

SUPPLEMENTARY ONLINE CONTENT

Supplemental Box 1. ICD-9-CM diagnostic and procedure codes

Supplemental Box 2. Calculation of mg-diazepam-equivalents from other benzodiazepines

Supplemental Table 1. Non-benzodiazepine medications for alcohol withdrawal syndrome (AWS)

Supplemental Figure 1. Patient sample

Supplemental Table 2. Comorbid Inpatient Diagnosis Categories, Labels, and ICD-9-CM Codes

Supplemental Table 3. Medications for alcohol withdrawal syndrome (AWS) received by medical inpatients in the Veterans Health Administration during 2013

Supplemental Table 4. Medications and benzodiazepine dosing strategies received by medical inpatients with alcohol withdrawal syndrome (AWS) in the Veterans Health Administration during 2013

Supplemental Figure 2. Proportion of medical inpatients receiving each benzodiazepine dosing strategy by hospital in the Veterans Health Administration during 2013

Supplemental Table 5. Adjusted associations between patient characteristics, hospital prescribing pattern, and each benzodiazepine dosing strategy for alcohol withdrawal syndrome (AWS) among medical inpatients in the Veterans Health Administration during 2013, with hospital site as a random effect

Supplemental Table 6. Associations between benzodiazepine dosing strategy for alcohol withdrawal syndrome (AWS) and cumulative benzodiazepine exposure, intensive care, and intubation during hospital days 0-10, unadjusted and adjusted for patient characteristics in the Veterans Health Administration during 2013, with hospital site as a random effect

Supplemental References

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

Supplemental Box 1. ICD-9-CM diagnostic and procedure codes

Alcohol Withdrawal Syndrome:

- Diagnostic Codes: 291.0, 291.3, 291.5, 291.8, 291.81
- Procedure Codes: 94.62, 94.63, 94.68, 94.69

Alcohol Use Disorder:

- Diagnostic Codes: 303.x and 305.0x

Intubation

- Procedure Codes: 31.1, 96.04, 96.05, 96.70, 96.71, 96.72

Supplemental Box 2. Calculation of mg-diazepam-equivalents from other benzodiazepines

10 mg of diazepam =

- 1 mg of lorazepam
- 25 mg of chlordiazepoxide
- 2 mg of midazolam
- 20 mg of oxazepam
- 20 mg of temazepam
- 0.5 mg of clonazepam
- 1 mg of alprazolam
- 15 mg of clorazepate

Supplemental Table 1. Non-benzodiazepine medications for alcohol withdrawal syndrome (AWS)

Medication	Mechanism
Baclofen ¹⁻³	GABA _B agonist
Carbamazepine ⁴⁻¹⁰	Stabilizes neuronal membranes by inhibiting voltage-sensitive sodium channels and/or calcium channels
Clonidine ¹⁰⁻¹³	α_2 agonist
Dexmedetomidine ¹⁴⁻²²	Selective α_2 agonist
Ethanol ²³⁻²⁵	GABA _A agonist, NMDA antagonist
Gabapentin ²⁶⁻³⁰	Stabilizes neuronal membranes by inhibiting voltage-gated calcium channels; structurally related to GABA but does not appear to bind receptor
Ketamine ³¹⁻³³	NMDA antagonist
Oxcarbazepine ³⁴	Stabilizes neuronal membranes by inhibiting voltage-sensitive sodium channels and/or calcium channels
Phenobarbital ^{26,35-39}	GABA _A agonist, NMDA antagonist
Pregabalin ⁴⁰	Stabilizes neuronal membranes by inhibiting voltage-gated calcium channels
Propofol ^{14,17,41-43}	GABA _A agonist, NMDA antagonist
Valproic acid ^{8,44-49}	Stabilizes neuronal membranes by inhibiting voltage-gated sodium channels; binding to presynaptic GABA _B receptors may increase release of GABA; increases GABA synthesis by activating glutamic acid decarboxylase

Legend: GABA = γ -aminobutyric acid; NMDA = *N*-methyl-D-aspartate

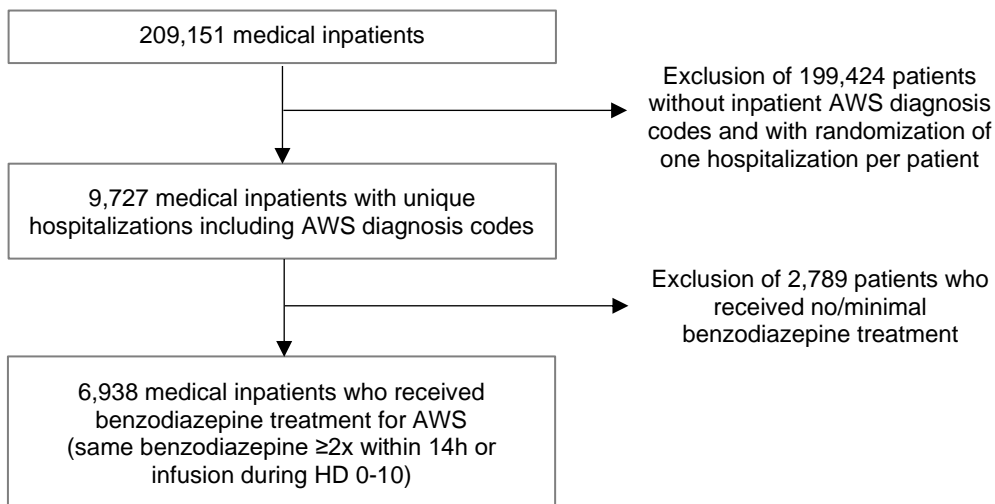
Supplemental Table 2. Comorbid Inpatient Diagnosis Categories, Labels, and ICD-9-CM Codes

Diagnosis Category	Diagnosis Label	ICD-9-CM Code
Mental health disorder	Schizophrenic disorders	295.x
	Episodic mood disorders (bipolar disorders, depressive disorders)	296.x, 311
	Delusional disorders	297.x
	Other nonorganic psychoses	298.x
	Anxiety, dissociative and somatoform disorders	300.x
	Personality disorders	301.x
	Eating disorders	307.x
	Acute reaction to stress	308.x
	Adjustment reaction (including PTSD)	309.x
	Other psychosocial circumstances (suicidal ideation and homicidal ideation)	V62.x
	Suicide	E950.x – E958.x
Nutrition, electrolyte, or acid-base disorder	Other disorders of pancreatic internal secretion	251.x
	Kwashiorkor	260.x
	Nutritional marasmus	261.x
	Other severe protein-calorie malnutrition	262.x
	Other and unspecified protein-calorie malnutrition	263.x
	Vitamin A deficiency	264.x
	Thiamine and niacin deficiency states	265.x
	Deficiency of b-complex components	266.x
	Ascorbic acid deficiency	267.x
	Vitamin D deficiency	268.x
	Other nutritional deficiencies	269.x
	Disorders of mineral metabolism	275.x
	Disorders of fluid electrolyte and acid-base balance	276.x
	Iron deficiency anemias	280.x
	Other deficiency anemias	281.x
GI tract disorder	Cholera	1.x
	Salmonella gastroenteritis	3
	Shigellosis	4.x
	Amebiasis (apart from causing liver injury, pneumonia, skin lesions)	6, 6.1, 6.2
	Other protozoal intestinal diseases	7.x
	Intestinal infections due to other organisms	8.x
	Ill-defined intestinal infections	9.x
	Tuberculosis of intestines peritoneum and mesenteric glands	14.x
	Tuberculosis of esophagus	17.8x
	Gastrointestinal anthrax	22.2
	Diphtheritic peritonitis	32.83
	Abdominal actinomycotic infections	39.2
	Toxin-producing bacterial infections	41.41, 41.42, 41.43, 41.49, 41.86
	Epidemic vomiting syndrome	78.82
	Syphilitic peritonitis	95.2
	Gonococcal peritonitis	98.86
	Chlamydia of peritoneum	98.86
	Candidiasis of the esophagus	112.84
	Candidiasis of the intestine	112.85
	Other cestode infections	123, 123.4
	Ancylostomiasis and necatoriasis	126.x
	Esophageal varices (bleeding, without bleeding, etc)	456.x
	Diseases of esophagus	530.x
	Gastric ulcers	531.x
	Duodenal ulcers	532.x
	Peptic ulcer site unspecified	533.x
	Gastrojejunal ulcer	534.x
	Gastritis and duodenitis	535.x
	Disorders of function of stomach	536.x
	Other disorders of stomach and duodenum	537.x
	Complications of bariatric procedures	539.01, 539.09, 539.81, 539.89
	Appendicitis	540, 540.1, 540.9, 541, 542, 543, 543.9
	Regional enteritis	555.x
Ulcerative enterocolitis	556.x	
Vascular insufficiency of intestine	557.x	

	Other and unspecified noninfectious gastroenteritis and colitis	558.1, 558.2, 558.3, 558.41, 558.42, 558.9
	Intestinal obstruction without mention of hernia	560.x
	Diverticula of intestine	562.x
	Functional digestive disorders not elsewhere classified	564.x
	Anal fissure and fistula	565.x
	Abscess of anal and rectal regions	566.x
	Peritonitis and retroperitoneal infections	567.x
	Other disorders of peritoneum	568.x
	Other disorders of intestine	569.x
	Gastrointestinal hemorrhage	578.x
	Intestinal malabsorption (apart from pancreatic steatorrhea)	579.x
	Other congenital anomalies of upper alimentary tract	750.x
	Other congenital anomalies of digestive system (apart from pancreaticobiliary and liver)	751.x
	Diarrhea	787.81
	Digestive system complication	997.4, 997.49
Liver injury	Amebic liver abscess	6.3
	Viral hepatitis	70.x
	Mumps hepatitis	72.71
	Secondary syphilitic hepatitis	91.62
	Syphilis of liver	95.3
	Echinococcus granulosus infection of the liver	122, 122.5, 122.8
	Hepatitis due to toxoplasmosis	130.5
	Acute and subacute necrosis of liver	570
	Chronic liver disease and cirrhosis	571.x
	Liver abscess and sequelae of chronic liver disease	572.x
	Other disorders of liver	573.x
	Congenital cystic disease of liver	751.62
Musculoskeletal or soft tissue disorder	Salmonella arthritis	3.23
	Salmonella osteomyelitis	3.24
	Amebic skin ulceration	6.6
	Tuberculosis of bones and joints	15.x
	Tuberculosis of skin and subcutaneous tissues	17.0x
	Cutaneous anthrax	22
	Cutaneous diphtheria	32.85
	Erysipelas	35
	Cutaneous actinomycotic infections	39
	Gangrene	40, 785.4
	Tropical pyomyositis	40.81
	Arthritis due to rubella	
	Leishmaniasis	85.x
	Syphilis of bone, muscle, synovium, tendon, or bursa	95.5, 95.6, 95.7
	Gonococcal arthritis, synovitis, tenosynovitis, bursitis, spondylitis, or other gonococcal infection of joint	98.5, 98.51, 98.52, 98.53, 98.59
	Dermatophytosis	110.x, 111.x
	Lipoma of skin or subcutaneous tissue	214, 214.1, 214.9
	Other benign neoplasm of connective or soft tissue	215.x
	Varicose veins of lower extremities	454.x
	Inguinal hernia	550.x
	Other hernias and complications of hernias	551.x, 552.x, 553.x
	Psoas muscle abscess and other retroperitoneal abscesses and infections	567.31, 567.38, 567.39
	Carbuncle or furuncle	680.x
	Cellulitis or abscess of soft tissue or skeletal sites	681.x, 682.x,
	Pilonidal cyst with or without abscess	685.x
	Pyoderma and other infections of skin and soft tissue	686.x
	Chronic ulcers of skin	707.x
	Arthropathy associated with infections	711.x
	Crystal arthropathies	712.x
	Rheumatoid arthritis and other inflammatory polyarthropathies	714.x
	Osteoarthritis and allied disorders	715.x
	Allergic and climacteric arthritis	716.2x, 716.3x
	Transient arthropathy	716.4x
Other arthritis	716.5x, 716.6x	
Other arthropathy	716.8x, 716.9x	

	Other joint derangement (e.g., effusions, hemarthrosis, stiffness)	717.x, 718.x, 719.x
	Ankylosing spondylitis, other inflammatory spondylopathies, and spondylosis (aside from traumatic)	720.x, 721.x
	Intervertebral disc disorders, disorders of the cervical region, and unspecified disorders of the back	722.x, 723.x, 724.x
	Polymyalgia rheumatica	725
	Peripheral enthesopathies and allied syndromes	726.x
	Other disorders of synovium tendon and bursa	727.x
	Other disorders of musculoskeletal tissues	728.x, 729.x, 737.x, 738.x, 782.2, 782.3
	Osteomyelitis	730.x
	Osteopathies and osteochondropathies	731.x, 732.x, 733.x
	Limb deformities and dysfunction	734.x, 735.x, 736.x, V49.x
	Complications peculiar to orthopedic procedures	996.4x, 996.77, 996.78, 996.79 996.9x, 997.6x
	Wound issues related to procedures	998.32, 998.81, 998.83
COPD	Chronic bronchitis	490.x, 491.x
	Emphysema	492, 492.8
	Chronic airway obstruction	496
Other substance use condition	Drug-induced mental disorders	292, 292.11, 292.12, 292.2 292.21, 292.8x, 292.9
	Drug dependence (opioid use disorders, sedative use disorders, cannabis use disorders, amphetamine use disorders, cocaine, hallucinogen, and other substance use disorders)	304.x
	Nondependent abuse of drugs (examples as above)	305.x
	Poisoning by analgesics, psychotropics, stimulants	965, 965.01, 965.02, 965.09, 969.6, 970.81, 970.89, 989.89 989.9, E850.0, E850.1, E854.1
Cardiac dysrhythmia		426.x, 427.x, 785, 785.1
Kidney injury	Syphilis of kidney	95.4
	Acute and chronic glomerulonephritis	580.x, 582.x
	Nephrotic syndrome	581.x
	Other nephritis or nephropathy	583.x
	Acute kidney failure	584.5, 584.6, 584.7, 584.8, 584.9
	Chronic kidney disease	403, 403.01, 403.1, 403.11, 403.9, 403.91, 404, 404.02, 404.1, 404.9, 405.01, 405.11, 405.91, 585.x
	Disorders resulting from impaired renal function	588.x
	Infections of kidney	590.x
	Hydronephrosis	591
	Other disorders of kidney and ureter	593.1, 593.71, 593.72, 593.73, 593.81, 593.89, 593.9
	Congenital anomalies of urinary system	753.x
Dialysis	V45.1, V45.11, V45.12, V56.0, V56.1, V56.2, V56.31, V56.32, V56.8	
Diabetes mellitus		249.x, 250.x, 357.2, 362.01, 362.02, 362.03, 362.04, 362.05, 362.06, 362.07
Trauma	Traumatic spondylopathy	721.7
	Pain due to trauma	338.11, 339.2, 339.21
	Trauma to specific body parts, including burns	388.11, 716.1x, 721.7, 800.x – 854.x, 860.x – 887.x, 890.x – 897.x, 900.x – 904.x, 910.x – 959.x
	Complications of trauma	518.5, 525.11
	Trauma from accidents, collisions, fights, other mechanisms	E800.x – E807.x, E810.x – E829.x, E831.x, E833.x – E838.x, E840.x – E849.x, E870.x, E880.x – E888.x, E890.x – E900.x, E902.x – E904.x, E906.x – E909.x, E914.x – E925.x, E960.x, E961.x, E963.x, E965.x, E966.x, E968.x, E970.x, E973.x – E976.x, E983.x, E985.x – E988.x, E990.x – E996.x, E998.x
Seizure		345.x, 780.3, 780.31, 780.32, 780.33, 780.39
Pancreaticobiliary disease	Mumps pancreatitis	72.3
	Cholelithiasis	574.x

	Other disorders of gallbladder or biliary tract	575.x, 576.x, 997.41
	Disease of pancreas	577, 577.1, 577.2, 577.8, 577.9
	Pancreatic steatorrhea	579.4
	Congenital anomaly of gallbladder, biliary system, or pancreas	751.6, 751.61, 751.62, 751.69
	Biliary atresia, congenital	751.61
Pneumonia	Infectious pneumonia	3.22, 6.4, 10.x, 11.x, 21.2, 22.1, 31.x, 39.1, 52.1, 55.1, 73, 95.1, 114, 114.4, 114.5, 114.9, 115.05, 115.15, 115.95, 130.4, 480 – 480.3, 480.8, 480.9, 481 – 482.32, 482.39, 482.4 – 482.42, 482.49, 482.8 – 482.84, 482.89, 482.9, 483, 483.1, 483.8, 484.1, 484.3, 484.5, 484.6, 484.7, 484.8, 485, 486, 487, 488.01, 488.11, 488.81, 510, 513, 997.31, 997.32,
	Non-infectious pneumonia	495.x, 500, 502 – 506, 516.3, 516.32, 516.33, 516.35 – 516.37, 516.5, 516.8, 516.9, 517.1, 518.3, 714.81
Sepsis/Shock		3.1, 22.3, 38.x, 40.82, 458.2, 458.21, 458.29, 458.8, 458.9, 785.5, 785.51, 785.52, 785.59, 995.x, 998
Congestive heart failure		398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 428.x, 429.83,
Malignancy		140.x – 165.x, 170.x – 176.x, 179, 180.x – 209.x, 233.x, 234, 234.8, 234.9, 238.6
Cerebrovascular disease	Vascular dementias	290.4, 290.41, 290.42, 290.43
	Retinal vascular occlusion	363.3x
	Subarachnoid hemorrhage	430
	Intracerebral hemorrhage	431
	Occlusion or stenosis of precerebral and cerebral arteries	432.x, 433.x, 434.x
	Transient cerebral ischemia	435.x
	Other cerebrovascular disease	436, 437.x, 438.x,
Myocardial infarction		410.x, 412



Supplemental Figure 1. Patient sample

Legend: AWS = alcohol withdrawal syndrome

Supplemental Table 3. Medications for alcohol withdrawal syndrome (AWS) received by medical inpatients in the Veterans Health Administration during 2013

Medications	n = 6,938	
	no.	(%)
Short-acting Benzodiazepines		
Lorazepam	5518	(79.5)
Midazolam	323	(4.7)
Oxazepam	237	(3.4)
Temazepam	159	(2.3)
Alprazolam	77	(1.1)
Clorazepate	49	(0.7)
Long-acting Benzodiazepines		
Chlordiazepoxide	2490	(35.9)
Diazepam	1003	(14.5)
Clonazepam	140	(2.0)
Non-benzodiazepine AWS medications		
Gabapentin	1149	(16.6)
Clonidine	686	(9.9)
Propofol	207	(3.0)
Valproic acid/Divalproex/Valproate	206	(3.0)
Dexmedetomidine	169	(2.4)
Baclofen	127	(1.8)
Carbamazepine	100	(1.4)
Phenobarbital	44	(0.6)
Pregabalin	32	(0.5)
Oxcarbazepine	4	(0.1)
Ethanol	0	(0.0)
Ketamine	0	(0.0)
Antipsychotics ^a		
Haloperidol	759	(10.9)
Quetiapine	564	(8.1)
Risperidone	232	(3.3)
Olanzapine	167	(2.4)
Chlorpromazine	28	(0.4)

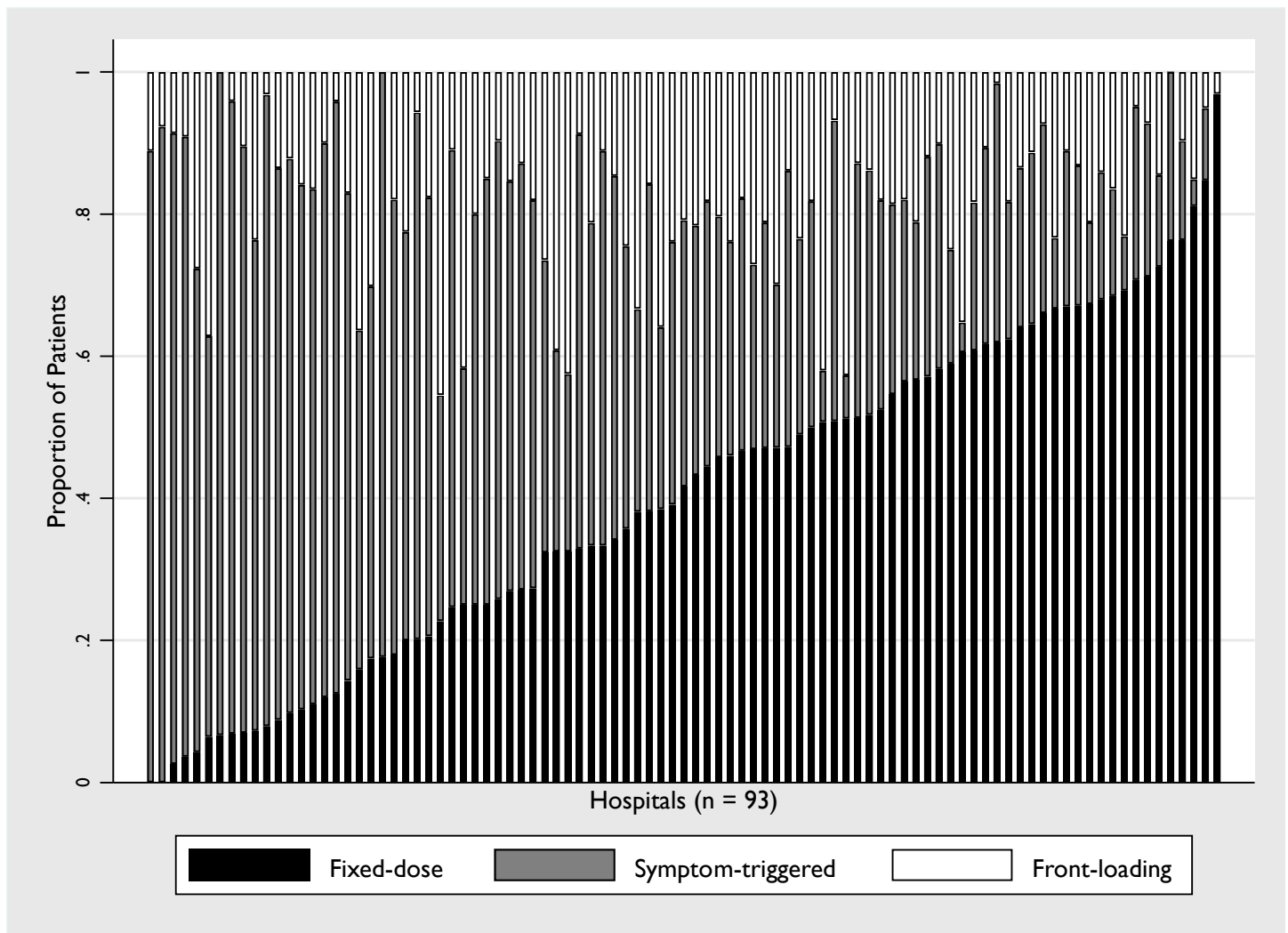
Legend: Treatments above are not mutually exclusive

^aCommon antipsychotic agents were included as possible adjuvant therapies, although antipsychotics are not considered primary treatment for AWS⁵⁰

Supplemental Table 4. Medications and benzodiazepine dosing strategies received by medical inpatients with alcohol withdrawal syndrome (AWS) in the Veterans Health Administration during 2013

	Fixed-dose		Symptom-triggered		Front-loading		p-value
	no.	(%)	no.	(%)	no.	(%)	
Received Short-acting Benzodiazepine	2,086	(73.7)	2,597	(89.3)	1,109	(92.4)	<0.001
Received Long-acting Benzodiazepine	1,654	(58.5)	1,140	(39.2)	688	(57.3)	<0.001
Received Non-Benzodiazepine AWS Medication	789	(27.9)	1,018	(35.0)	423	(35.3)	<0.001
Received Antipsychotic Medication	518	(18.3)	662	(22.8)	331	(27.6)	<0.001

Legend: chi-squared tests were used to assess differences across groups



Supplemental Figure 2. Proportion of medical inpatients receiving each benzodiazepine dosing strategy by hospital in the Veterans Health Administration during 2013

Supplemental Table 5. Adjusted associations between patient characteristics, hospital prescribing pattern, and benzodiazepine dosing strategy for alcohol withdrawal syndrome (AWS) among medical inpatients in the Veterans Health Administration during 2013, with hospital site as a random effect

	Fixed-dose Therapy				Symptom-triggered Therapy				Front-loading Therapy			
	OR	(95% CI)	Pred %	(95% CI)	OR	(95% CI)	Pred %	(95% CI)	OR	(95% CI)	Pred %	(95% CI)
<40 yo	ref.		36.5	(31.5-41.5)	ref.		44.4	(39.6-49.2)	ref.		17.5	(13.8-21.1)
40-49 yo	1.0	(0.8-1.4)	37.3	(33.2-41.3)	0.9	(0.7-1.2)	42.3	(38.6-46.0)	1.1	(0.8- 1.5)	19.0	(16.3-21.6)
50-59 yo	1.2	(0.9-1.5)	39.0	(35.6-42.4)	0.8	(0.6-1.0)	40.5	(37.6-43.4)	1.1	(0.9- 1.5)	19.2	(17.4-21.0)
60-69 yo	1.3	(1.0-1.6)	40.5	(37.1-44.0)	0.9	(0.7-1.2)	42.8	(39.8-45.7)	0.9	(0.6- 1.2)	15.5	(13.9-17.1)
70+ yo	1.7**	(1.2-2.4)	46.2	(41.0-51.4)	0.9	(0.6-1.2)	41.9	(37.2-46.7)	0.6**	(0.4- 0.8)	10.9	(8.0-13.7)
Male	1.1	(0.8-1.5)	39.7	(36.5-42.8)	0.9	(0.6-1.2)	41.8	(39.2-44.4)	1.1	(0.7- 1.6)	17.1	(15.9-18.3)
White	ref.		38.6	(35.4-41.8)	ref.		42.6	(39.9-45.3)	ref.		17.4	(16.1-18.8)
Black	1.4**	(1.2-1.6)	44.6	(40.6-48.7)	0.8*	(0.7-1.0)	39.2	(35.6-42.7)	0.8*	(0.7- 1.0)	15.1	(12.9-17.2)
Hispanic/Latinx	0.7	(0.5-1.0)	33.3	(27.4-39.1)	1.1	(0.8-1.5)	45.0	(39.0-51.0)	1.2	(0.9- 1.6)	19.5	(15.1-24.0)
Other Race	1.3	(0.9-1.8)	42.9	(35.8-50.0)	0.7*	(0.5-0.9)	35.2	(28.9-41.5)	1.1	(0.8- 1.7)	19.4	(13.9-24.9)
Unknown Race	1.1	(0.8-1.6)	41.0	(34.6-47.3)	1.0	(0.8-1.4)	43.3	(37.4-49.3)	0.8	(0.6- 1.2)	14.7	(10.4-19.0)
Single	0.9	(0.8-1.1)	39.4	(36.3-42.6)	1.1	(1.0-1.3)	42.3	(39.6-44.9)	0.9	(0.8- 1.1)	16.9	(15.7-18.2)
Homeless	1.1	(1.0-1.2)	40.7	(37.1-44.3)	1.0	(0.9-1.1)	41.5	(38.4-44.6)	0.9	(0.8- 1.1)	16.3	(14.5-18.1)
Prior year AUD	1.2*	(1.0-1.5)	40.1	(37.0-43.3)	1.0	(0.8-1.2)	41.8	(39.2-44.5)	0.8*	(0.6- 1.0)	16.7	(15.4-17.9)
Prior year AWS	0.9*	(0.8-1.0)	38.3	(35.0-41.6)	1.0	(0.9-1.1)	41.8	(39.0-44.6)	1.3**	(1.1- 1.5)	18.6	(17.0-20.2)
Mental health disorders	0.9	(0.8-1.0)	38.8	(35.5-42.1)	1.2*	(1.0-1.3)	43.2	(40.3-46.0)	1.0	(0.8- 1.1)	16.8	(15.3-18.3)
Nutrition, electrolyte, or acid-base DO	1.0	(0.9-1.2)	39.9	(36.5-43.2)	0.9	(0.8-1.1)	41.4	(38.5-44.2)	1.0	(0.9- 1.2)	17.4	(15.8-18.9)
GI tract DO	1.0	(0.9-1.2)	40.2	(36.7-43.7)	1.0	(0.9-1.1)	41.5	(38.6-44.5)	1.0	(0.9- 1.1)	16.9	(15.2-18.6)
Liver injury	1.0	(0.9-1.1)	39.8	(36.3-43.3)	1.0	(0.9-1.1)	41.6	(38.6-44.7)	1.0	(0.9- 1.2)	17.3	(15.6-19.1)
Musculoskeletal or soft tissue DO	1.0	(0.9-1.1)	39.3	(35.7-42.8)	1.1	(1.0-1.2)	43.1	(40.0-46.2)	0.9	(0.8- 1.0)	16.1	(14.3-17.9)
COPD	1.1	(1.0-1.3)	41.0	(37.2-44.7)	0.9	(0.8-1.1)	41.1	(37.8-44.4)	0.9	(0.8- 1.1)	16.1	(14.1-18.2)
Other substance use condition	0.9	(0.8-1.1)	38.7	(34.9-42.5)	1.1	(0.9-1.3)	43.4	(39.9-46.8)	1.0	(0.8- 1.1)	16.7	(14.5-18.9)
Cardiac dysrhythmia	0.9	(0.8-1.1)	38.6	(34.7-42.5)	1.0	(0.9-1.2)	42.1	(38.6-45.7)	1.1	(0.9- 1.3)	18.0	(15.6-20.4)
Kidney injury	0.8**	(0.6-0.9)	35.3	(31.3-39.3)	1.1	(0.9-1.3)	43.5	(39.7-47.4)	1.3**	(1.1- 1.6)	20.2	(17.4-23.0)
Diabetes mellitus	1.1	(0.9-1.3)	40.6	(36.5-44.8)	1.0	(0.8-1.2)	41.5	(37.7-45.2)	0.9	(0.8- 1.1)	16.3	(13.7-18.9)
Trauma	0.9	(0.7-1.1)	37.5	(33.3-41.8)	1.0	(0.9-1.2)	42.6	(38.6-46.6)	1.1	(0.9- 1.4)	18.5	(15.6-21.4)
Seizure	1.1	(0.9-1.4)	41.7	(37.2-46.1)	0.7**	(0.6-0.8)	35.9	(32.0-39.9)	1.3**	(1.1- 1.7)	20.8	(17.8-23.9)
Pancreaticobiliary disease	0.8*	(0.6-0.9)	35.6	(31.3-40.0)	1.2	(1.0-1.4)	44.8	(40.7-49.0)	1.1	(0.9- 1.4)	18.4	(15.4-21.3)
Pneumonia	0.8*	(0.6-1.0)	35.1	(30.3-39.8)	0.9	(0.8-1.2)	41.0	(36.3-45.6)	1.5**	(1.2- 2.0)	22.8	(18.9-26.7)
Sepsis/Shock	0.8	(0.6-1.0)	35.8	(30.8-40.9)	1.0	(0.8-1.3)	42.3	(37.4-47.2)	1.2	(0.9- 1.6)	19.5	(15.8-23.1)
Congestive heart failure	0.8	(0.6-1.1)	36.2	(30.8-41.6)	1.2	(0.9-1.6)	45.6	(40.1-51.0)	1.1	(0.8- 1.4)	17.8	(13.6-21.9)
Malignancy	1.3	(0.9-1.7)	43.8	(37.5-50.1)	1.0	(0.7-1.4)	41.9	(35.8-48.1)	0.6*	(0.4- 1.0)	11.9	(7.8-16.0)
Cerebrovascular disease	1.0	(0.7-1.4)	39.7	(33.0-46.3)	1.0	(0.7-1.4)	41.3	(34.7-47.9)	1.0	(0.7- 1.6)	17.7	(12.4-23.0)
Myocardial infarction	0.7	(0.5-1.1)	34.3	(26.8-41.7)	0.8	(0.5-1.2)	38.4	(30.9-46.0)	1.7*	(1.1- 2.5)	24.6	(17.8-31.4)
Not top-tercile hospital for prescribing dosing strategy of interest	ref.		26.7	(23.0-30.4)	ref.		27.1	(23.9-30.3)	ref.		12.3	(11.1-13.6)
Top-tercile hospital for prescribing dosing strategy of interest	6.5**	(4.5-9.3)	65.0	(59.2-70.9)	8.3**	(6.1-11.3)	72.0	(67.4-76.7)	3.0**	(2.5- 3.6)	28.8	(25.9-31.6)

Legend: OR = Odds Ratio, CI = Confidence Interval, DO = Disorder, GI = Gastrointestinal, COPD = Chronic obstructive pulmonary disease, ** = p<0.01, * = p<0.05

Hospital intraclass correlation coefficient for fixed-dose therapy = 0.16 (95% CI 0.11-0.21), symptom-triggered therapy = 0.11 (95% CI 0.07-0.15), front-loading therapy = 0.02 (95% CI 0.01-0.05)

Supplemental Table 6. Associations between benzodiazepine dosing strategy for alcohol withdrawal syndrome (AWS) and cumulative benzodiazepine exposure, intensive care, and intubation, unadjusted and adjusted for patient characteristics in the Veterans Health Administration in 2013

	Cumulative Benzodiazepine ^a (mixed-effects linear regression)				ICU Care (mixed-effects logistic regression)				Intubation (mixed-effects logistic regression)			
	Unadj. coef.	(95% CI)	Adj. coef.	(95% CI)	Unadj. OR	(95% CI)	Adj. OR	(95% CI)	Unadj. OR	(95% CI)	Adj. OR	(95% CI)
Fixed-dose	ref.		ref.		ref.		ref.		ref.		ref.	
Symptom-triggered	30.5**	(13.5-47.5)	26.4**	(9.4-43.4)	1.7**	(1.5-2.0)	1.7**	(1.4-2.0)	1.6**	(1.2-2.2)	1.5*	(1.1-2.1)
Front-loading	175.9**	(155.3-196.4)	168.8**	(148.2-189.4)	3.0**	(2.6-3.6)	2.2**	(1.8-2.6)	5.6**	(4.2-7.4)	4.9**	(3.5-6.9)
Age			-1.3**	(-2.1- -0.6)			1.0	(1.0-1.0)			1.0	(1.0-1.0)
Male			9.7	(-32.0-51.4)			0.9	(0.6-1.4)			1.4	(0.5-3.7)
White			ref.				ref.			ref.		
Black			-34.3**	(-54.6- -13.9)			1.1	(0.9-1.3)			0.7	(0.5-1.1)
Hispanic/Latinx			-10.6	(-48.5-27.2)			0.9	(0.6-1.3)			1.0	(0.6-1.9)
Other Race			-17.4	(-60.2-25.5)			1.0	(0.7-1.5)			0.7	(0.3-1.6)
Unknown Race			10.6	(-28.5-49.7)			1.2	(0.9-1.8)			1.4	(0.8-2.5)
Single			6.2	(-11.4-23.7)			1.0	(0.8-1.2)			0.9	(0.6-1.1)
Homeless			8.5	(-7.5-24.5)			0.7**	(0.6-0.9)			0.8	(0.6-1.1)
Mental health disorders			3.6	(-11.5-18.6)			0.6**	(0.6-0.8)			0.5**	(0.4-0.7)
Nutrition, electrolyte, or acid-base disorder			22.1**	(7.3-36.9)			1.4**	(1.2-1.6)			1.7**	(1.3-2.3)
GI tract disorder			5.9	(-9.0-20.9)			1.4**	(1.2-1.6)			1.4**	(1.1-1.8)
Liver injury			6.6	(-8.8-22.0)			1.0	(0.9-1.1)			1.2	(0.9-1.6)
Musculoskeletal or soft tissue disorder			6.6	(-9.1-22.2)			1.0	(0.9-1.2)			0.8	(0.6-1.1)
COPD			1.6	(-16.4-19.5)			1.1	(0.9-1.3)			1.1	(0.8-1.5)
Other substance use condition			20.2*	(1.5-38.8)			1.0	(0.9-1.2)			1.0	(0.6-1.4)
Cardiac dysrhythmia			39.7**	(19.9-59.5)			2.2**	(1.8-2.6)			2.0**	(1.5-2.6)
Kidney injury			27.4*	(5.2-49.6)			2.2**	(1.8-2.6)			2.6**	(2.0-3.4)
Diabetes mellitus			-9.2	(-30.6-12.1)			1.3**	(1.1-1.6)			0.9	(0.6-1.3)
Trauma			6.2	(-16.6-29.1)			1.6**	(1.3-1.9)			1.7**	(1.2-2.5)
Seizure			6.0	(-17.8-29.8)			1.9**	(1.6-2.4)			1.4	(0.9-2.1)
Pancreaticobiliary disease			19.1	(-5.3-43.5)			1.2	(1.0-1.5)			1.0	(0.7-1.5)
Pneumonia			32.1*	(3.1-61.1)			3.4**	(2.6-4.3)			6.7**	(5.0-9.0)
Sepsis/Shock			-19.8	(-50.1-10.5)			4.5**	(3.5-5.8)			4.7**	(3.5-6.4)
Congestive heart failure			-1.7	(-35.5-32.1)			1.4*	(1.1-1.9)			1.6*	(1.1-2.5)
Malignancy			-4.7	(-43.7-34.3)			1.3	(0.9-1.8)			1.3	(0.8-2.3)
Cerebrovascular disease			-8.4	(-51.1-34.3)			1.5*	(1.0-2.2)			1.6	(0.9-2.7)
Myocardial infarction			28.2	(-21.4-77.7)			3.4**	(2.2-5.3)			3.8**	(2.2-6.4)
Cumulative BZD ^a (for AWS Severity)			-	-			1.0**	(1.0-1.0)			1.0**	(1.0-1.0)

Legend: ICU = intensive care unit, GI = Gastrointestinal, COPD = Chronic obstructive pulmonary disease, ^amg-diazepam-equivalents, ** p<0.01, * p<0.05

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