)
Flaxseed extract	supplement	188	7,174	3.8	9.2	0.44	(0.16 - 1.24)
Ascorbic acid	supplement	566	6,796	1.4	2.9	0.46	(0.18 - 1.17)
Loratadine	antihistamine	756	6,606	0.9	1.9	0.47	(0.17 - 1.29)
*B Streptococcus pneumoniae serotype X	vaccine	617	6,745	2.5	4.1	0.47	(0.22 - 0.99)
Diphtheria toxoid vaccine, inactivated	vaccine	1,171	6,191	1.1	2	0.51	(0.23 - 1.09)
Tetanus toxoid vaccine, inactivated	vaccine	1,174	6,188	1.1	2	0.51	(0.23 - 1.10)
Acellular pertussis vaccine, inactivated	vaccine	1,124	6,238	1.2	2	0.53	(0.24 - 1.15)
Methylprednisolone acetate	corticosteroid	399	6,963	1.2	2.8	0.54	(0.17 - 1.76)
Omega-3 fatty acids	supplement	436	6,926	3.3	5.1	0.59	(0.27 - 1.27)
Meloxicam	NSAID	591	6,771	1.5	3.2	0.61	(0.25 - 1.50)
Pseudoephedrine	decongestant	952	6,410	0.6	1.5	0.61	(0.21 - 1.79)
Fluticasone	corticosteroid	2,161	5,201	1.3	2.1	0.64	(0.35 - 1.16)
Bismuth subsalicylate	antidiarrheal	171	7,191	2.8	3.6	0.65	(0.17 - 2.48)
Naproxen	NSAID	984	6,378	1.1	2	0.66	(0.28 - 1.54)
Ibuprofen	NSAID	3,518	3,844	1.1	1.7	0.66	(0.37 - 1.20)
Cefdinir	antibiotic	298	7,064	1.7	1.4	0.68	(0.15 - 3.20)
*C Streptococcus pneumoniae type X	vaccine	515	6,847	3.5	5	0.71	(0.35 - 1.45)
Fluticasone propionate	corticosteroid	900	6,462	1.4	2	0.72	(0.32 - 1.62)
Vitamin B12	supplement	670	6,692	2.4	2.9	0.73	(0.34 - 1.60)
Varicella zoster virus glycoprotein E	vaccine	222	7,140	2.9	6.1	0.75	(0.24 - 2.37)
Benzonatate	antitussive	636	6,726	2	2.8	0.77	(0.34 - 1.75)
Tamsulosin	alpha 1 blocker	219	7,143	5.5	6.9	0.79	(0.32 - 1.94)
Escitalopram	antidepressant	500	6,862	1.4	1.4	0.8	(0.24 - 2.67)
Azelastine	antihistamine	482	6,880	2	2.8	0.81	(0.32 - 2.04)
Amoxicillin	antibiotic	1,713	5,649	1.3	1.4	0.81	(0.41 - 1.62)
Duloxetine	antidepressant	294	7,068	2.3	3	0.81	(0.27 - 2.42)
Ranitidine	antacid	252	7,110	1.9	2.4	0.81	(0.22 - 3.00)
Tetracaine	anesthetic	200	7,162	2.5	2.6	0.82	(0.21 - 3.15)
Cetirizine	antihistamine	1,390	5,972	1.3	1.6	0.84	(0.40 - 1.74)
Ropivacaine	anesthetic	220	7,142	2.7	3.6	0.84	(0.26 - 2.75)
Valacyclovir	antiviral	453	6,909	1.3	2	0.85	(0.26 - 2.70)

Lutein	supplement	149	7,213	5.6	7.3	0.86	(0.30 - 2.44)
Ketorolac	NSAID	553	6,809	1.4	2	0.86	(0.31 - 2.38)
Zolpidem	hypnotic	241	7,121	2.4	3.8	0.88	(0.27 - 2.88)
Diclofenac sodium	NSAID	342	7,020	3.3	4.2	0.89	(0.37 - 2.12)
Diclofenac	NSAID	610	6,752	2.6	3.4	0.9	(0.42 - 1.90)
Hydrochlorothiazide	antihypertensive	714	6,648	3.5	4.8	0.91	(0.48 - 1.70)
Ketoconazole	antifungal	230	7,132	2.1	2.1	0.94	(0.24 - 3.79)
Butalbital	barbituate	348	7,014	2	2.3	0.95	(0.32 - 2.84)
Losartan	antihypertensive	464	6,898	3.8	5	0.95	(0.46 - 1.98)
Fish oils	supplement	442	6,920	3.5	3.8	0.97	(0.45 - 2.11)
Tropicamide	ophthalmic agent	352	7,010	3.2	3.2	0.97	(0.38 - 2.47)
Eicosapentaenoate	supplement	225	7,137	3.5	4	0.98	(0.34 - 2.83)
Trazodone	antidepressant	341	7,021	2.8	2.8	0.99	(0.36 - 2.71)
Methylprednisolone	corticosteroid	876	6,486	2.1	2.5	1	(0.48 - 2.04)

Other abbreviations and acronyms. *A Streptococcus pneumoniae serotype X: Streptococcus pneumoniae serotype (1, 19A, 3, 5, 6A, 7F) capsular antigen diphtheria CRM197 protein conjugate vaccine; *B Streptococcus pneumoniae serotype X: Streptococcus pneumoniae serotype (14, 18C, 19F, 23F, 4, 6B, 9V) capsular antigen diphtheria CRM197 protein conjugate vaccine; *C Streptococcus pneumoniae type X: Streptococcus pneumoniae type (1, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 2, 20, 22F, 23F, 3, 33F, 4, 5, 6B, 7F, 8, 9N, 9V) capsular polysaccharide antigen; NSAID: nonsteroidal anti-inflammatory drug; PDE5 inhibitor: phosphodiesterase type 5 inhibitor.

eTable 6 Association between drug exposure and in ICU (cumulative severity).

TCe/u, total count of drug exposed/unexposed patients; **SRe/u**, severity rate of drug exposed/unexposed patients computed after overlap weighting with propensity score; **OR**, odds ratio; **CI**, confidence interval. The association results are arranged in the ascending order of OR values. The statistically significant results at the 0.05 level are emphasized in bold.

Drug name	Drug class	TCe	TCu	SRe	SRu	OR	95% CI
*A Streptococcus pneumoniae serotype X	vaccine	391	7,001	2.8	5.4	0.39	(0.17 - 0.89)
*B Streptococcus pneumoniae serotype X	vaccine	618	6,774	2.7	4.9	0.41	(0.20 - 0.83)
Diphtheria toxoid vaccine, inactivated	vaccine	1,172	6,220	1.2	2.6	0.42	(0.21 - 0.87)
Tetanus toxoid vaccine, inactivated	vaccine	1,175	6,217	1.2	2.6	0.42	(0.21 - 0.87)
Acellular pertussis vaccine, inactivated	vaccine	1,125	6,267	1.3	2.5	0.44	(0.21 - 0.91)
Flaxseed extract	supplement	189	7,203	4.3	9.9	0.44	(0.17 - 1.18)
Dextromethorphan	antitussive	900	6,492	0.8	2	0.45	(0.17 - 1.17)
Sildenafil	PDE5 inhibitor	182	7,210	3.7	7.6	0.51	(0.18 - 1.45)
Fexofenadine	antihistamine	560	6,832	1.2	2.6	0.52	(0.19 - 1.38)
Methylprednisolone acetate	corticosteroid	400	6,992	1.5	3.4	0.52	(0.18 - 1.51)
Naproxen	NSAID	985	6,407	1.2	2.5	0.55	(0.25 - 1.20)
Clavulanate	antibiotic	872	6,520	1.4	2.4	0.57	(0.26 - 1.25)
Pseudoephedrine	decongestant	954	6,438	0.8	1.9	0.6	(0.24 - 1.54)
*C Streptococcus pneumoniae type X	vaccine	516	6,876	3.7	5.9	0.61	(0.31 - 1.20)
Omega-3 fatty acids	supplement	439	6,953	4	5.7	0.64	(0.32 - 1.30)
Ascorbic acid	supplement	571	6,821	2.3	3.4	0.65	(0.30 - 1.41)
Bismuth subsalicylate	antidiarrheal	172	7,220	3.4	4.2	0.65	(0.19 - 2.18)
Fluticasone	corticosteroid	2,169	5,223	1.6	2.6	0.65	(0.39 - 1.11)
Varicella zoster virus glycoprotein E	vaccine	223	7,169	3.3	6.8	0.66	(0.23 - 1.89)
Fluticasone propionate	corticosteroid	902	6,490	1.6	2.5	0.66	(0.32 - 1.39)
Loratadine	antihistamine	761	6,631	1.6	2.3	0.68	(0.30 - 1.54)
Meloxicam	NSAID	595	6,797	2.1	3.7	0.69	(0.32 - 1.49)
Betamethasone	corticosteroid	238	7,154	2.5	3.6	0.72	(0.23 - 2.24)
Escitalopram	antidepressant	501	6,891	1.6	1.8	0.72	(0.24 - 2.13)
Ibuprofen	NSAID	3,531	3,861	1.5	2.1	0.73	(0.44 - 1.22)
Ketoconazole	antifungal	230	7,162	2.1	2.5	0.76	(0.20 - 2.82)
Diclofenac sodium	NSAID	343	7,049	3.6	4.9	0.8	(0.35 - 1.80)
Azelastine	antihistamine	484	6,908	2.4	3.3	0.8	(0.34 - 1.85)
Ropivacaine	anesthetic	221	7,171	3.2	4.2	0.81	(0.28 - 2.39)
Codeine	opioid	345	7,047	2.7	4	0.81	(0.32 - 2.08)
Eicosapentaenoate	supplement	225	7,167	3.5	4.6	0.82	(0.30 - 2.27)
Tetracaine	anesthetic	201	7,191	2.9	3.2	0.83	(0.24 - 2.85)
Zolpidem	hypnotic	243	7,149	3.2	4.4	0.84	(0.29 - 2.40)
Lutein	supplement	150	7,242	6.3	7.9	0.85	(0.32 - 2.25)

Duloxetine	antidepressant	296	7,096	2.9	3.5	0.85	(0.32 - 2.28)
Butalbital	barbituate	349	7,043	2.2	2.8	0.86	(0.31 - 2.37)
Vitamin B12	supplement	676	6,716	3.3	3.5	0.88	(0.45 - 1.72)
Tamsulosin	alpha 1 blocker	222	7,170	6.7	7.5	0.88	(0.38 - 2.03)
Valacyclovir	antiviral	455	6,937	1.7	2.4	0.88	(0.32 - 2.43)
Amoxicillin	antibiotic	1,721	5,671	1.7	1.8	0.89	(0.48 - 1.62)
Folic acid	supplement	422	6,970	3	2.8	0.89	(0.37 - 2.15)
Diclofenac	NSAID	614	6,778	3.2	4.1	0.9	(0.46 - 1.75)
Benzonatate	antitussive	641	6,751	2.7	3.3	0.9	(0.44 - 1.85)
Cetirizine	antihistamine	1,396	5,996	1.7	2	0.9	(0.47 - 1.71)
Testosterone	androgen	287	7,105	3.1	3.4	0.91	(0.33 - 2.48)
Methylprednisolone	corticosteroid	879	6,513	2.4	3	0.91	(0.47 - 1.76)
Phenol	anesthetic	339	7,053	1.5	1.6	0.91	(0.25 - 3.29)
Losartan	antihypertensive	467	6,925	4.4	5.8	0.91	(0.47 - 1.80)
Ketorolac	NSAID	556	6,836	1.9	2.5	0.92	(0.38 - 2.21)
Alprazolam	benzodiazepine	334	7,058	2.4	2.8	0.93	(0.31 - 2.74)
Cefdinir	antibiotic	300	7,092	2.3	1.7	0.93	(0.26 - 3.35)
Tropicamide	ophthalmic agent	354	7,038	3.8	3.7	0.95	(0.41 - 2.23)
Adenosine monophosphate	antiarrhythmic agent	178	7,214	4.2	4.5	0.97	(0.30 - 3.11)
Ranitidine	antacid	254	7,138	2.7	3	0.97	(0.32 - 3.00)
Menthol	topical skin product	366	7,026	3.2	2.8	0.98	(0.39 - 2.45)
Docosahexaenoate	supplement	171	7,221	2.9	2.9	0.99	(0.26 - 3.74)
Diethylstilbestrol	estrogen	175	7,217	6.1	7.1	0.99	(0.38 - 2.58)
Fish oils	supplement	445	6,947	4.1	4.3	0.99	(0.49 - 2.03)
Pamidronate	bisphosphonate derivative	244	7,148	4.7	4.1	1	(0.39 - 2.56)
Trazodone	antidepressant	343	7,049	3.4	3.3	1	(0.40 - 2.47)
Esomeprazole	antacid	172	7,220	3.4	4.2	1	(0.30 - 3.37)

Other abbreviations and acronyms. *A Streptococcus pneumoniae serotype X: Streptococcus pneumoniae serotype (1, 19A, 3, 5, 6A, 7F) capsular antigen diphtheria CRM197 protein conjugate vaccine; *B Streptococcus pneumoniae serotype X: Streptococcus pneumoniae serotype (14, 18C, 19F, 23F, 4, 6B, 9V) capsular antigen diphtheria CRM197 protein conjugate vaccine; *C Streptococcus pneumoniae type X: Streptococcus pneumoniae type (1, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 2, 20, 22F, 23F, 3, 33F, 4, 5, 6B, 7F, 8, 9N, 9V) capsular polysaccharide antigen; NSAID: nonsteroidal anti-inflammatory drug; PDE5 inhibitor: phosphodiesterase type 5 inhibitor.

eTable 7 Association between drug exposure and hospitalized-mild (cumulative severity).

TCe/u, total count of drug exposed/unexposed patients; **SRe/u**, severity rate of drug exposed/unexposed patients computed after overlap weighting with propensity score; **OR**, odds ratio; **CI**, confidence interval. The association results are arranged in the ascending order of OR values. The statistically significant results at the 0.05 level are emphasized in bold.

Drug name	Drug class	TCe	TCu	SRe	SRu	OR	95% CI
Ethinyl estradiol	estrogen	749	7,019	1	2.8	0.37	(0.14 - 0.99)
Clotrimazole	antifungal	160	7,608	4.3	9	0.4	(0.14 - 1.15)
Turmeric extract	supplement	154	7,614	5.8	14.2	0.4	(0.17 - 0.98)
Triamcinolone acetonide	corticosteroid	154	7,614	5.1	11.2	0.41	(0.15 - 1.07)
Flaxseed extract	supplement	206	7,562	11.6	23.6	0.41	(0.22 - 0.77)
Levonorgestrel	estrogen	507	7,261	1.2	3.4	0.42	(0.15 - 1.18)
Ubidecarenone	supplement	131	7,637	7.5	16.3	0.44	(0.19 - 1.02)
*C Streptococcus pneumoniae type X	vaccine	552	7,216	9.4	16.8	0.47	(0.31 - 0.72)
Methylprednisolone acetate	corticosteroid	413	7,355	4.5	10	0.48	(0.26 - 0.89)
*A Streptococcus pneumoniae serotype X	vaccine	419	7,349	9.1	14.9	0.49	(0.30 - 0.80)
Estradiol	estrogen derivative	576	7,192	3.1	6.2	0.51	(0.26 - 0.97)
Biotin	supplement	209	7,559	7.2	12.3	0.51	(0.24 - 1.09)
Estrogens	estrogen	316	7,452	4.4	8.5	0.53	(0.26 - 1.09)
*B Streptococcus pneumoniae serotype X	vaccine	667	7,101	9.4	14.1	0.55	(0.37 - 0.82)
Oseltamivir	antiviral	557	7,211	3.4	6	0.55	(0.29 - 1.04)
Pseudoephedrine	decongestant	978	6,790	3.3	6.3	0.58	(0.35 - 0.94)
Omega-3 fatty acids	supplement	475	7,293	10.7	15.7	0.6	(0.39 - 0.94)
Psyllium	antidiarrheal	116	7,652	6.8	11.4	0.61	(0.22 - 1.67)
Eicosapentaenoate	supplement	237	7,531	8.2	13	0.61	(0.32 - 1.18)
Glucosamine	supplement	113	7,655	8.7	15.2	0.62	(0.25 - 1.55)
Haemophilus influenzae type b	vaccine	373	7,395	4.5	6.7	0.64	(0.32 - 1.27)
Varicella zoster virus glycoprotein E	vaccine	241	7,527	10.3	17.6	0.64	(0.35 - 1.19)
Betamethasone	corticosteroid	250	7,518	7.1	10.6	0.65	(0.33 - 1.29)
Azelastine	antihistamine	507	7,261	6.7	10.1	0.66	(0.40 - 1.10)
Dextromethorphan	antitussive	933	6,835	4.3	6.6	0.66	(0.42 - 1.06)
Tetanus toxoid vaccine, inactivated	vaccine	1,233	6,535	5.8	8	0.67	(0.47 - 0.97)
Estrogens, conjugated (USP)	estrogens	121	7,647	8.3	12.7	0.67	(0.26 - 1.72)
Fexofenadine	antihistamine	586	7,182	5.5	8.3	0.67	(0.40 - 1.12)
Ibuprofen	NSAID	3,655	4,113	5.2	7.4	0.68	(0.51 - 0.90)
Fluticasone	corticosteroid	2,271	5,497	5.7	8.3	0.68	(0.50 - 0.91)
Diphtheria toxoid vaccine, inactivated	vaccine	1,231	6,537	5.9	8	0.68	(0.48 - 0.98)
Calcium citrate	calcium salt	116	7,652	7.8	12	0.68	(0.27 - 1.75)
Acellular pertussis vaccine, inactivated	vaccine	1,181	6,587	5.9	8	0.69	(0.47 - 0.99)
Naproxen	NSAID	1,029	6,739	5.3	8	0.69	(0.46 - 1.03)

Tadalafil	PDE5 inhibitor	131	7,637	12.3	18.1	0.71	(0.34 - 1.50)
Clobetasol	corticosteroid	156	7,612	8.2	10.5	0.71	(0.31 - 1.66)
Follicle stimulating hormone	gonadotropin	134	7,634	4.5	6.6	0.73	(0.23 - 2.30)
Nitrofurantoin, monohydrate	antibiotic	210	7,558	4.8	6.6	0.73	(0.28 - 1.87)
Cetirizine	antihistamine	1,447	6,321	5.1	7	0.73	(0.51 - 1.05)
Fluticasone propionate	corticosteroid	947	6,821	6.2	8	0.73	(0.49 - 1.10)
Phentermine	anorexiant	123	7,645	5	6.5	0.74	(0.22 - 2.47)
Sildenafil	PDE5 inhibitor	203	7,565	13.8	18.3	0.76	(0.41 - 1.39)
Loratadine	antihistamine	797	6,971	5.9	7.7	0.76	(0.48 - 1.18)
Lutein	supplement	167	7,601	15.9	20	0.78	(0.41 - 1.46)
Adalimumab	DMARD	132	7,636	6	8.4	0.78	(0.28 - 2.15)
Lamotrigine	anticonvulsant	160	7,608	5	6.1	0.78	(0.27 - 2.24)
Vitamin B12	supplement	728	7,040	9.6	11.3	0.8	(0.54 - 1.19)
Naproxen sodium	NSAID	137	7,631	7.9	10	0.8	(0.33 - 1.97)
Testosterone	androgen	302	7,466	7.8	9.8	0.81	(0.43 - 1.51)
Benzonatate	antitussive	680	7,088	8.1	10.1	0.82	(0.53 - 1.24)
Cortisone	corticosteroid	179	7,589	9.3	11.9	0.82	(0.39 - 1.72)
Diethylstilbestrol	estrogen	193	7,575	14.7	18.1	0.82	(0.45 - 1.50)
Diclofenac sodium	NSAID	375	7,393	11.4	13.9	0.85	(0.53 - 1.39)
Lufenuron	antiparasitic/antifungal	217	7,551	9.5	10.3	0.87	(0.44 - 1.71)
Oxymetazoline	adrenergic agonist agent	1,206	6,562	6.6	7.1	0.87	(0.61 - 1.26)
Fish oils	supplement	479	7,289	10.7	12.4	0.88	(0.56 - 1.38)
Meloxicam	NSAID	640	7,128	8.7	10.7	0.9	(0.59 - 1.37)
Finasteride	5-alpha reductase inhibitor	106	7,662	13.8	15	0.91	(0.39 - 2.09)
Ascorbic acid	supplement	618	7,150	9.5	10.3	0.91	(0.59 - 1.38)
Desoxycorticosterone	corticosteroid	159	7,609	11.2	12	0.92	(0.43 - 1.96)
Tretinoin	antineoplastic agent	230	7,538	3.5	4.4	0.92	(0.33 - 2.58)
Ketoconazole	antifungal	244	7,524	7.7	8	0.93	(0.45 - 1.89)
Norethindrone	contraceptive	441	7,327	2.6	3.1	0.93	(0.38 - 2.28)
Methylprednisolone	corticosteroid	933	6,835	7.9	9.3	0.93	(0.64 - 1.35)
Varicella-zoster virus vaccine live (Oka-Merck) strain	vaccine	165	7,603	9.7	8.4	0.94	(0.41 - 2.14)
Fiber	supplement	699	7,069	7.4	8.3	0.94	(0.61 - 1.45)
Docosahexaenoate	supplement	181	7,587	8.3	8.9	0.94	(0.43 - 2.05)
Thioguanine	antineoplastic agent	252	7,516	12.4	13.6	0.94	(0.53 - 1.68)
Celecoxib	NSAID	182	7,586	11.4	12.9	0.94	(0.47 - 1.89)
Mometasone	corticosteroid	222	7,546	8.5	9.6	0.95	(0.46 - 1.95)
Diclofenac	NSAID	667	7,101	10.5	11.8	0.95	(0.65 - 1.40)
Phenol	anesthetic	354	7,414	5.7	5.8	0.97	(0.49 - 1.92)
Metoprolol succinate	antihypertensive	195	7,573	16.3	17.3	0.98	(0.54 - 1.77)

Hepatitis A vaccine (inactivated) strain HM175	vaccine	189	7,579	7.4	6.8	0.99	(0.41 - 2.35)
Hepatitis A Vaccine, Inactivated	vaccine	166	7,602	6	5.8	0.99	(0.36 - 2.73)
Valacyclovir	antiviral	482	7,286	7.2	8	1	(0.58 - 1.71)
Guaifenesin	expectorant	1,293	6,475	8.3	8.1	1	(0.71 - 1.40)

Other abbreviations and acronyms. *A Streptococcus pneumoniae serotype X: Streptococcus pneumoniae serotype (1, 19A, 3, 5, 6A, 7F) capsular antigen diphtheria CRM197 protein conjugate vaccine; *B Streptococcus pneumoniae serotype X: Streptococcus pneumoniae serotype (14, 18C, 19F, 23F, 4, 6B, 9V) capsular antigen diphtheria CRM197 protein conjugate vaccine; *C Streptococcus pneumoniae type X: Streptococcus pneumoniae type (1, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 2, 20, 22F, 23F, 3, 33F, 4, 5, 6B, 7F, 8, 9N, 9V) capsular polysaccharide antigen; NSAID: nonsteroidal anti-inflammatory drug; PDE5 inhibitor: phosphodiesterase type 5 inhibitor; DMARD: disease-modifying antirheumatic drugs.

eTable 8 Association between drug exposure and on ventilator (exclusive severity).

TCe/u, total count of drug exposed/unexposed patients; **SRe/u**, severity rate of drug exposed/unexposed patients computed after overlap weighting with propensity score; **OR**, odds ratio; **CI**, confidence interval. The association results are arranged in the ascending order of OR values.

Drug name	Drug class	TCe	TCu	SRe	SRu	OR	95% CI
*A Streptococcus pneumoniae serotype X	vaccine	384	6,928	1.3	2.1	0.52	(0.15 - 1.81)
Tetanus toxoid vaccine, inactivated	vaccine	1,168	6,144	0.7	1.1	0.53	(0.19 - 1.44)
Diphtheria toxoid vaccine, inactivated	vaccine	1,165	6,147	0.7	1.1	0.53	(0.19 - 1.44)
Acellular pertussis vaccine, inactivated	vaccine	1,118	6,194	0.7	1.1	0.55	(0.20 - 1.52)
Ascorbic acid	supplement	562	6,750	0.8	1.4	0.59	(0.17 - 2.03)
Vitamin B12	supplement	657	6,655	0.9	1.4	0.6	(0.19 - 1.86)
*B Streptococcus pneumoniae serotype X	vaccine	608	6,704	1.4	1.9	0.62	(0.23 - 1.69)
Fluticasone	corticosteroid	2,147	5,165	0.7	1.2	0.65	(0.30 - 1.41)
Ibuprofen	NSAID	3,505	3,807	0.7	1	0.69	(0.32 - 1.46)
Cetirizine	antihistamine	1,381	5,931	0.6	0.9	0.7	(0.27 - 1.85)
Amlodipine	antihypertensive	474	6,838	1.8	2.7	0.73	(0.27 - 1.93)
Losartan	antihypertensive	451	6,861	1.6	2.4	0.73	(0.26 - 2.07)
Amoxicillin	antibiotic	1,703	5,609	0.7	0.9	0.74	(0.30 - 1.84)
Fluticasone propionate	corticosteroid	894	6,418	0.8	1.1	0.74	(0.25 - 2.18)
Sildenafil	PDE5 inhibitor	180	7,132	2.6	3.4	0.81	(0.21 - 3.16)
Benzonatate	antitussive	630	6,682	1.1	1.3	0.82	(0.27 - 2.45)
Tamsulosin	alpha 1 blocker	212	7,100	3.2	3.7	0.85	(0.26 - 2.73)
Naproxen	NSAID	981	6,331	0.8	1	0.88	(0.31 - 2.47)
Omega-3 fatty acids	supplement	429	6,883	2.1	2.2	0.89	(0.32 - 2.47)
Ketorolac	NSAID	550	6,762	0.9	1.1	0.89	(0.25 - 3.22)
Tropicamide	ophthalmic agent	345	6,967	1.4	1.5	0.9	(0.24 - 3.43)
Meloxicam	NSAID	589	6,723	1.1	1.4	0.94	(0.31 - 2.86)
Dexamethasone	corticosteroid	880	6,432	1	1.1	0.97	(0.36 - 2.62)
*C Streptococcus pneumoniae type X	vaccine	505	6,807	2.1	2.1	0.99	(0.38 - 2.60)

Other abbreviations and acronyms. *A Streptococcus pneumoniae serotype X: Streptococcus pneumoniae serotype (1, 19A, 3, 5, 6A, 7F) capsular antigen diphtheria CRM197 protein conjugate vaccine; *B Streptococcus pneumoniae serotype X: Streptococcus pneumoniae serotype (14, 18C, 19F, 23F, 4, 6B, 9V) capsular antigen diphtheria CRM197 protein conjugate vaccine; *C Streptococcus pneumoniae type X: Streptococcus pneumoniae type (1, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 2, 20, 22F, 23F, 3, 33F, 4, 5, 6B, 7F, 8, 9N, 9V) capsular polysaccharide antigen; NSAID: nonsteroidal anti-inflammatory drug; PDE5 inhibitor: phosphodiesterase type 5 inhibitor.

eTable 9 Association between drug exposure and in ICU (exclusive severity).

TCe/u, total count of drug exposed/unexposed patients; **SRe/u**, severity rate of drug exposed/unexposed patients computed after overlap weighting with propensity score; **OR**, odds ratio; **CI**, confidence interval. The association results are arranged in the ascending order of OR values. The statistically significant results at the 0.05 level are emphasized in bold.

Drug name	Drug class	TCe	TCu	SRe	SRu	OR	95% CI
Diphtheria toxoid vaccine, inactivated	vaccine	1,164	6,166	0.6	1.5	0.34	(0.12 - 0.93)
Tetanus toxoid vaccine, inactivated	vaccine	1,167	6,163	0.6	1.5	0.34	(0.12 - 0.93)
Acellular pertussis vaccine, inactivated	vaccine	1,117	6,213	0.6	1.5	0.35	(0.13 - 0.97)
Naproxen	NSAID	978	6,352	0.5	1.5	0.4	(0.13 - 1.22)
*A Streptococcus pneumoniae serotype X	vaccine	385	6,945	1.4	2.6	0.42	(0.13 - 1.35)
*B Streptococcus pneumoniae serotype X	vaccine	609	6,721	1.5	2.5	0.46	(0.18 - 1.19)
Flaxseed extract	supplement	185	7,145	2.3	3.8	0.62	(0.16 - 2.38)
Fluticasone propionate	corticosteroid	895	6,435	0.9	1.4	0.63	(0.24 - 1.69)
*C Streptococcus pneumoniae type X	vaccine	505	6,825	1.9	2.8	0.65	(0.26 - 1.66)
Sildenafil	PDE5 inhibitor	180	7,150	2.8	4.2	0.68	(0.19 - 2.37)
Dextromethorphan	antitussive	899	6,431	0.7	1.1	0.68	(0.22 - 2.06)
Amoxicillin	antibiotic	1,706	5,624	0.8	1.1	0.68	(0.30 - 1.54)
Clavulanate	antibiotic	868	6,462	0.9	1.3	0.68	(0.25 - 1.84)
Diclofenac sodium	NSAID	336	6,994	1.8	2.5	0.72	(0.24 - 2.22)
Thyrotropin	thyroid product	468	6,862	1.1	1.4	0.74	(0.21 - 2.58)
Morphine sulfate	opioid	659	6,671	1.3	1.6	0.76	(0.29 - 2.04)
Cetirizine	antihistamine	1,384	5,946	0.9	1.2	0.78	(0.33 - 1.82)
Fluticasone	corticosteroid	2,155	5,175	1.1	1.4	0.79	(0.41 - 1.54)
Omega-3 fatty acids	supplement	430	6,900	2.1	2.6	0.79	(0.30 - 2.11)
Tropicamide	ophthalmic agent	346	6,984	1.7	2	0.8	(0.25 - 2.60)
Fexofenadine	antihistamine	559	6,771	1	1.4	0.81	(0.26 - 2.56)
Dexamethasone	corticosteroid	881	6,449	1.1	1.5	0.82	(0.33 - 2.06)
Vitamin B12	supplement	662	6,668	1.7	1.9	0.84	(0.34 - 2.05)
Fish oils	supplement	434	6,896	1.8	2.2	0.84	(0.30 - 2.33)
Calcium carbonate	supplement	307	7,023	1.6	2	0.84	(0.23 - 3.01)
Vitamin D	supplement	1,408	5,922	1.2	1.4	0.85	(0.40 - 1.81)
Ketorolac	NSAID	551	6,779	1.1	1.4	0.86	(0.27 - 2.71)
Diclofenac	NSAID	604	6,726	1.8	2.2	0.86	(0.36 - 2.06)
Meloxicam	NSAID	591	6,739	1.5	1.9	0.86	(0.33 - 2.26)
Loratadine	antihistamine	757	6,573	1	1.3	0.87	(0.31 - 2.40)
Iron	supplement	1,230	6,100	1.1	1.1	0.89	(0.37 - 2.14)
Azelastine	antihistamine	479	6,851	1.4	1.7	0.89	(0.30 - 2.67)
Pseudoephedrine	decongestant	953	6,377	0.7	1.1	0.91	(0.31 - 2.65)
Methylprednisolone	corticosteroid	869	6,461	1.3	1.6	0.92	(0.38 - 2.21)

Cephapirin	antibiotic	520	6,810	1.5	1.4	0.92	(0.31 - 2.77)
Doxycycline	antibiotic	690	6,640	1.4	1.5	0.93	(0.36 - 2.40)
Ibuprofen	NSAID	3,516	3,814	1	1.2	0.93	(0.49 - 1.77)
Trazodone	antidepressant	337	6,993	1.8	1.7	0.95	(0.28 - 3.24)
Oxymetazoline	adrenergic agonist agent	1,140	6,190	1.2	1.2	0.95	(0.41 - 2.20)
Amlodipine	antihypertensive	480	6,850	2.9	3.3	0.96	(0.42 - 2.18)
Zolpidem	hypnotic	240	7,090	2.1	2.1	0.97	(0.25 - 3.68)
Tamsulosin	alpha 1 blocker	214	7,116	4	4.1	0.97	(0.33 - 2.83)
Folic acid	supplement	416	6,914	1.7	1.5	0.97	(0.31 - 3.08)
Varicella zoster virus glycoprotein E	vaccine	221	7,109	2.6	3.1	0.97	(0.27 - 3.47)
Ascorbic acid	supplement	567	6,763	1.7	1.7	0.99	(0.38 - 2.59)

Other abbreviations and acronyms. *A Streptococcus pneumoniae serotype X: Streptococcus pneumoniae serotype (1, 19A, 3, 5, 6A, 7F) capsular antigen diphtheria CRM197 protein conjugate vaccine; *B Streptococcus pneumoniae serotype X: Streptococcus pneumoniae serotype (14, 18C, 19F, 23F, 4, 6B, 9V) capsular antigen diphtheria CRM197 protein conjugate vaccine; *C Streptococcus pneumoniae type X: Streptococcus pneumoniae type (1, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 2, 20, 22F, 23F, 3, 33F, 4, 5, 6B, 7F, 8, 9N, 9V) capsular polysaccharide antigen; NSAID: nonsteroidal anti-inflammatory drug; PDE5 inhibitor: phosphodiesterase type 5 inhibitor.

eTable 10 Association between drug exposure and hospitalized-mild (exclusive severity).

TCe/u, total count of drug exposed/unexposed patients; **SRe/u**, severity rate of drug exposed/unexposed patients computed after overlap weighting with propensity score; **OR**, odds ratio; **CI**, confidence interval. The association results are arranged in the ascending order of OR values. The statistically significant results at the 0.05 level are emphasized in bold.

Drug name	Drug class	TCe	TCu	SRe	SRu	OR	95% CI
Turmeric extract	supplement	150	7,474	3.3	10.4	0.32	(0.11 - 0.97)
Ethinyl estradiol	estrogen	748	6,876	0.8	2.3	0.4	(0.14 - 1.17)
Flaxseed extract	supplement	197	7,427	7.9	17.3	0.4	(0.19 - 0.84)
*C Streptococcus pneumoniae type X	vaccine	529	7,095	6.1	12.6	0.42	(0.25 - 0.69)
Clotrimazole	antifungal	158	7,466	3.1	6.6	0.44	(0.13 - 1.43)
Methylprednisolone acetate	corticosteroid	407	7,217	3.2	7.5	0.46	(0.22 - 0.94)
Eicosapentaenoate	supplement	229	7,395	5	9.6	0.5	(0.23 - 1.12)
*A Streptococcus pneumoniae serotype X	vaccine	407	7,217	6.6	11	0.52	(0.30 - 0.91)
Glucosamine	supplement	109	7,515	5.4	11.2	0.52	(0.17 - 1.61)
Estradiol	estrogen derivative	572	7,052	2.5	4.8	0.52	(0.25 - 1.08)
Psyllium	antidiarrheal	113	7,511	4.4	8.3	0.54	(0.16 - 1.83)
Omega-3 fatty acids	supplement	456	7,168	7.2	11.5	0.56	(0.33 - 0.95)
Ubidecarenone	supplement	130	7,494	6.8	12.1	0.56	(0.23 - 1.41)
Pseudoephedrine	decongestant	970	6,654	2.5	4.7	0.57	(0.33 - 0.99)
Triamcinolone acetonide	corticosteroid	154	7,470	5.1	8.3	0.57	(0.21 - 1.56)
Biotin	supplement	206	7,418	5.8	9.2	0.58	(0.25 - 1.32)
Estrogens	estrogen	314	7,310	3.7	6.6	0.58	(0.26 - 1.29)
*B Streptococcus pneumoniae serotype X	vaccine	647	6,977	7	10.4	0.59	(0.38 - 0.93)
Clobetasol	corticosteroid	151	7,473	5.2	7.7	0.59	(0.22 - 1.62)
Azelastine	antihistamine	495	7,129	4.5	7.4	0.61	(0.33 - 1.10)
Betamethasone	corticosteroid	244	7,380	4.9	7.8	0.62	(0.28 - 1.36)
Oseltamivir	antiviral	554	7,070	2.9	4.5	0.64	(0.32 - 1.27)
Calcium citrate	calcium salt	113	7,511	5.3	8.8	0.64	(0.22 - 1.92)
Varicella zoster virus glycoprotein E	vaccine	233	7,391	7.3	12.9	0.65	(0.32 - 1.31)
Ibuprofen	NSAID	3,608	4,016	3.7	5.6	0.65	(0.47 - 0.90)
Estrogens, conjugated (USP)	estrogens	118	7,506	5.9	9.4	0.65	(0.22 - 1.90)
Nitrofurantoin, monohydrate	antibiotic	207	7,417	3.4	5.1	0.65	(0.22 - 1.94)
Cetirizine	antihistamine	1,423	6,201	3.5	5.2	0.68	(0.44 - 1.03)
Fluticasone	corticosteroid	2,232	5,392	4.2	6.1	0.68	(0.48 - 0.95)
Lutein	supplement	157	7,467	10.7	14.7	0.71	(0.34 - 1.48)
Lamotrigine	anticonvulsant	157	7,467	3.2	4.4	0.72	(0.21 - 2.47)
Diethylstilbestrol	estrogen	182	7,442	9.7	13.2	0.72	(0.35 - 1.47)
Testosterone	androgen	293	7,331	5	7.1	0.72	(0.34 - 1.52)
Fexofenadine	antihistamine	579	7,045	4.4	6.1	0.73	(0.41 - 1.30)

Naproxen	NSAID	1,017	6,607	4.2	5.9	0.74	(0.47 - 1.16)
Dextromethorphan	antitussive	926	6,698	3.6	4.9	0.75	(0.45 - 1.26)
Fluticasone propionate	corticosteroid	932	6,692	4.7	5.9	0.76	(0.48 - 1.20)
Tetanus toxoid vaccine, inactivated	vaccine	1,218	6,406	4.6	5.9	0.76	(0.50 - 1.14)
Acellular pertussis vaccine, inactivated	vaccine	1,166	6,458	4.7	5.9	0.77	(0.51 - 1.15)
Benzonatate	antitussive	662	6,962	5.7	7.5	0.77	(0.47 - 1.25)
Mometasone	corticosteroid	214	7,410	5.1	7	0.77	(0.32 - 1.83)
Vitamin B12	supplement	702	6,922	6.8	8.4	0.77	(0.49 - 1.22)
Diphtheria toxoid vaccine, inactivated	vaccine	1,216	6,408	4.7	5.9	0.77	(0.52 - 1.16)
Naproxen sodium	NSAID	134	7,490	5.9	7.4	0.78	(0.28 - 2.19)
Haemophilus influenzae type b	vaccine	371	7,253	4	5	0.78	(0.37 - 1.66)
Oxymetazoline	adrenergic agonist agent	1,179	6,445	4.4	5.3	0.79	(0.51 - 1.21)
Loratadine	antihistamine	785	6,839	4.5	5.7	0.79	(0.48 - 1.31)
Varicella-zoster virus vaccine live (Oka-Merck) strain	vaccine	158	7,466	5.7	6	0.79	(0.29 - 2.15)
Metoprolol succinate	antihypertensive	181	7,443	10.1	12.5	0.8	(0.39 - 1.63)
Fish oils	supplement	460	7,164	7.1	9.1	0.8	(0.47 - 1.36)
*D Neisseria meningitidis serogroup X	vaccine	171	7,453	2.9	3.5	0.82	(0.23 - 2.99)
Fiber	supplement	681	6,943	5	6.2	0.85	(0.51 - 1.40)
Diclofenac sodium	NSAID	362	7,262	8.3	10.3	0.85	(0.49 - 1.48)
Docosahexaenoate	supplement	176	7,448	5.7	6.6	0.85	(0.34 - 2.13)
Sodium sulfate	laxative	188	7,436	8.4	10.2	0.86	(0.40 - 1.84)
Sildenafil	PDE5 inhibitor	196	7,428	10.9	13.1	0.86	(0.43 - 1.74)
Norethindrone	contraceptive	438	7,186	1.9	2.5	0.86	(0.31 - 2.41)
Tadalafil	PDE5 inhibitor	128	7,496	10.4	13.2	0.87	(0.38 - 2.01)
Cortisone	corticosteroid	175	7,449	7.3	8.7	0.89	(0.39 - 2.03)
Thioguanine	antineoplastic agent	242	7,382	8.8	10	0.89	(0.46 - 1.73)
Tretinoin	antineoplastic agent	228	7,396	2.7	3.4	0.9	(0.28 - 2.86)
Methylprednisolone	corticosteroid	911	6,713	5.8	6.8	0.92	(0.60 - 1.40)
Diclofenac	NSAID	646	6,978	7.7	8.7	0.94	(0.60 - 1.46)
Hydrochlorothiazide	antihypertensive	767	6,857	9.7	11.1	0.96	(0.65 - 1.41)
Ketoconazole	antifungal	239	7,385	5.8	5.9	0.96	(0.43 - 2.15)
Meloxicam	NSAID	627	6,997	6.9	7.9	0.96	(0.60 - 1.54)
Phenol	anesthetic	349	7,275	4.3	4.4	0.96	(0.44 - 2.10)
Hepatitis A vaccine (inactivated) strain HM175	vaccine	185	7,439	5.4	5.1	0.97	(0.36 - 2.63)
Methocarbamol	skeletal muscle relaxant	163	7,461	7.3	8.3	0.98	(0.40 - 2.39)
Lufenuron	antiparasitic/antifungal	213	7,411	7.9	7.6	0.99	(0.47 - 2.10)
Ascorbic acid	supplement	604	7,020	7.5	7.5	1	(0.62 - 1.60)
Guaifenesin	expectorant	1,260	6,364	6	5.9	1	(0.68 - 1.47)
Amlodipine	antihypertensive	530	7,094	11.3	12.2	1	(0.65 - 1.54)

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