Supplemental Online Content

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

eTable 1a. Elements of Preimplementation Non–Intensive Care Unit Order Set for Alcohol Withdrawal Syndrome

Pathway	Treatment	Dosing
Observation (Criteria: CIWA-Ar <8) Measure CIWA-Ar every 6 hours with no medication orders		
Withdrawal Prophylaxis (Criteria: CIWA-Ar <8) Measure CIWA-Ar every 6 hours with diazepam or lorazepam		
	Diazepam (mild risk)	Day 1: 10 mg by mouth every 8 hours Day 2: 10 mg by mouth every 12 hours Day 3: 10 mg by mouth every daily
	Lorazepam (mild risk)[a]	Day 1: 1 mg by mouth every 8 hours Day 2: 1 mg by mouth every 12 hours Day 3: 1 mg by mouth every daily
	Diazepam (moderate risk)	Day 1: 10 mg by mouth every 6 hours Day 2: 10 mg by mouth every 8 hours Day 3: 10 mg by mouth every 12 hours
	Lorazepam (moderate risk)[a]	Day 1: 1 mg by mouth every 6 hours Day 2: 1 mg by mouth every 8 hours Day 3: 1 mg by mouth every 12 hours
	Diazepam (severe risk)	Day 1 to 2: 10 mg by mouth every 6 hours Day 3: 10 mg by mouth every 8 hours Day 4: 10 mg by mouth every 12 hours
	Lorazepam (severe risk)[a]	Day 1: 2 mg by mouth every 6 hours Day 2: 2 mg by mouth every 8 hours Day 3: 2 mg by mouth every 12 hours
Active Withdrawal Treatment (Criteria: CIWA-Ar ≥8) Measure CIWA-Ar every 4 hours with diazepam or lorazepam		
	Diazepam	CIWA-Ar score 8-13: 10 mg by mouth every hour as needed CIWA-Ar score 14-20: 15 mg by mouth every hour as needed CIWA-Ar score ≥21: 20 mg by mouth every hour as needed
	Lorazepam[a]	CIWA-Ar score 8-13: 1 mg by mouth every hour as needed CIWA-Ar score 14-20: 2 mg by mouth every hour as needed CIWA-Ar score ≥21: 4 mg by mouth every hour as needed
IV Fluids and Other Medications Thiamine, folic acid, multivitamin, and maintenance fluid		
	Thiamine	Day 1 to 5: 100 mg by mouth 2 times daily
	Folic Acid	Day 1+: 1 mg by mouth daily
	Multivitamin	Day 1+: 1 tablet by mouth daily
	Maintenance fluid	Day 1+: 20 mEq/L potassium chloride in 5% dextrose and 0.45% sodium chloride at 100 mL/hr by IV route continuously

[a]May be administered by IV route if patient is unable to tolerate oral dosing.

Abbreviations: CIWA-Ar, Clinical Institute Withdrawal Assessment for Alcohol, revised.[8]

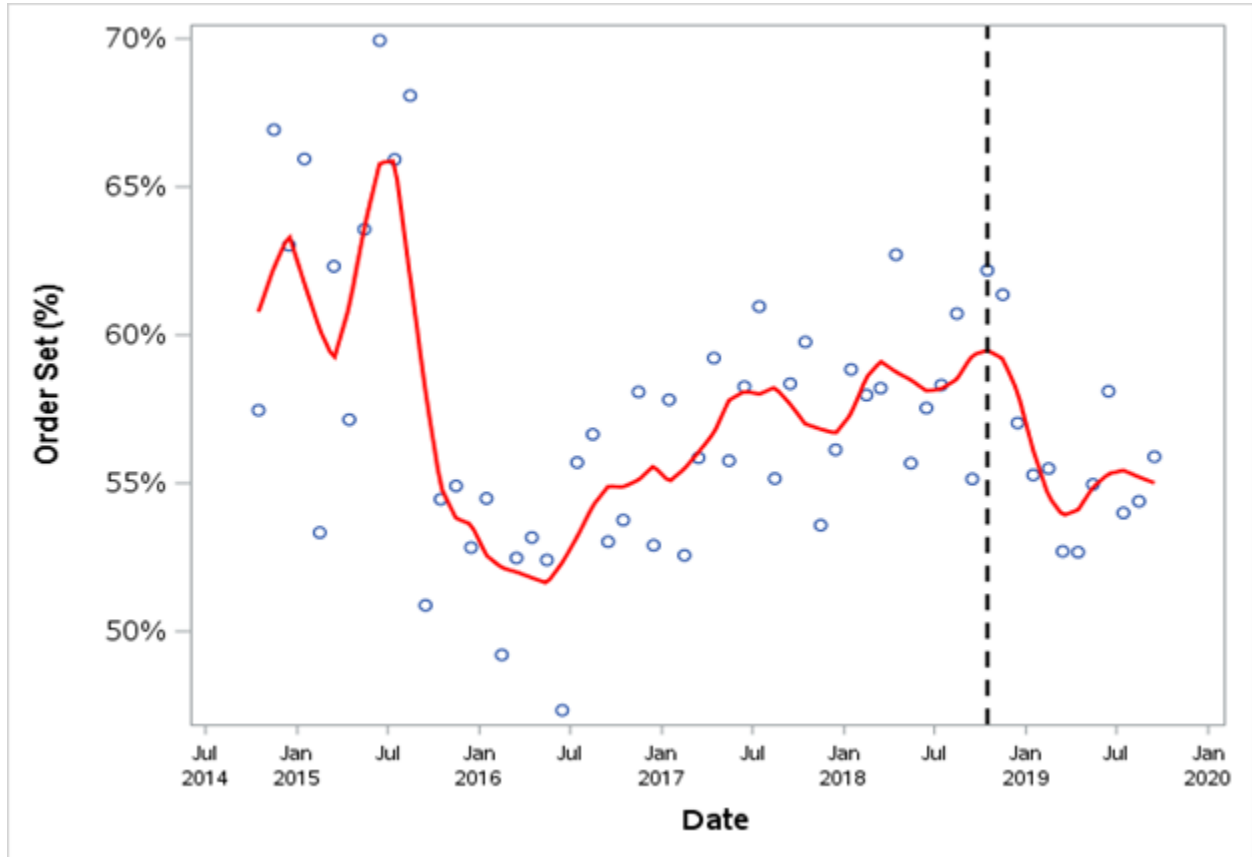**eTable 1b.** Elements of Preimplementation Non–Intensive Care Unit Order Set for Alcohol Withdrawal Syndrome

ICU Acute Alcohol Withdrawal
Discontinue any other sedatives, hypnotics, central nervous system depressants, or tranquilizers
Measure CIWA-Ar every 15 minutes after every lorazepam dose, every 2 hours while awake, and 4 hours while asleep

Loading
1. Start lorazepam using *Dose Scale A* based on CIWA-Ar
2. Reassess CIWA-Ar score 15 minutes after administering the 1st dose and if needed give 2nd dose per *Dose Scale A*
3. Reassess CIWA-Ar score 30 minutes after administering the 1st dose
4. If CIWA-Ar score is ≤15, continue to use *Dose Scale A*
5. If CIWA-Ar score if >15, move to *Dose Scale B* and administer lorazepam dose per protocol

Monitoring
Measure CIWA-Ar every 15 minutes after every lorazepam dose, every 2 hours while awake, and 4 hours while asleep

Escalation
1. If using *Dose Scale A* and 2 doses of lorazepam within 30 minutes fail to improve a CIWA-AR score of greater than 15, move to *Dose Scale B* and give Lorazepam dose per protocol
2. If using *Dose Scale B* and 2 doses of lorazepam within 30 minutes fail to improve a CIWA-Ar score of greater than 20, notify physician

CIWA-Ar Score	Dose Scale A	Dose Scale B
>20	4 mg IV	6 mg IV
16-20	3 mg IV	5 mg IV
11-15	2 mg IV	4 mg IV
6-10	1 mg IV	3 mg IV
0-5	0 mg IV	0 mg IV

[a]May be administered by IV route if patient is unable to tolerate oral dosing.
Abbreviations: CIWA-Ar, Clinical Institute Withdrawal Assessment for Alcohol, revised;[8] ICU, intensive care unit.

eFigure 1. Proportion of Potential Patients With Alcohol Withdrawal and Alcohol Withdrawal Order Set Use

The blue circles represent quarterly proportions while the red line displays a smooth fitted line. The dotted black line represents the implementation of the novel benzodiazepine-sparing orderset.

eTable 2. Outcomes by First Clinical Institute Withdrawal Assessment for Alcohol, Revised Score Value Category

	First CIWA-Ar value			
	Low (<8)	**Medium (8-14)**	**High (≥15)**	***P* value**
Inpatient mortality	145 (1.7)	24 (0.9)	16 (0.8)	.001
Length of stay, days	4.7 ± 7.6	4.5 ± 6.1	4.6 ± 6.7	.32
ICU admission	2,213 (25.3)	692 (26.9)	711 (34.0)	<.001
Readmission	1,463 (17.0)	432 (16.9)	354 (17.1)	.99

Abbreviations: CIWA-Ar, Clinical Institute Withdrawal Assessment for Alcohol, revised;[8] ICU, intensive care unit.

eTable 3. Difference-in-Differences Adjusted Outcomes in Sensitivity Analyses[a]

Including hospitalizations: (1) with at least on alcohol withdrawal-relevant medication administration[b]; (2) with at least one benzodiazepine administered[c]; and (2) within the 12-month periods before and after implementation.

Outcome	Difference-in-differences change		
	At least one AWS-relevant medication given	At least one benzodiazepine given	12 month pre- and post- periods
Inpatient mortality	0.70 (0.28-1.75); *P*=.45	0.70 (0.26-1.88); *P*=.48	0.68 (0.52-0.89); *P*=.005
Length of stay, days[d]	0.65 (0.50-0.85); *P*=.001	0.56 (0.41-0.76); *P*<.001	0.96 (0.93-0.99); *P*=.02
ICU admission	0.65 (0.50 – 0.84); *P*=.001	0.56 (0.42-0.75); *P*<.001	1.00 (0.91 – 1.10); *P*=.97
Readmission	0.70 (0.48-1.04); *P*=.07	0.61 (0.38-0.98); *P*=.04	0.88 (0.79-0.98); *P*=.02[e]

[a]*Adjusted models include age, gender, COPS2, LAPS2, prior alcohol withdrawal hospitalization, maximum CIWA-Ar value, CIWA-Ar value recordings, observation status, month of year, weekend admission, urine toxicology assessed, and facility.*
[b]*Includes any benzodiazepine, clonidine, dexmedetomidine, gabapentin, phenobarbital, and/or valproic acid.*
[c]*Includes alprazolam, chlordiazepoxide, diazepam, lorazepam, midazolam, oxazepam, and/or temazepam.*
[d]*Assumed a gamma distribution and log-link in the GEE model.*
[e]*Parallel slopes in pre-period assumption not met.*
Abbreviations: AWS, alcohol withdrawal; CIWA-Ar, Clinical Institute Withdrawal Assessment for Alcohol, revised;[8] CI, confidence interval; COPS2, Comorbidity Point Score, version 2;[29] ICU, intensive care unit; LAPS2, Laboratory Acute Physiology Score, version 2;[29]."

eTable 4. Baseline Characteristics of Hospitalizations for Alcohol Withdrawal Syndrome With Use of Alcohol Withdrawal-Relevant Medication[a]

Characteristic	With use of an orderset		Without use of an orderset	
	Pre-implementation (n = 6,835)	Post-implementation (n = 3,696)	Pre-implementation (n = 2,987)	Post-implementation (n = 1,680)
Age, mean (SD), years	53.1 (13.5)	53.6 (14.2)	58.8 (13.9)	60.0 (14.6)
Male, (%)	4,753 (69.5)	2,556 (69.2)	1,942 (65.0)	1,075 (64.0)
Observation admission, (%)	714 (10.4)	298 (8.1)	186 (6.2)	41 (2.4)
Weekend admission, (%)	1,791 (26.2)	970 (26.2)	497 (16.6)	320 (19.0)
LAPS2, mean (SD)	68.2 (37.5)	74.6 (39.7)	50.6 (43.7)	70.2 (48.2)
COPS2, mean (SD)	40.2 (43.3)	41.4 (47.5)	58.7 (55.4)	65.9 (64.6)
Urine toxicology checked (%)	2,934 (42.9)	1,802 (48.8)	496 (16.6)	409 (24.3)
Had ≥1 prior hospitalization for AWS within prior 6 months, (%)	2,345 (34.3)	1,333 (36.1)	632 (21.2)	377 (22.4)
Had ≥1 CIWA-Ar value recorded, (%)	6,798 (99.5)	3,610 (97.7)	439 (14.7)	100 (6.0)
Elixhauser comorbidities[b]				
Alcohol abuse, (%)	5,495 (80.4)	3,204 (86.7)	2,864 (95.9)	1,655 (98.5)
Hypertension[c], (%)	3,984 (58.3)	2,212 (59.8)	1,945 (65.1)	1,157 (68.9)
Fluid and electrolyte disorders, (%)	4,212 (61.6)	2,406 (65.1)	1,355 (45.4)	1,001 (59.6)
Peripheral vascular disease, (%)	2,347 (34.3)	1,526 (41.3)	1,560 (52.2)	1,070 (63.7)
Liver disease, (%)	3,050 (44.6)	1,855 (50.2)	1,074 (36.0)	690 (41.1)
Hospital outcomes				
Inpatient mortality, (%)	96 (1.4)	82 (2.2)	94 (3.1)	124 (7.4)
Length of stay, mean (SD), d	5.0 (8.6)	4.7 (5.6)	6.1 (10.9)	6.8 (9.3)
ICU admission, (%)	2,042 (29.9)	1,057 (28.6)	765 (25.6)	523 (31.1)
Readmission within 30 days, (%)	1,211 (18.0)	580 (16.0)	577 (19.9)	345 (22.2)

[a]Includes any benzodiazepine, clonidine, dexmedetomidine, gabapentin, phenobarbital, and/or valproic acid.
[b]Includes only the 5 most common comorbidities.
[c]Includes complicated and uncomplicated hypertension.
Abbreviations: AWS, alcohol withdrawal; CIWA-Ar, Clinical Institute Withdrawal Assessment for Alcohol, revised;[8] COPS2, Comorbidity Point Score, version 2;[29] ICU, intensive care unit; IQR, interquartile range; LAPS2, Laboratory Acute Physiology Score, version 2;[29] SD, standard deviation.

eTable 5. Baseline Characteristics of Hospitalizations for Alcohol Withdrawal Syndrome With Use ≥1 Benzodiazepine[a]

Characteristic	With use of an orderset		Without use of an orderset	
	Pre-implementation (n = 6,431)	Post-implementation (n = 2,823)	Pre-implementation (n = 2,114)	Post-implementation (n = 920)
Age, mean (SD), years	52.6 (13.3)	52.7 (13.8)	57.9 (14.0)	58.8 (14.8)
Male, (%)	4,488 (69.8)	1,943 (68.8)	1,372 (64.9)	575 (62.5)
Observation admission, (%)	668 (10.4)	231 (8.2)	144 (6.8)	25 (2.7)
Weekend admission, (%)	1,686 (26.2)	750 (26.6)	354 (16.7)	192 (20.9)
LAPS2, mean (SD)	68.8 (37.2)	76.3 (39.9)	51.4 (44.5)	76.9 (49.1)
COPS2, mean (SD)	39.7 (43.1)	40.3 (46.3)	53.1 (51.9)	59.7 (60.5)
Urine toxicology checked (%)	2,842 (44.2)	1,443 (51.1)	393 (18.6)	260 (28.3)
Had ≥1 prior hospitalization for AWS within prior 6 months, (%)	2,238 (34.8)	1,058 (37.5)	437 (20.7)	185 (20.1)
Had ≥1 CIWA-Ar value recorded, (%)	6,401 (99.5)	2,776 (98.3)	396 (18.7)	66 (7.2)
Elixhauser comorbidities[b]				
Alcohol abuse, (%)	5,111 (79.5)	2,393 (84.8)	2,016 (95.4)	905 (98.4)
Hypertension[c], (%)	3,684 (57.3)	1,656 (58.7)	1,323 (62.6)	607 (66.0)
Fluid and electrolyte disorders, (%)	3,979 (61.9)	1,862 (66.0)	956 (45.2)	561 (61.0)
Peripheral vascular disease, (%)	2,126 (33.1)	1,096 (38.8)	1,046 (49.5)	571 (62.1)
Liver disease, (%)	2,883 (44.8)	1,452 (51.4)	767 (36.3)	373 (40.5)
Hospital outcomes				
Inpatient mortality, (%)	92 (1.4)	74 (2.6)	77 (3.6)	97 (10.5)
Length of stay, mean (SD), d	5.1 (8.7)	4.9 (5.9)	6.4 (11.8)	8.1 (11.1)
ICU admission, (%)	1,939 (30.2)	872 (30.9)	572 (27.1)	338 (36.7)
Readmission within 30 days, (%)	1,134 (17.9)	445 (16.2)	383 (18.8)	178 (21.6)

[a]Includes alprazolam, chlordiazepoxide, diazepam, lorazepam, midazolam, oxazepam, and/or temazepam.
[b]Includes only the 5 most common comorbidities.
[c]Includes complicated and uncomplicated hypertension.
Abbreviations: AWS, alcohol withdrawal; CIWA-Ar, Clinical Institute Withdrawal Assessment for Alcohol, revised;[8] COPS2, Comorbidity Point Score, version 2;[29] ICU, intensive care unit; IQR, interquartile range; LAPS2, Laboratory Acute Physiology Score, version 2;[29] SD, standard deviation.

eTable 6. Baseline Characteristics of Hospitalizations for Alcohol Withdrawal Syndrome 12 mo Before and After Implementation

Characteristic	With use of an orderset		Without use of an orderset	
	Pre-implementation (n = 2,568)	Post-implementation (n = 4,652)	Pre-implementation (n = 1,881)	Post-implementation (n = 3,709)
Age, mean (SD), years	53.6 (14.2)	54.7 (14.7)	59.4 (15.0)	61.7 (15.3)
Male, (%)	1,775 (69.1)	3,244 (69.7)	1,309 (69.6)	2,475 (66.7)
Observation admission, (%)	246 (9.6)	327 (7.0)	114 (6.1)	94 (2.5)
Weekend admission, (%)	699 (27.2)	1,239 (26.6)	359 (19.1)	795 (21.4)
LAPS2, mean (SD)	67.8 (37.7)	73.8 (39.7)	54.5 (43.6)	69.4 (45.8)
COPS2, mean (SD)	39.8 (43.6)	40.4 (46.9)	60.3 (58.0)	63.1 (62.0)
Urine toxicology checked (%)	1,130 (44.0)	2,129 (45.8)	325 (17.3)	777 (20.9)
Had ≥1 prior hospitalization for AWS within prior 6 months, (%)	822 (32.0)	1,545 (33.2)	364 (19.4)	719 (19.4)
Had ≥1 CIWA-Ar value recorded, (%)	2,543 (99.0)	4,525 (97.3)	210 (11.2)	159 (4.3)
Elixhauser comorbidities[a]				
Alcohol abuse, (%)	2,164 (84.3)	4,145 (89.1)	1,816 (96.5)	3,654 (98.5)
Hypertension[b], (%)	1,501 (58.5)	2,814 (60.5)	1,232 (65.5)	2,555 (68.9)
Fluid and electrolyte disorders, (%)	1,548 (60.3)	2,942 (63.2)	844 (44.9)	2,086 (56.2)
Peripheral vascular disease, (%)	935 (36.4)	2,006 (43.1)	990 (52.6)	2,335 (63.0)
Liver disease, (%)	1,110 (43.2)	2,229 (47.9)	669 (35.5)	1,515 (40.8)
Hospital outcomes				
Inpatient mortality, (%)	41 (1.6)	93 (2.0)	32 (1.7)	166 (4.5)
Length of stay, mean (SD), d	4.4 (6.8)	4.4 (5.4)	4.6 (6.6)	5.2 (7.0)
ICU admission, (%)	641 (25.0)	1,229 (26.4)	397 (21.1)	841 (22.7)
Readmission within 30 days, (%)	451 (17.8)	718 (15.7)	392 (21.2)	766 (21.6)

[a]Includes only the 5 most common comorbidities.
[b]Includes complicated and uncomplicated hypertension.
Abbreviations: AWS, alcohol withdrawal; CIWA-Ar, Clinical Institute Withdrawal Assessment for Alcohol, revised;[8] COPS2, Comorbidity Point Score, version 2;[29] ICU, intensive care unit; IQR, interquartile range; LAPS2, Laboratory Acute Physiology Score, version 2;[29] SD, standard deviation.

eMethods. SAS Code for Difference-in-Differences Analysis

```
%macro did(outcome,dist,link,where);
PROC GEE DATA = etohrx;
&where.;
class post mrn orig_fac_id os mon;
model &outcome.(event='1')=age_at_admit male cops2 laps2 prior_hosp obs_only admit_weekend mon
urinetox post os os*post time0 time1 os*time0 os*time1 orig_fac_id/dist=&dist. link=&link.;
REPEATED subject = MRN/ type=exch covb corrw;
lsmeans os*post/cl ilink;
estimate os*post 1 -1 -1 1/cl ilink;
output out=adj pred=p0;
ods output GEEEmpPEst=geeest lsmeans=lsm estimates=diff parameterestimates=beta;
run;

data beta;
set beta;
outcome="&outcome.";
if parameter eq 'time0*os' and level1 eq 'No';
if "&link." eq "identity" and outcome eq 'los_day' then outcome='los_linear';
if "&link." eq "identity" and outcome eq 'lorazepam_tot' then outcome='lor_linear';
run;

data betas;
        set betas beta;
        run;

        data diff;
        set diff;
        outcome="&outcome.";
        if "&link." eq "identity" and outcome eq 'los_day' then outcome='los_linear';
        if "&link." eq "identity" and outcome eq 'lorazepam_tot0' then outcome='lor_linear';
        run;

        data lsme;
        set lsm;
        outcome="&outcome.";
        if "&link." eq "identity" and outcome eq 'los_day' then outcome='los_linear';
        if "&link." eq "identity" and outcome eq 'lorazepam_tot0' then outcome='lor_linear';
        run;

        data lsmes;
        set lsmes lsme;
        run;

        data diffs;
        set diffs diff;
        run;
        %mend;
```

Legend: &where, used to remove deaths for the readmission outcome; &link, LOG link for POISSON and GAMMA distributions and IDENTITY for normal; &dist, GAMMA and NORMAL for length of stay and POISSON for the binary outcomes; Time0, denotes the month number starting with month=1 until the end of the study; Time1, set to 0 for months in the pre-period and has values 1 to number of months in the post period.