1) What is the accuracy of a tool and/or clinical judgement for the a) assessment b) monitoring of patients at risk of acute alcohol withdrawal? 2) Does the assessment and monitoring of patients with acute alcohol withdrawal improve patient outcomes?								
Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow-up	Outcome measures	Source of funding
DeCarolis DD, Rice KL, Ho L et al. Symptom-driven lorazepam protocol for treatment of severe alcohol withdrawal delirium in the intensive care unit. *Pharmacotherapy.* 2007; 27(4):510-518. Ref ID: 16	Retrospective case series 3	N=40 (36 patients)	Patients admitted to a medical ICO with a primary diagnosis of severe alcohol withdrawal Exclusion criteria: patients who were admitted to ICU for other conditions and who developed alcohol withdrawal syndrome coincidentally Patient population: symptom-triggered (24 episodes) Mean age 51 yrs, m:f 23:1, baseline MINDS 25 Preprotocol group (16 episodes) Mean age 48 yrs, m:f 16:0, baseline MINDS 27	Protocol-treated patients N=24 (21 patients) Minnesota Detoxification Scale (MINDS) to monitor symptoms. Treatment: Lorazepam administered as intermittent intravenous doses, progressing to a continuous intravenous infusion according to the MINDS score Assessments performed every 15 mins to 2 hrs depending on MINDS score	Non-protocol patients N=16 (15 patients) Patients treated according to physician preference; the standard local practice was administration of a continuous infusion of midazolam without a protocol	Length of hospital stay	Time to reach a MINDS score of less than 20 (control of severe symptoms)re Total dose of benzodiazepine in lorazepam-equivalent milligrams Amount of time receiving continuous benzodiazepine infusion Length of ITU say Length of hospital stay Complications of treatment Polypharmacy (use of multiple benzodiazepine products)	None reported
Effect Symptom-triggered vs pre-protocol The symptom-triggered protocol compared to the pre-protocol was associated with significantly: Less time to reach a MINDS score of less than 20 (symptom control) (19 vs 8; p=0.002) Lower cumulative benzodiazepine dose (1044 vs 1677 lorazepam equivalent; p<0.05). Less time receiving continuous-infusion benzodiazepine (52 vs 122 hrs; p=0.001)								

There was no significant difference between the symptom-triggered and pre-protocol groups on: Mean length of ITU stay (ns) Mean length of hospital stay (ns) Complications Pre-protocol group: There were 7 treatment-related complications (44%). Symptom-triggered group: There were 6 treatment-related complications (25%)								
Foy A, Kay J, Taylor A. The course of alcohol withdrawal in a general hospital. *QJM - Monthly Journal of the Association of Physicians.* 1997; 90(4):253-261. Ref ID: 492	Prospective case series 3	N=539	Patients with alcohol withdrawal Inclusion criteria (one or more of the following): 100 g alcohol daily or more; admission with an alcohol-related diagnosis; previous documented alcohol withdrawal and still drinking; a blood alcohol level of 0.2% without impairment of consciousness, and who had an Alcohol Withdrawal Scale (AWS) ≥ 10 Patient population: Male:female 437:102, mean age 52 yrs, mean alcohol consumption 150 g/daily, primary diagnosis (N): alcohol withdrawal/intoxication 90, musco-skeletal disease 85, neurological disease 62, GI/liver/pancreatic disease 115, carcinoma/infection/other 66	Alcohol Withdrawal Scale (AWS) – modification of the CIWA-A Loading dose diazepam 20 mg if: Two scores of 15 or more or one of 20 then consider treatment but the decision to treat, dose and technique was at the discretion of the treating team Timing of assessment If AWS ≥ 10 assess every two hourse, if ≥ 15 then hourly	NA	Length of treatment	Withdrawal onset defined as when CIWA-A first reached or exceeded 10 Resolution time defined as when the score returned to 10 or less and remained < 10. Reaction defined as seizures, hallucinations or delirium at any time within 10 days of admission	None reported
Effect Incidence on admission: 68/539 (30 were not related alcohol/unclear aetiology) patients were admitted with seizures 19/539 patients with hallucinations								

31/539 patients with delirium 9/539 patients had both delirium and seizures 79/539 patients had a definite complication of alcohol withdrawal on admission After admission: 113/539 patients had complication of alcohol withdrawal Early identification and monitoring Patients whose monitoring was delayed were three times more likely to have complications compared with those who were identified in the first 24 hrs (25/52 vs 71/408; p<0.001) Factors associated with any complication Delaying sedation (13/50, OR 1.5 (95%CI 0.7 to 3.1) Delay > 24 hrs first assessment (25/52, OR 4.0; 95%CI 2.7 to 7.6) Age > 70 yrs (18/55, OR 1.8 (95%CI 1.0 to 3.7) Seizure on admission (27/68, OR 4.1; 95%CI 1.7 to 10.0) Factors associated with delirium Age > 70 yrs (10/55, OR 2.0 (95%CI 0.74 to 5.2) Delay > 24 hrs first assessment (20/52, OR 8.1; 95%CI 3.7 to 17.7) The following were not significant associated with delirium Seizure on admission (ns) Delaying sedation (ns) Factors associated with hallucinations: Seizure on admission (16/68, OR 2.1; 1.1 to 4.0) Delay > 24 hrs first assessment (18/52, OR 3.2; 95%CI 1.6 to 6.0) Factors not associated with hallucinations Age > 70 yrs (ns) Delaying sedation (ns)								
Foy A, March S, Drinkwater V. Use of an objective clinical scale in the assessment and management of alcohol withdrawal in a	Prospective case series 3	N=203	Patients aged 20 to 75 yrs admitted under the care of physicians in all specialities, general and orthopaedic surgeons who were identified at risk of alcohol withdrawal within the first 24 hrs. Inclusion criteria included: intake of 100 g of	Withdrawal scale derived from the CIWA-Ar (simplified for use in a general hospital). Assessments every 4 hrs by an alcohol unit	NA	Length of admission	Severity of alcohol withdrawal (confusion, hallucinations, seizures), highest score prior to	None reported

large general hospital. *Alcoholism: Clinical & Experimental Research.* 1988; 12(3):360-364. Ref ID: 70			alcohol daily for 10 yrs or more; previous documented treatment for alcohol withdrawal; document current alcohol related problems in health, social life, employment Exclusion criteria: patients who had suffered a fit within the first 24 hrs preceding the admission (they may have already developed alcohol withdrawa) Patient population: Male: female 161:42, top 6 admission diagnosis were cirrhosis, fractured femur, alcohol dependence for detoxification, Gastrointestinal haemorrhage, pancreatitis, chronic obstructive airways disease	nurse for the first 24 to 48 hrs. If score > 10 then assessments every 2 hrs If score > 15 then assessments every hour Treatment: If score > 15 on 2 consecutive occasions or above 20 once then: Loading dose technique of 20 mg diazepam at 2 hr intervals until score fallen to less than 10			development of complications or prior to discharge, use of benzodiazepines	

Effect
110/204 patients had a score of greater than 15 and received at least one dose of diazepam 20 mg.
15/93 of those patients who score less than 15 received prophylactic treatment with at least diazepam 20 mg
The mean dose of diazepam was 50 mg

Complications
37/204 patients suffered complicated alcohol withdrawal reactions (N=4 seizures, N=33 confusion with or without hallucinations, N=0 hallucinations alone)
The score was significantly higher in patients who developed complication (confusion, hallucinations or seizures) compared to those patients who did not developed complications:
(mean highest score 21.8 vs 15.6, $p<0.001$)

Prophylactic effect of treatment on different scores
Of the 110/204 patients who had scores greater than 15, 75 were treated of whom 11 developed severe withdrawal. In the 35 who were not treated, 21 developed severe withdrawal. The relative risk of severe withdrawal in those remaining untreated was 3.72 (95% 2.85 to 4.85).

Of the 93 patients who had scores less than 15, 15 were treated and none had severe withdrawal. 5/78 who were untreated developed severe withdrawal. The relative risk of remaining untreated was 1.92 (95%CI 0.27 to 13.6).

Severe withdrawal in patients with low scores or with apparent adequate treatment 11/75 patients who received apparently adequate treatment still went on to develop signs of severe withdrawal. 5/78 patients with scores less than 15 went on to develop severe withdrawal A multivariate analysis reported that liver disease (OR 0.25; 95%CI 0.20 to 0.80; p=0.02) and postoperative status (OR 3.10; 95%CI 1.35 to 7.09; p=0.008) were associated with inappropriate placement on the CIWA-Ar protocol, with the former less likely and the latter more likely to experience inappropriate placement.								
Hecksel KA, Bostwick JM, Jaeger TM et al. Inappropriate use of symptom-triggered therapy for alcohol withdrawal in the general hospital. *Mayo Clinic Proceedings.* 2008; 83(3):274-279. Ref ID: 965	Retrospective case series 3	N=124 episodes (N=121 patients) (random selection from 495)	Patients who received symptom-triggered therapy according to the CIWA-Ar protocol Setting: Medical and surgical patients admitted to a general hospital Patient population: 73% male, 88% white, mean age 56 yrs	Appropriate symptom-triggered therapy N=60	Inappropriate symptom-triggered therapy N=64	NA	Appropriateness of symptom-triggered therapy Adverse events	None reported
Effect Symptom-triggered therapy was deemed appropriate if a medical record document heavy alcohol consumption (defined as > 2 drinks per day in women and > 4 drinks per day in men and in the week before hospital admission) and a history of alcohol abuse or dependence. The CIWA-Ar depends on the ability to communicate and is therefore inappropriate in people who cannot communicate. They also therefore could not be intubated or delirious. 60/124 (48%) patients met both inclusion criteria (drinking history and communication) for symptom-triggered therapy. 9/64 (14%) did not meet the criteria had been drinking heavily just before surgery but had been unable to communicate 35/64 (55%) did not have a recent history of heavy drinking but were able to communicate 20/64 (31%) had been neither drinking heavily recently or were able to communicate. 11 of these 20 had non-alcohol delirium. Non-drinkers who were able to communicate were significantly more likely to be placed on symptom-triggered therapy than drinkers who could communicate (36 vs 13%; p=0.003) Adverse events N=7 DT N=1 seizure N=2 DT and seizure N=1 death There was no significant difference between those patients who received appropriate and those that received inappropriate therapy with respect the incidence of adverse events (ns)								
Morgan T, Kofoed L, Petersen DB. Clinical	Retrospective before/after	N=197	**Inclusion Criteria**: patients who had	Post-pathway	Pre-pathway	6 months and 1	Length of stay, total benzodiazepine prescribed,	Not reported

pathway effects on treatment of the alcohol withdrawal syndrome. *South Dakota Journal of Medicine.* 1996; 49(6):195-200.	time series (case series) 3		undergone screening for admission to this unit, meeting criteria for needing hospitalization to treat uncomplicated alcohol withdrawal syndrome. **Exclusion Criteria**: patients who did not fall into the centres protocol (no details provided) Setting: 28 bed psychiatric unit in the Sioux Falls VA Medical Center **Patient Characteristics**: 'Before' group: all patients were male, average age 49.3 yrs 'After' group: 1 female in the group, average age 44.0 yrs. '1 yr after' group: all patients were male, average age 48.8 yrs.	N=56 Pathway for uncomplicated alcohol withdrawal incorporating the use of the CIWA-Ar Move towards symptom-triggered dosing but clinicians made decisions independently benzodiazepine prescribing One year after pathway implementation N=75 Pathway included a protocol for benzodiazepine dosing according to a symptom-triggered CIWA-Ar based schedule	N=66 No standard assessment scale. Implied that fixed-dosing scheduling used but not explicitly stated	year after initiation of the pathway.	patient outcomes (frequency of complications, percentage completing detox)	

Effect Size

Outcomes

1. **Length of stay (LOS)**
   - *All patients*: decreased significantly following initiation of pathway, from a mean 6.67 (SD 5.14) days before to 5.25 (SD 3.50) after, and 4.31 (SD 2.96) days 1 year after (t=3.28, p=0.0014, df 101)
   - *Detoxification completers*: decreased significantly following initiation of pathway, from a mean 7.35 (SD 5.18) days before to 5.76 (SD 3.45)days after, and 4.77 (SD 2.91) days 1 year after (t=3.33, p=0.0013, df 86)

- *Non-completers*: mean days increased from 2.33 (SD 1.66) days to 2.90 (SD 2.81) days after, then dropped to 1.64 (SD 1.50) days 1 year after. **2. Total benzodiazepine prescribed** - Mean mg per episode of PRN benzodiazepine: o *All patients*: episodes initially dropped from 20.7 (SD 32.0) to 16.1 (SD 18.0) after, and then increased to 21.5 (SD29.4) 1 year after. - Mean mg of benzodiazepine per episode as scheduled medication (diazepam equivalents): o *All patients*: decreased significantly following initiation of the pathway from 74.6 (SD 92.7) mg to 31.4 (SD 47.5) mg after (t=3.3, p=0.0013, df 100), and to 9.9 (SD 32.2) 1 year after (t=5.4, p<0.0001, df 79). o The mg amount for the non-completers was lower than for completers due to the shorter LOS for the non-completers. - Mean mg of benzodiazepine per episode-total (diazepam equivalents): o Decreased from 95.3 (SD 100.2) diazepam equivalents (mg) to 47.5 (SD 56.6) after pathway initiated (t=3.3, p=0.0013, df 105), and dropped further to 31.4 (SD 41.9) 1 year after (t=4.8, p<0.0001, df 85). o Similar significant reductions in mean total benzodiazepine prescribed per episode were found in both completer and non-completer groups. **3. Patient outcomes** - No serious complications were noted during chart review for before initiation of the pathway, after or 1 year after. **Authors' conclusion:** The data showed that initiation of a clinical pathway incorporating CIWA-Ar assessment led to decreased LOS, decreased reliance on scheduled benzodiazepine prescribing, and decreased exposure to benzodiazepine per detoxification episode.								
Pletcher MJ, Fernandez A, May TA et al. Unintended consequences of a quality improvement program designed to improve treatment of alcohol withdrawal in hospitalized patients. *Joint Commission Journal on Quality & Patient Safety.* 2005; 31(3):148-157. Ref ID: 1024	Retrospective before and after study 3	N=500 (randomly selected from N=2642 eligible patients)	Patients with alcohol-related discharge diagnosis (ICD-9) Setting: General hospital Patient population: post-pathway Mean age 46 yrs, 79% male, 40% white, symptomatic withdrawal on admission 44%, > 7 alcohol drinks per day 51%, previous alcohol withdrawal 30%, previous DT 10%, previous alcohol withdrawal seizure 24% pre-pathway Mean age 45 yrs, 80% male, 41% white, symptomatic withdrawal on admission 39%, > 7 alcohol drinks per day 54%,	Post-protocol N=202 Guideline and protocol recommending: CIWA monitoring for all patients with or at risk of developing alcohol withdrawal. However due to concern about efficacy in patients with acute concurrent illness they recommended fixed dose scheduling for at risk or symptomatic patients with CIWA monitoring to allow for extra doses as-needed. Education campaign	Pre-protocol N=188 Fixed-schedule dosing without the use of standard monitoring	NA	Documentation Medication	National Institutes for Health

			previous alcohol withdrawal 32%, previous alcohol withdrawal seizure 26%, previous DT 12%	also recommended lorazepam instead of chlordiazepoxide or diazepam. Standard order form implemented				

Effect
Post- vs pre- pathway
Evidence that the pathway was followed:
There was a significant difference post-pathway compared to pre-pathway on:
The use of the optional standardised order form increased (24 vs 9%; p<0.001)
CIWA score documentation in nursing notes increased 40 vs 8%; p<0.001)
Proportion of patients over age 65 yrs (N=13) treated with chlordiazepoxide decreased (20 vs 100%; p<0.05)
Proportion of patients transferred to a higher level of care decreased (17 vs 22%; OR (adj) 0.6 (95%CI 0.3 to 1.0)
Proportion of patients who died increased (3.5 vs 2.7%; OR (adj) 2.1 (95%CI 1.0 to 4.6)

There was no significant different post- and pre- pathway for:
Medication use
Proportion treated with benzodiazepine (76 vs 75%; ns)
Median total dose of benzodiazepine (16 vs 22; ns)
Proportion treated with lorazepam (64 vs 65%; ns)
Proportion treated with chloridazepoxide (52 vs 45%; ns)

There was a significant increase in the median benzodiazepine dose post-pathway compared with pre-pathway in patients:
with cirrhosis (p<0.05) but not without cirrhosis (ns)
with APACHE III score 5 but not scores 1 to 4 (ns)

Length of stay (median 4 vs 3 days, p value or OR not reported)

Two-year follow-up
Pre-pathway vs two year follow-up
Two years after the implementation of the pathway compared with the pre-pathway there was an increase in:
The proportion of deaths (2.2 vs 3.3%; OR (adj) 1.2 (95%CI 0.6 to 2.4)
The length of stay (median 3 vs 4 days; OR (adj) -3% (-14% to 8%)

Complications
There was no significant different post vs pre-pathway for the incidence of:
Seizures (3.5 vs 3.2%; OR (adj) 0.9; 95%CI 0.3 to 3.0)

Delirium (41 vs 35%; OR (adj) 1.2 (0.8 to 1.9)								
Repper-DeLisi J, Stern TA, Mitchell M et al. Successful implementation of an alcohol-withdrawal pathway in a general hospital. *Psychosomatics.* 2008; 49(4):292-299. Ref ID: 1001	Retrospective case series 3	N=80	Patients with alcohol withdrawal Setting: medical and surgical patients admitted to a general hospital Inclusion criteria: If the records indicated alcohol consumption within two weeks of admission and/or withdrawal or treatment for alcohol withdrawal during the index admission Patient population Post-pathway: mean age 47 yrs, 85% male, 30% alcohol withdrawal, 10% alcohol withdrawal seizure, 35% with one or more co-morbid condition Pre-pathway: mean age 50 yrs, 75% male, 43% alcohol withdrawal, 13% alcohol withdrawal seizure, 35% with one or more co-morbid condition The groups were well matched at baseline except that more patients in the post-pathway group had undergone previous detoxification compared to the pre-pathway group (78 vs 43%, p<0.01)	Post-pathway N=40 Pathway developed to: Increase recognition of those at risk of withdrawal and to treat patients before they became symptomatic. Also, to facilitate aggressive treatment of alcohol withdrawal Assessment consisted of: CAGE, vital signs, alcohol history, withdrawal signs, delirium, risk factors. Treatment: fixed dose benzodiazepines Training and education program	Pre-pathway N=40 Benzodiazepines at the discretion of staff i.e. without a protocol	NA	Frequency of assessment and monitoring Complications	None reported
Effect Pre vs post –pathway There was a significant difference post-pathway when compared to pre-pathway with respect to: Frequency of vital sign checks (controlling for delirium) (No. of vital sign checks over three days 26 vs 20; p<0.05) The proportion of patients who received their benzodiazepine medication as a standing or fixed-dose compared to as-needed or prn over the first three days of hospitalisation (pday oay one p<0.05; day two p<0.01; and day three p<0.05)								

There was no significant difference pre and post pathway with respect to: The proportion of patients who were consulted about the amount and frequency of their alcohol consumption, including CAGE documentation (ns) The median dose of lorazepam equivalent (ns) The incidence of DT (ns)								
Stanley KM, Worrall CL, Lunsford SL et al. Efficacy of a symptom-triggered practice guideline for managing alcohol withdrawal syndrome in an academic medical center. *Journal of Addictions Nursing.* 2007; 18(4):207-216. Ref ID: 758	Before and after (two groups) 3	N=188	Patients at risk of alcohol withdrawal admitted to the surgery or internal medicine services Patient population: Mean age 48 yrs, 85% male, 52% African American. There were no significant differences at baseline	Guideline managed patients N=106 The guideline comprised of: Symptom-triggered dosing schedule, guideline on how to manage a seizure or delirium and patients with specified comorbid conditions. Monitor using the Alcohol Withdrawal Scale type indicator every two to four hours according to score	Non-guideline managed patients N=82 Patients were identified by medical record documentation of a discharge diagnosis of alcohol withdrawal, or the combination of benzodiazepine, thiamine, folic acid and multivitamin. Prior to the guideline benzodiazepines were given around the clock and/or as needed and these vitamin supplements were commonly prescribed for patients with suspected or known alcohol abose	Length of hospital stay	Amount of medication Length of hospital stay	None reported
Effect Guideline vs non-guideline managed patients: Patients who received the practice guidelines compared to those who did not received significantly: less lorazepam (7.8 vs 23.3; p<0.01)								

more clonidine (0.2 vs 0.05; p<0.01) Patients managed by a guideline compared to those that were not were significantly more likely to receive drug therapy (34 vs 11%; p<0.01) Patients managed by a guideline compared to those that were not were significantly less likely to be discharged on tapered benzodiazepine therapy (11 vs 54%; p<0.01) There was no significant different between guideline and non-guideline managed patients: On the amount of haloperidol (4.0 vs 5.9; ns) On the length of hospital stay (6.4 vs 6.3 days; ns)								
Wetterling T, Kanitz RD, Besters B et al. A new rating scale for the assessment of the alcohol-withdrawal syndrome (AWS scale). *Alcohol & Alcoholism.* 1997; 32(6):753-760. Ref ID: 959	Prospective case series 3	N=387	Development phase: Adults with chronic alcohol abuse admitted to a detoxification unit N=132 Patient characteristics: M:F 101:31, mean age 44 yrs, mean number of past detoxifications 5 Validation phase: N=256 Patients with long-standing alcohol dependence (DSM-IV) admitted for detoxification to an psychiatric emergency ward Patient characteristics M:F 198:58, mean age 45 yrs, median no. past detoxifications 5	Symptom-based protocol N=256 Alcohol Withdrawal Scale (AWS) derived from the CIWA-Ar Six items on somatic symptoms (pulse rate, diastolic blood pressure, temperature, breathing rate, sweating, tremor) Five items on mental symptoms (agitation, contact, orientation, hallucinations, anxiety) AWS administered every 2 hrs Treatment protocol: Mild AWS – no medication Moderate AWS –	Non-protocol group (validation phase) N=131 Patients were treated without reference to a rating scale	Duration of treatment	Prescription of clomethiazole, duration of medical treatment, applied dosage of clomethiazole	None reported

				carbamazepine upto 900mg/day Severe AWS - clomethiazole				

Effect
AWS characteristics
The inter-rater reliability between 20 trained nurses and three senior practioners was κ=0.67 to 1.00 for all 11 items

Of those patients identified as low risk (AWS < 10, N=211) 6 developed symptoms of delirium.
Of those patients identified as high risk (AWS $\geq$ 10, N=45) 21 developed symptoms of delirium.
According to the treatment protocol nearly one half of the patients received no medication and a further 31.6% received only carbamazepine, 22.7% clomethiazole or benzodiazepines. Medication was initiated or changed during the course of AWS in 19 patients (7.4%) based on changes in the AWS scale score

AWS controlled treatment protocol vs non-rating scale protocol
Medication dose
An AWS controlled treatment protocol compared to a non-rating scale protocol resulted in a significant:
Increase in the number of patients receiving clomethiazole (64/131 (49%) vs 58/256 (23%), p<0.001)
Decrease in the amount of applied dose of clomethiazole per patient (5061 vs 7680 mg/patient, p<0.001)

Duration of treatment
AWS controlled treatment protocol vs non-rating scale protocol
An AWS controlled treatment protocol compared to a non-rating scale protocol resulted in a significant:
Decrease in the duration of treatment (2.7 vs 3.8 days, p<0.001)

Delerium tremens
There was no significant difference between the number of patients who developed delirium tremens in the AWS controlled protocol compared with the non-rating scale protocol (ns)