

Supplementary Online Content

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eTable 1. Complications and contraindications to medications

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Complications and contraindications to medications

ICD-9 / ICD-10 Codes	Description
<i>All Drugs</i>	
977	Poisoning by other and unspecified drugs and medicinal substances
T50	Poisoning by diuretics and other and unspecified drugs, medicaments and biological substances
T78	Adverse effects, not elsewhere classified
<i>Antiplatelet and anticoagulant agents</i>	
<i>Hemorrhage</i>	
285.1	Acute post-hemorrhage anemia
286.5	Hemorrhagic D/O due to circulating anticoagulant (use E code to identify cause if drug induced)
286.7	Acquired coagulation factor deficiency (use E code to identify cause if drug induced)
430	Subarachnoid hemorrhage
431	Intracerebral hemorrhage
432	Other and unspecific intracranial hemorrhage
459.0	Hemorrhage, unspecified / Spontaneous hemorrhage NEC
531.0	Gastric ulcer—acute with hemorrhage
531.2	Gastric ulcer—acute with hemorrhage and perforation
531.4	Gastric ulcer—chronic or unspecified with hemorrhage
531.6	Gastric ulcer—chronic or unspecified with hemorrhage and perforation
532.0	Duodenal ulcer—acute with hemorrhage
532.2	Duodenal ulcer—acute with hemorrhage and perforation
532.4	Duodenal ulcer—chronic or unspecified with hemorrhage
532.6	Duodenal ulcer—chronic or unspecified with hemorrhage and perforation
533.0	Peptic ulcer Dx, site unspecified—acute with hemorrhage
533.2	Peptic ulcer Dx, site unspecified—acute with hemorrhage and perforation
533.4	Peptic ulcer Dx, site unspecified—chronic or unspecified with hemorrhage
533.6	Peptic ulcer Dx, site unspecified—chronic or unspecified with hemorrhage and perforation
534.0	Gastrojejunal ulcer—acute with hemorrhage
534.2	Gastrojejunal ulcer—acute with hemorrhage and perforation
534.4	Gastrojejunal ulcer—chronic or unspecified with hemorrhage
534.6	Gastrojejunal ulcer—chronic or unspecified with hemorrhage and perforation
535	Gastritis and duodenitis
537.8	Disorders of the stomach and duodenum, other specified disorders of the stomach and duodenum
562.0	Diverticula of the intestine—small intestine
562.1	Diverticula of the intestine—colon
568.8	Other disorders of the peritoneum, other specified disorders of the peritoneum (hemoperitoneum--non-traumatic)
569.3	Hemorrhage of rectum and anus
569.8	Other disorders of the intestine, other specified disorders of the intestine(angiodysplasia with hemorrhage)
578.0	Hematemesis
578.1	Blood in stool (melena)
578.9	Hemorrhage GI tract, unspecified
599.7	Hematuria
719.1	Hemarthrosis
784.7	Epistaxis
786.3	Hemoptysis
790.92	Abnormal coagulation profile
D65-69	Coagulation defects, purpura and other haemorrhagic conditions
K25-K28	Gastric and Duodenal Ulcers
K29.0	Acute haemorrhagic gastritis
K55	Vascular disorders of intestine

ICD-9 / ICD-10 Codes	Description
160	Subarachnoid haemorrhage
161	Intracerebral haemorrhage
162	Other nontraumatic intracranial haemorrhage
184	Haemorrhoids
185	Oesophageal varices
M25.0	Haemarthrosis
R04	Haemorrhage from respiratory passages
<i>Poisoning</i>	
972, T46	Poisoning by agents primarily affecting the cardiovascular system
Statins	
<i>Liver Disease</i>	
570	Acute and subacute necrosis of liver
571	Chronic liver disease and cirrhosis
572	Liver abscess and sequelae of chronic liver disease
573	Other disorders of liver
070	Viral hepatitis
078.5	cytomegalic inclusion virus hepatitis
B15-B19	Viral hepatitis
K70-K77	Liver disease
<i>Rhabdomyolysis</i>	
728	Disorders of muscle
359	Muscular dystrophies and other myopathies
M60	Myositis
M62	Other disorders of muscle
<i>Poisoning</i>	
972, T46	Poisoning by agents primarily affecting the cardiovascular system
Acid suppressors	
973, T47	Poisoning by agents primarily affecting the gastrointestinal system
Respiratory Inhalers	
975, T48	Poisoning by agents primarily acting on the smooth and skeletal muscles and respiratory system
L-Thyroxine	
T38	Poisoning by hormones and their synthetic substitutes and antagonists, not elsewhere classified
T49	Poisoning by topical agents primarily affecting skin and mucous membrane and by ophthalmological, otorhinolaryngological and dental drugs

eTable 2. Study analysis exclusions

Groups	Statins	Antiplatelets/ anticoagulants	L- Thyroxine	Respiratory Inhalers	Gastric acid suppressors
Hospitalized					
Initial N	105300	35040	60792	6031	62830
Contraindications ^a	896	3206	13	1	4
Deaths within 90 days of index	7082	3786	5209	881	5727
Analysis cohort	97533	28721	55570	5149	57099
Control					
Initial N	109099	21582	65052	2680	46337
Contraindications ^a	0	0	0	0	0
Deaths within 90 days of index	155	92	125	22	145
Analysis cohort	108944	21490	64927	2658	46192
Total	206,477	50,211	120,497	7,807	103,291

^aSee eTable 1.

eTable 3. Detailed data for each medication group

	Hospitalizations			Control
	All	Without ICU Stay	With ICU Stay	
HMG co-A reductase inhibitors (Statins)				
N	97,533	87,395	10,138	108,944
Age at index, mean (\pm SD)	75.6 (5.67)	75.7 (5.71)	74.8 (5.29)	
Male, n (%)	54,424 (55.8)	47,822 (54.7)	6,602 (65.1)	53,445 (49.1)
Low income status*, n (%)	21,747 (22.3)	19,687 (22.5)	2,060 (20.3)	23,764 (21.8)
Number of drugs prescribed in the year prior to index, median (IQR)	13 (9-17)	12 (9-17)	13 (10-18)	9 (6-12)
Patients with primary care visits in the year prior to index, n (%)	96,045 (98.5)	86,063 (98.5)	9,982 (98.5)	106,293 (97.6)
Number of primary care visits, median (IQR)				
90 days before admission	3 (1-4)	3 (1-4)	3 (1-4)	2 (1-3)
90 days after index date	3 (2-5)	3 (1-5)	3 (2-5)	2 (1-3)
Number of internal medicine and subspecialist visits, median (IQR)				
90 days before admission	1 (0-2)	1 (0-2)	1 (0-3)	0 (0-1)
90 days after index date	1 (0-2)	1 (0-2)	2 (1-3)	0 (0-1)
Hospital admission category, n (%)				
Emergent / Urgent	66,327 (68)	60,189 (68.9)	6,138 (60.5)	N / A
Elective	31,202 (32)	27,202 (31.1)	4,000 (39.5)	N / A
Missing	4 (0)	4 (0)		N / A
Hospital LOS				
Mean (\pm SD)	4.1 (3.06)	3.8 (2.89)	6.4 (3.42)	N / A
Median (IQR)	3 (2-6)	3 (2-5)	6 (4-8)	N / A
ICU Stay, n (%)	10,138 (10.4)	N / A	10,138 (100)	N / A
ICU LOS				
Mean (\pm SD)	2.7 (1.6)	N / A	2.7 (1.6)	N / A
Median (IQR)	2 (2-3)	N / A	2 (2-3)	N / A
Teaching hospital, n (%)	25,608 (26.3)	21,479 (24.6)	4,129 (40.7)	N / A
Outcomes				
Drug Discontinuation, n (%)	13,277 (13.6)	11,793 (13.5)	1,484 (14.6)	11,627 (10.7)
Odds Ratios (CI)				
Univariate	1.32 [1.28, 1.35]	1.31 [1.27, 1.34]	1.44 [1.35, 1.52]	1.00
Univariate (Hospitalizations Only)	-	1.00	1.10 [1.04, 1.17]	-
Multivariate	1.34 [1.30, 1.38]	1.32 [1.29, 1.36]	1.48 [1.39, 1.57]	1.00
Multivariate (Hospitalizations Only)	-	1.00	1.12 [1.05, 1.18]	-
* Low income status \equiv individual income below \$16,018 or couples income below \$24,175				
Antiplatelet or Anticoagulant Agents				
N	28,721	26,298	2,423	21,490
Age at index, mean (\pm SD)	77.8 (6.22)	77.9 (6.25)	76.3 (5.74)	
Male, n (%)	15,771 (54.9)	14,315 (54.4)	1,456 (60.1)	11,320 (52.7)

	Hospitalizations			Control
	All	Without ICU Stay	With ICU Stay	
Low income status*, n (%)	7,402 (25.8)	6,855 (26.1)	547 (22.6)	5,377 (25)
Number of drugs prescribed in the year prior to index, median (IQR)	14 (10-18)	14 (10-18)	14 (11-19)	10 (7-14)
Patients with primary care visits in the year prior to index, n (%)	28,337 (98.7)	25,952 (98.7)	2,385 (98.4)	21,025 (97.8)
Number of primary care visits, median (IQR)				
90 days before admission	4 (2-6)	4 (2-6)	4 (2-6)	4 (2-5)
90 days after index date	5 (3-7)	5 (3-7)	5 (3-7)	3 (2-5)
Number of internal medicine and subspecialist visits, median (IQR)				
90 days before admission	1 (0-2)	1 (0-2)	1 (0-3)	0 (0-1)
90 days after index date	1 (0-2)	1 (0-2)	2 (0-3)	0 (0-1)
Hospital admission category, n (%)				
Emergent / Urgent	22,309 (77.7)	20,564 (78.2)	1,745 (72)	N / A
Elective	6,411 (22.3)	5,733 (21.8)	678 (28)	N / A
Missing	1 (0)	1 (0)		N / A
Hospital LOS				
Mean (\pm SD)	4.3 (3.22)	4.1 (3.11)	6.4 (3.61)	N / A
Median (IQR)	3 (2-6)	3 (2-6)	6 (4-9)	N / A
ICU Stay, n (%)	2,423 (8.4)	N / A	2,423 (100)	N / A
ICU LOS				
Mean (\pm SD)	2.7 (1.62)	N / A	2.7 (1.62)	N / A
Median (IQR)	2 (2-3)	N / A	2 (2-3)	N / A
Teaching hospital, n (%)	6,293 (21.9)	5,508 (20.9)	785 (32.4)	N / A
Outcomes				
Drug Discontinuation, n (%)	5,564 (19.4)	5,012 (19.1)	552 (22.8)	2,535 (11.8)
Odds Ratios (CI)				
Univariate	1.8 [1.71, 1.89]	1.76 [1.67, 1.85]	2.21 [1.99, 2.45]	1.00
Univariate (Hospitalizations Only)	-	1.00	1.25 [1.13, 1.38]	-
Multivariate	1.88 [1.78, 1.98]	1.85 [1.75, 1.95]	2.31 [2.07, 2.57]	1.00
Multivariate (Hospitalizations Only)	-	1.00	1.26 [1.14, 1.4]	-
* Low income status \equiv individual income below \$16,018 or couples income below \$24,175				
L-thyroxine				
N	55,570	51,476	4,094	64,927
Age at index, mean (\pm SD)	77 (6.35)	77.1 (6.39)	76.2 (5.87)	
Male, n (%)	13,499 (24.3)	12,172 (23.6)	1,327 (32.4)	11,906 (18.3)
Low income status*, n (%)	15,117 (27.2)	14,073 (27.3)	1,044 (25.5)	15,910 (24.5)
Number of drugs prescribed in the year prior to index, median (IQR)	12 (9-17)	12 (8-17)	13 (10-18)	8 (5-12)
Patients with primary care visits in the year prior to index, n (%)	54,644 (98.3)	50,632 (98.4)	4,012 (98)	63,002 (97)
Number of primary care visits, median (IQR)				
90 days before admission	3 (1-4)	3 (1-4)	3 (1-4)	2 (1-3)
90 days after index date	3 (2-5)	3 (1-5)	3 (2-6)	2 (1-3)
Number of internal medicine and subspecialist				

	Hospitalizations			Control
	All	Without ICU Stay	With ICU Stay	
visits, median (IQR)				
90 days before admission	1 (0-2)	1 (0-2)	1 (0-3)	0 (0-1)
90 days after index date	1 (0-2)	1 (0-2)	2 (0-3)	0 (0-0)
Hospital admission category, n (%)				
Emergent / Urgent	39,211 (70.6)	36,400 (70.7)	2,811 (68.7)	N / A
Elective	16,355 (29.4)	15,073 (29.3)	1,282 (31.3)	N / A
Missing	4 (0)	3 (0)	1 (0)	N / A
Hospital LOS				
Mean (\pm SD)	4.3 (3.14)	4.1 (3.04)	6.4 (3.47)	N / A
Median (IQR)	3 (2-6)	3 (2-6)	6 (4-9)	N / A
ICU Stay, n (%)	4,094 (7.4)	N / A	4,094 (100)	N / A
ICU LOS				
Mean (\pm SD)	2.7 (1.59)	N / A	2.7 (1.59)	N / A
Median (IQR)	2 (2-3)	N / A	2 (2-3)	N / A
Teaching hospital, n (%)	12,705 (22.9)	11,244 (21.8)	1,461 (35.7)	N / A
Outcomes				
Drug Discontinuation, n (%)	6,831 (12.3)	6,217 (12.1)	614 (15)	7,114 (11)
Odds Ratios (CI)				
Univariate	1.14 [1.10, 1.18]	1.12 [1.08, 1.16]	1.43 [1.31, 1.57]	1.00
Univariate (Hospitalizations Only)	-	1.00	1.28 [1.17, 1.41]	-
Multivariate	1.19 [1.14, 1.23]	1.17 [1.12, 1.21]	1.51 [1.38, 1.66]	1.00
Multivariate (Hospitalizations Only)	-	1.00	1.28 [1.17, 1.4]	-
* Low income status \equiv individual income below \$16,018 or couples income below \$24,175				
Respiratory inhalers				
N	5,149	4,777	372	2,658
Age at index, mean (\pm SD)	76.1 (5.87)	76.1 (5.89)	75 (5.4)	
Male, n (%)	2,768 (53.8)	2,560 (53.6)	208 (55.9)	1,315 (49.5)
Low income status*, n (%)	1,838 (35.7)	1,710 (35.8)	128 (34.4)	945 (35.6)
Number of drugs prescribed in the year prior to index, median (IQR)	16 (12-21)	15 (11-20)	17 (12-22)	12 (8-16)
Patients with primary care visits in the year prior to index, n (%)	5,055 (98.2)	4,692 (98.2)	363 (97.6)	2,568 (96.6)
Number of primary care visits, median (IQR)				
90 days before admission	3 (1-5)	3 (1-5)	3 (1-5)	2 (1-3)
90 days after index date	3 (2-5)	3 (2-5)	3 (2-5.5)	2 (1-3)
Number of internal medicine and subspecialist visits, median (IQR)				
90 days before admission	1 (0-2)	1 (0-2)	1 (0-2)	0 (0-1)
90 days after index date	1 (0-2)	1 (0-2)	1 (0-3)	0 (0-1)
Hospital admission category, n (%)				
Emergent / Urgent	4,424 (85.9)	4,119 (86.2)	305 (82)	N / A
Elective	725 (14.1)	658 (13.8)	67 (18)	N / A
Missing				N / A
Hospital LOS				
Mean (\pm SD)	4.9 (3.33)	4.7 (3.22)	7.5 (3.68)	N / A

	Hospitalizations			Control
	All	Without ICU Stay	With ICU Stay	
Median (IQR)	4 (2-7)	4 (2-6)	7 (5-10)	N / A
ICU Stay, n (%)	372 (7.2)	N / A	372 (100)	N / A
ICU LOS				
Mean (\pm SD)	2.9 (1.86)	N / A	2.9 (1.86)	N / A
Median (IQR)	2 (2-4)	N / A	2 (2-4)	N / A
Teaching hospital, n (%)	1,004 (19.5)	894 (18.7)	110 (29.6)	N / A
Outcomes				
Drug Discontinuation, n (%)	231 (4.5)	211 (4.4)	20 (5.4)	79 (3)
Odds Ratios (CI)				
Univariate	1.53 [1.18, 1.99]	1.51 [1.16, 1.96]	1.85 [1.12, 3.07]	1.00
Univariate (Hospitalizations Only)	-	1.00	1.23 [0.77, 1.97]	-
Multivariate	1.52 [1.16, 1.99]	1.49 [1.14, 1.97]	1.84 [1.10, 3.08]	1.00
Multivariate (Hospitalizations Only)	-	1.00	1.26 [0.78, 2.02]	-
* Low income status \equiv individual income below \$16,018 or couples income below \$24,175				
Gastric acid suppressors				
N	57,099	52,738	4,361	46,192
Age at index, mean (\pm SD)	77 (6.26)	77.1 (6.29)	76.1 (5.73)	
Male, n (%)	25,706 (45)	23,360 (44.3)	2,346 (53.8)	18,286 (39.6)
Low income status*, n (%)	17,028 (29.8)	15,857 (30.1)	1,171 (26.9)	13,305 (28.8)
Number of drugs prescribed in the year prior to index, median (IQR)	14 (10-19)	14 (10-19)	15 (11-20)	11 (7-15)
Patients with primary care visits in the year prior to index, n (%)	56,176 (98.4)	51,897 (98.4)	4,279 (98.1)	45,007 (97.4)
Number of primary care visits, median (IQR)				
90 days before admission	3 (1-5)	3 (1-5)	3 (1-5)	2 (1-3)
90 days after index date	3 (2-5)	3 (2-5)	4 (2-6)	2 (1-3)
Number of internal medicine and subspecialist visits, median (IQR)				
90 days before admission	1 (0-2)	1 (0-2)	1 (0-3)	0 (0-1)
90 days after index date	1 (0-2)	1 (0-2)	2 (0-3)	0 (0-1)
Hospital admission category, n (%)				
Emergent / Urgent	42,082 (73.7)	39,048 (74)	3,034 (69.6)	N / A
Elective	15,014 (26.3)	13,687 (26)	1,327 (30.4)	N / A
Missing	3 (0)	3 (0)		N / A
Hospital LOS				
Mean (\pm SD)	4.3 (3.13)	4.1 (3.03)	6.4 (3.52)	N / A
Median (IQR)	3 (2-6)	3 (2-6)	6 (4-9)	N / A
ICU Stay, n (%)	4,361 (7.6)	N / A	4,361 (100)	N / A
ICU LOS				
Mean (\pm SD)	2.7 (1.64)	N / A	2.7 (1.64)	N / A
Median (IQR)	2 (2-3)	N / A	2 (2-3)	N / A
Teaching hospital, n (%)	13,173 (23.1)	11,633 (22.1)	1,540 (35.3)	N / A
Outcomes				
Drug Discontinuation, n (%)	7,394 (12.9)	6,724 (12.7)	670 (15.4)	4,330 (9.4)

	Hospitalizations			Control
	All	Without ICU Stay	With ICU Stay	
Odds Ratios (CI)				
Univariate	1.44 [1.38, 1.50]	1.41 [1.36, 1.47]	1.75 [1.61, 1.92]	1.00
Univariate (Hospitalizations Only)	-	1.00	1.24 [1.14, 1.35]	-
Multivariate	1.5 [1.44, 1.57]	1.48 [1.41, 1.54]	1.87 [1.71, 2.05]	1.00
Multivariate (Hospitalizations Only)	-	1.00	1.26 [1.16, 1.38]	-
* Low income status ≡ individual income below \$16,018 or couples income below \$24,175				