

Supplementary

Table S1 The numbers of participating csDDIs and usage frequencies of each ATC category

ATC Classification (first level), Frequency, n (%)	second level	Frequency, n (%)	Numbers of participating csDDIs combinations, n (%)		
			Lexicomp (n=366)	Micromedex (n=740)	DDInter (n=245)
Alimentary Tract and Metabolism (A), 16478 (24.53)	A02	2685 (4.00)	37 (10.11)	37 (5)	9 (1.22)
	A03	1227 (1.83)	7 (1.91)	21 (2.84)	1 (0.14)
	A04	36 (0.05)	1 (0.27)	6 (0.81)	2 (0.27)
	A05	871 (1.30)	2 (0.55)	0	0
	A06	787 (1.17)	0	4 (0.54)	0
	A07	1136 (1.69)	10 (2.73)	5 (0.68)	1 (0.14)
	A09	610 (0.91)	0	0	0
	A10	4434 (6.60)	151 (41.26)	188 (25.41)	11 (1.49)
	A11	2762 (4.11)	9 (2.46)	4 (0.54)	0
	A12	1851 (2.76)	17 (4.64)	4 (0.54)	1 (0.14)
	A14	21 (0.03)	0	0	0
	A16	58 (0.09)	0	1 (0.14)	0
	Blood and Blood Forming Organs (B), 7800 (11.61)	B01	4941 (7.36)	33 (9.02)	115 (15.54)
B02		119 (0.18)	0	0	0
B03		2409 (3.59)	11 (3.01)	4 (0.54)	2 (0.27)
B05		331 (0.49)	8 (2.19)	3 (0.41)	16 (2.16)
Cardiovascular System (C), 18763 (27.93)	C01	2385 (3.55)	4 (1.09)	33 (4.46)	11 (1.49)
	C02	161 (0.24)	2 (0.55)	1 (0.14)	0
	C03	561 (0.84)	6 (1.64)	22 (2.97)	16 (2.16)
	C05	355 (0.53)	0	1 (0.14)	0
	C07	2557 (3.81)	3 (0.82)	22 (2.97)	14 (1.89)
	C08	3269 (4.87)	9 (2.46)	32 (4.32)	10 (1.35)
	C09	3231 (4.81)	25 (6.83)	66 (8.92)	49 (6.62)
	C10	6244 (9.29)	12 (3.28)	47 (6.35)	24 (3.24)
	D05	13 (0.02)	0	0	0
	Dermatologicals (D), 13 (0.02)	D05	13 (0.02)	0	0
D05		13 (0.02)	0	0	0
Genito Urinary System and Sex Hormones (G), 1915 (2.85)	G03	25 (0.04)	2 (0.55)	1 (0.14)	1 (0.14)
	G04	1890 (2.81)	5 (1.37)	23 (3.11)	2 (0.27)
Systemic Hormonal Preparations, Excl. Sex Hormones and Insulins (H), 1070 (1.59)	H01	14 (0.02)	0	4 (0.54)	0
	H02	538 (0.8)	9 (2.46)	15 (2.03)	9 (1.22)
	H03	305 (0.45)	3 (0.82)	1 (0.14)	0
	H05	213 (0.32)	0	1 (0.14)	0
Antinfectives for Systemic Use (J), 2690 (4.00)	J01	1970 (2.93)	35 (9.56)	88 (11.89)	31 (4.19)
	J02	28 (0.04)	2 (0.55)	4 (0.54)	2 (0.27)
	J04	374 (0.56)	1 (0.27)	1 (0.14)	1 (0.14)
	J05	267 (0.40)	1 (0.27)	3 (0.41)	0
	J06	16 (0.02)	0	0	0
	J07	35 (0.05)	0	0	0
	J07	35 (0.05)	0	0	0
Antineoplastic and Immunomodulating Agents (L), 2626 (3.91)	L01	788 (1.17)	4 (1.09)	15 (2.03)	9 (1.22)
	L02	982 (1.46)	0	16 (2.16)	5 (0.68)
	L03	136 (0.20)	0	0	0
	L04	720 (1.07)	34 (9.29)	36 (4.86)	57 (7.7)
Musculo-Skeletal System (M), 3727 (5.55)	M01	2090 (3.11)	38 (10.38)	101 (13.65)	12 (1.62)
	M02	493 (0.73)	13 (3.55)	0	0
	M03	317 (0.47)	5 (1.37)	0	0
	M04	371 (0.55)	0	2 (0.27)	2 (0.27)
	M05	456 (0.68)	2 (0.55)	2 (0.27)	0
Nervous System (N), 7727 (11.50)	N01	18 (0.03)	0	1 (0.14)	0
	N02	391 (0.58)	33 (9.02)	41 (5.54)	28 (3.78)
	N03	802 (1.19)	29 (7.92)	52 (7.03)	18 (2.43)
	N04	625 (0.93)	11 (3.01)	10 (1.35)	2 (0.27)
	N05	2118 (3.15)	69 (18.85)	127 (17.16)	24 (3.24)
	N06	3061 (4.56)	26 (7.1)	227 (30.68)	70 (9.46)
	N07	712 (1.06)	13 (3.55)	1 (0.14)	0
Antiparasitic Products, Insecticides and Repellents (P), 263 (0.39)	P01	263 (0.39)	0	16 (2.16)	9 (1.22)
Respiratory System (R), 3453 (5.14)	R01	649 (0.97)	4 (1.09)	22 (2.97)	5 (0.68)
	R03	1147 (1.71)	18 (4.92)	32 (4.32)	3 (0.41)
	R05	853 (1.27)	1 (0.27)	2 (0.27)	0
	R06	803 (1.20)	18 (4.92)	10 (1.35)	4 (0.54)
	R07	1 (0)	0	0	0
	S01	316 (0.47)	7 (1.91)	9 (1.22)	5 (0.68)
	Sensory Organs (S), 316 (0.47)	S01	316 (0.47)	7 (1.91)	9 (1.22)
V03		127 (0.19)	2 (0.55)	1 (0.14)	1 (0.14)
V06		204 (0.30)	0	0	0
Various (V), 336 (0.50)	V03	127 (0.19)	2 (0.55)	1 (0.14)	1 (0.14)
	V08	5 (0.01)	0	0	0

Table S2 Univariate and multivariate analyses of potential csDDIs assessed within a single period

Variables	Detected by Lexicomp (n=1832)				Detected by Micromedex (n=2904)				Detected by DDInter (n=912)						
	n (%)	Univariate Analysis		Multivariate Analysis		n (%)	Univariate Analysis		Multivariate Analysis		n (%)	Univariate Analysis		Multivariate Analysis	
		Person Chi-Square	OR	95% CI	Person Chi-Square		OR	95% CI	Person Chi-Square	OR		95% CI			
Gender															
Female	888 (9.7)	5.95*	1.0	–	1189 (13.0)	31.829**	1.0	–	407 (4.4)	0.499	1.0	–			
Male	944 (8.7)		–	–	1715 (15.8)		–	–	505 (4.7)		–	–			
Age															
65–69	656 (8.4)	9.194	1.0	–	986 (12.7)	40.661**	1.0	–	326 (4.2)	6.992	–	–			
70–74	437 (9.7)		1.184**	1.075–1.304	687 (15.2)		1.138*	1.012–1.279	223 (4.9)		–	–			
75–79	276 (9.7)		1.115	0.997–1.248	435 (15.3)		0.954	0.833–1.093	129 (4.5)		–	–			
80–84	221 (9.6)		1.062	0.940–1.200	375 (16.2)		0.927	0.802–1.072	117 (5.1)		–	–			
85–89	159 (9.9)		0.962	0.835–1.108	263 (16.4)		0.793*	0.671–0.937	78 (4.9)		–	–			
90–94	75 (9.1)		0.953	0.788–1.153	144 (17.5)		0.869	0.699–1.080	37 (4.5)		–	–			
≥95	8 (8.4)		0.924	0.546–1.563	14 (14.7)		0.56	0.298–1.052	2 (2.1)		–	–			
No. of departments															
1	852 (6.1)	3**	1.0	–	1381 (10.0)	1036.25**	1.0	–	467 (3.4)	309.652**	1.0	–			
2–3	626 (12.9)		0.974	0.871–1.091	1028 (21.2)		0.672**	0.594–0.759	272 (5.6)		0.75*	0.622–0.904			
4–6	310 (26.5)		1.242	0.957–1.611	437 (37.3)		0.53**	0.419–0.669	151 (12.9)		0.99	0.725–1.352			
≥7	44 (42.3)		10.357**	3.894–27.546	58 (55.8)		0.959	0.584–1.575	22 (21.2)		1.887*	1.031–3.456			
No. of medications															
1–4	502 (3.8)	2**	1.0	–	727 (5.4)	3046.981**	1.0	–	274 (2.0)	808.638**	1.0	–			
5–9	804 (16.0)		9.267**	8.482–10.125	1427 (28.3)		6.992**	6.261–7.808	378 (7.5)		4.479**	3.767–5.326			
≥10	526 (33.3)		44.859**	36.591–54.995	750 (47.5)		19.466**	16.328–23.208	260 (16.5)		12.64**	9.866–16.195			
Department patient visited															
Cardiology	763 (11.5)	64.747**	1.536**	1.406–1.677	1617 (24.4)	773.506**	1.685**	1.521–1.866	433 (6.5)	87.706**	–	–			
Neurology	415 (12.6)	56.935**	1.946**	1.754–2.160	837 (25.5)	380.207**	2.305**	2.057–2.582	235 (7.2)	60.722**	1.278*	1.079–1.513			
Gastroenterology	283 (11.3)	16.073**	0.353**	0.308–0.404	384 (15.4)	1.645	0.569**	0.489–0.661	150 (6.0)	13.648**	0.777*	0.630–0.959			
Orthopedics	451 (19.5)	333.668**	1.396**	1.235–1.579	448 (19.3)	48.664**	0.865*	0.749–0.998	114 (4.9)	0.763	–	–			
Pneumology	313 (13.7)	63.846**	0.605**	0.530–0.690	505 (22.1)	119.444**	–	–	143 (6.3)	17.094**	0.719*	0.580–0.890			
Urinary	170 (8.4)	1.656	0.526**	0.456–0.606	303 (14.9)	0.312	–	–	98 (4.8)	0.379	–	–			
Endocrinology	462 (27.7)	753.518**	2.634**	2.303–3.014	523 (31.4)	417.045**	2.415**	2.107–2.768	76 (4.6)	0	–	–			
TCM	204 (15.2)	62.799**	0.412**	0.348–0.489	290 (21.6)	57.909**	0.671**	0.563–0.799	85 (6.3)	10.325*	0.568**	0.434–0.745			
Nephrology	107 (10.3)	1.639	–	–	150 (14.4)	0.012	–	–	50 (4.8)	0.147	–	–			
Oncology	65 (6.9)	5.903*	0.522**	0.422–0.647	75 (8.0)	33.808**	–	–	35 (3.7)	1.56	–	–			

*, P<0.05; **, P<0.001.

Table S3 The potential csDDIs detected by both Lexicomp and Micromedex and their frequencies

Object drug and class	Interacting drug and class	Lexicomp Rating	Micromedex Rating	Frequency under different assessment cycles, n		
				Single prescription	Single day	Single period
Alpha-/Beta-Agonists	Serotonin/Norepinephrine Reuptake Inhibitors	D	Major	0	2	2
Alpha1-Agonists	Monoamine Oxidase Inhibitors	X	Major	2	2	2
Alpha1-Blockers	Alpha1-Blockers	X	Major	2	4	4
Amlodipine	Simvastatin	D	Major	12	15	15
Angiotensin-Converting Enzyme Inhibitors	Angiotensin II Receptor Blockers	D	Major	10	15	18
Anti-Parkinson Agents (Dopamine Agonist)	Antipsychotic Agents (Second Generation [Atypical])	D	Major	2	8	10
Aspirin	Dabigatran Etexilate	D	Major	9	12	12
Aspirin	Nonsteroidal Anti-Inflammatory Agents (COX-2 Selective)	D	Major	2	11	15
Aspirin	Ticagrelor	D	Major	72	83	83
Atorvastatin	Clarithromycin	D	Major	0	1	3
Atorvastatin	Cyclosporine	X	Major	2	5	6
Beta-Blockers	Rivastigmine	X	Major	2	2	2
Carbamazepine	Quetiapine	D	Major	0	1	1
Cardiac Glycosides	Amiodarone	D	Major	1	1	1
Cilostazol	Omeprazole	D	Major	0	1	1
Citalopram	Escitalopram	X	Major	2	2	3
Citalopram	Omeprazole	D	Major	0	1	2
Clopidogrel	CYP2C19 Inhibitors (Strong)	D	Major	0	1	1
Clopidogrel	Omeprazole/Esomeprazole	X	Major	6	17	25
Clopidogrel	Repaglinide	D	Major	6	15	15
CNS Depressants	Opioid Agonists	D	Major	17	20	22
CNS Depressants	Oxycodone	D	Major	2	107	117
CNS Depressants	Zolpidem	D	Major	53	102	112
Cyclosporine (Systemic)	Antifungal Agents (Azole Derivatives, Systemic)	D	Major	0	1	1
CYP3A4 Inducers (Moderate)	Clarithromycin	D	Major	1	1	1
Dabigatran Etexilate	Nonsteroidal Anti-Inflammatory Agents (Nonselective)	D	Major	0	3	3
Diltiazem	Simvastatin	D	Major	1	2	2
Domperidone	CYP3A4 Inhibitors (Moderate)	X	Major	1	1	1
Domperidone	Ondansetron	D	Major	1	1	1
Domperidone	QT-prolonging Agents (Moderate Risk)	D	Major	1	1	1
Felodipine	CYP3A4 Inducers (Strong)	D	Major	1	1	1
Felodipine	CYP3A4 Inhibitors (Strong)	D	Major	0	1	1
Gefitinib	Inhibitors of the Proton Pump (PPIs and PCABs)	D	Major	0	0	1
Hormonal Contraceptives	CYP3A4 Inducers (Weak)	D	Major	0	1	1
Insulins	Dipeptidyl Peptidase-IV Inhibitors	D	Major	24	31	31
Insulins	Liraglutide	D	Major	18	21	21
Insulins	Pioglitazone	D	Major	1	3	3
Ivabradine	CYP3A4 Inhibitors (Moderate)	X	Major	3	5	6
Lamotrigine	Valproate Products	D	Major	3	3	3
Lev amlodipine	Simvastatin	D	Major	21	24	25
Levofloxacin	Amiodarone	X	Major	0	1	1
Loop Diuretics	Nonsteroidal Anti-Inflammatory Agents	D	Major	1	3	3
Methotrexate	Inhibitors of the Proton Pump (PPIs and PCABs)	D	Major	1	3	4
Methotrexate	Leflunomide	D	Major	46	46	46
Methotrexate	Nonsteroidal Anti-Inflammatory Agents	D	Major	12	13	13
Metoclopramide	Promethazine	X	Major	1	4	4
Nonsteroidal Anti-Inflammatory Agents	Nonsteroidal Anti-Inflammatory Agents	X	Major	3	8	12
QT-prolonging Miscellaneous Agents (Moderate Risk)	QT-prolonging Strong CYP3A4 Inhibitors (Moderate Risk)	X	Major	0	2	2
Rivaroxaban	Antiplatelet Agents (P2Y12 Inhibitors)	D	Major	3	3	3
Rivaroxaban	Aspirin	D	Major	2	4	5
Rivaroxaban	Nonsteroidal Anti-Inflammatory Agents (Nonselective)	D	Major	0	2	2
Rosuvastatin	Brand Name	D	Major	1	3	3
Salicylates	Ginkgo Biloba	D	Major	113	161	169
Salicylates	Methotrexate	D	Major	1	2	2
Salicylates	Nonsteroidal Anti-Inflammatory Agents (Nonselective)	D	Major	9	54	63
Selective Serotonin Reuptake Inhibitors	Nonsteroidal Anti-Inflammatory Agents (Nonselective)	D	Major	0	8	11
Selegiline	Selective Serotonin Reuptake Inhibitors	X	Contraindicated	0	1	1
Serotonergic Non-Opioid CNS Depressants	Selegiline	X	Contraindicated	1	1	1
Sildenafil	CYP3A4 Inhibitors (Strong)	X	Contraindicated	0	0	1
Sulfamethoxazole and Trimethoprim	Methotrexate	D	Major	1	1	1
Sulfonylureas	Alpha-Glucosidase Inhibitors	D	Major	24	24	24
Sulfonylureas	Dipeptidyl Peptidase-IV Inhibitors	D	Major	47	51	51
Sulfonylureas	Thiazolidinediones	D	Major	3	3	3
Tenofovir Products	Nonsteroidal Anti-Inflammatory Agents	D	Major	0	1	1
Tetracyclines	Magnesium Salts	D	Major	0	1	1
Tiotropium	Anticholinergic Agents	X	Major	9	12	15
Tolvaptan	CYP3A4 Inhibitors (Moderate)	D	Major	1	1	1
Vitamin K Antagonists	Ginkgo Biloba	D	Major	1	1	1