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a) What are the benefits and risks of unplanned 'emergency' detoxification (medically assisted withdrawal) in acute medical settings vs discharge? b) What criteria should be used to admit a patient with AAW for 'unplanned emergency' detoxification?								
Reference	Study type Evidence level	Number of patients	Patient characteristics	Intervention  Treatment regimen	Comparison	Length of follow-up	Outcome measures Associations Statistical analysis	Source of funding
Duka T, Townshend JM, Collier K et al. Impairment in cognitive functions after multiple detoxifications in alcoholic inpatients. <i>Alcoholism: Clinical &amp; Experimental Research</i> . 2003; 27(10):1563-1572. Ref ID: 87	Prospective cohort 2++	N=85	Patients undergoing detoxification in an inpatient setting. All patients had ceased pharmacological therapy for the treatment of withdrawal for at least two weeks	Two or more medically supervised detoxifications N=6  Total number of previous detoxifications (including unsupervised and medically supervised): ANCOVA not performed (results not reported)  Treatment regimen: chlormethiazole (mean dose 192 mg, probably fixed dose)	One or fewer medically assisted detoxifications (LO) N=36  Mild to moderate social alcohol drinkers recruited from a University  N=43	NA	Stroop colour naming task, maze learning vigilance task	Medical research council
Effect There were no significant differences (ANCOVA) were reported between patients with a high number of previous detoxifications and those with a low number on the stroop task, maze learning or vigilance tasks (ns)								
Malcolm R, Roberts JS,	Prospective cohort 2++	N=136	Patients with alcohol dependence and	Lorazepam and carbamazepine	Previous detoxifications >	NA	Statistical analysis:	None reported

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<p>Wang W et al. Multiple previous detoxifications are associated with less responsive treatment and heavier drinking during an index outpatient detoxification. <i>Alcohol</i>. 2000; 22(3):159-164. Ref ID: 97</p>			<p>withdrawal (DSM-IV)</p> <p>Inclusion: ≥ 26 Mini mental state examination CIWA-Ar ≥ 10</p> <p>Exclusion: substance abuse, history of head injury but patients with a history of alcohol related seizures were included</p> <p>Setting: Patients recruited via a trial comparing lorazepam and carbamazepine in the outpatients treatment of alcohol withdrawal</p> <p>Patient population: mean age 73%, 87% white, mean no. of standard drinks in 14 days prior to detoxification 177, mean alcohol dependence scale score 22, mean number of years drinking 21 yrs, 73% male</p> <p>No significant differences were reported at baseline</p>	<p>fixed dose regimen</p> <p>Previous detoxifications ≤ 1</p> <p>N=103</p> <p>Lorazepam N=58</p> <p>Carbamazepine N=45</p>	<p>1 (range 2 to 5)</p> <p>N=33</p> <p>Lorazepam N=17</p> <p>Carbamazepine N=16</p>		<p>ANCOVA and logistic regression</p>	
<p>Effect Low vs high detoxifications Patients who had undergone multiple detoxifications compared with those with 0 to 1 previous detoxification had:</p>								

DRAFT FOR CONSULTATION

A significantly slower rate of decline on the CIWA-Ar from day one to four of the detoxification (no data reported p<0.05)

There was no significant difference between patients with 0 to 1 previous detoxifications compared with those with multiple detoxifications on: CIWA-Ar score at baseline (no data reported ns)

<p>Schuckit MA, Tipp JE, Reich T et al. The histories of withdrawal convulsions and delirium tremens in 1648 alcohol dependent subjects. <i>Addiction</i>. 1995; 90(10):1335-1347. Ref ID: 1013</p>	<p>Prospective cohort 2++</p>	<p>N=1648</p>	<p>Patients who were alcohol dependent (DSM-III-R)  Setting: Not specified  Patient population: Mean age 38 yrs, 33% female, 77% Caucasian, mean age of alcohol dependence 24 yrs</p>	<p>History of severe withdrawal  Presence of DTs and/or seizures)  N=211</p>	<p>Control (no history of severe withdrawal)  N=1437</p>	<p>NA</p>	<p>Outcomes taken from Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA)  Association between a history of DT and convulsion and: Drinking history Withdrawal episodes (***) Withdrawal symptoms  Univariate tests and regression</p>	<p>National Institute for Alcohol Abuse and Alcoholism</p>
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Effect  
Incidence  
188/1648 (11%) patients experienced delirium tremens, including 31 (2% of the total sample and 17% of those with DTs) who ever had a grand mal convulsion during withdrawal.  
Another 23 people (1%) of the total had a history of convulsions but not history of DTs. In total 211/1648 (13%) (range 1 to 45) reported DTs and/or a history of convulsions.  
Multivariate hierarchical logistic regression model  
A history of DTs and/or convulsions compared with no history of DTs and/or convulsions was significantly associated with:  
A higher number of drinks in 24 hrs (lifetime) (41 vs 25) (OR 1.02, 95%CI 1.01 to 1.03; p<0.001)  
A history of more withdrawal episodes (28 vs 16) (OR 1.01, 95%CI 1.00 to 1.02; p<0.01)

Univariate analyses  
Patients with a history of DTs and/or convulsions compared to those without was associated with a significantly:  
Longer period of heavy drinking (excluding abstinence periods) (13 vs 10 yrs; p<0.001)

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<p>Days of drinking per week (drinkers, last six months) (41 vs 25; p&lt;0.001)                  Number of withdrawal symptoms (worst episode) (6 vs 4; p&lt;0.001)</p> <p>None of the factors were significant predictors of DTs and/or convulsions in the multivariate analysis</p>								
<p>Wetterling T, Driessen M, Kanitz RD et al. The severity of alcohol withdrawal is not age dependent. <i>Alcohol &amp; Alcoholism</i>. 2001; 36(1):75-78. Ref ID: 122</p>	<p>Prospective cohort 2++</p>	<p>N=723</p>	<p>Patients with alcohol withdrawal</p> <p>Setting: Alcohol detoxification unit in a general hospital (patients with acute medical or surgical disorders)</p> <p>Patient population: M:F 518:205, mean age 43 yrs</p>	<p>Age groups compared: ≤ 29 yrs, 30 to 59 yrs and ≥ 60 yrs</p> <p>Treatment regimen: symptom-triggered carbamazepine</p>	<p>See intervention</p>	<p>NA</p>	<p>Association between age and severity of alcohol withdrawal</p> <p>Severity of alcohol withdrawal and drinking history, number of prior detoxifications (no definition provided)</p> <p>Statistical analysis: univariate and regression</p>	<p>None reported</p>
<p>Effect</p> <p>The incidence of DT was 8.4% for the total population</p> <p>Logistic regression analysis</p> <p>Withdrawal severity (maximum AWS score) was not predicted by:</p> <p>Age (ns)</p> <p>Duration of alcohol dependence (ns)</p> <p>Alcohol intake/day (ns)</p> <p>Prior detoxification (ns)</p>								
<p>Booth BM, Blow FC. The kindling hypothesis: further evidence from a U.S. national study</p>	<p>Retrospective cohort 2+</p>	<p>N=6818</p>	<p>Patients admitted for a short detoxification episode (0 to 5 days) with alcohol dependence (ICD-9)</p> <p>Setting: medical centre</p> <p>Exclusion criteria:</p>	<p>Withdrawal problems</p> <p>N=461</p> <p>Unspecified seizures</p> <p>N=193</p>	<p>No withdrawal problems</p> <p>N=6357</p> <p>No unspecified seizures</p> <p>N=6625</p>	<p>NA</p>	<p>No. of hospitalisations (determined by hospital notes) and seizure frequency and withdrawal problems (DT, alcoholic</p>	<p>National institute for alcoholism and alcohol abuse</p>

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<p>of alcoholic men. <i>Alcohol &amp; Alcoholism</i>. 1993; 28(5):593-598. Ref ID: 200</p>			<p>females, admission for rehabilitation</p>	<p>Treatment regimen: not specified</p>			<p>hallucinations, alcoholic dementia) Statistical analysis: univariate and multivariate analysis</p>	
<p><b>Effect</b> During the index period 461/6818 (7%) experienced withdrawal problems (DT, alcoholic hallucinations, alcoholic dementia) 193/6818 (3%) had unspecified seizures</p> <p><b>Three years before index detoxification</b> Withdrawal problem (DT, alcoholic hallucinations, alcoholic dementia) vs no withdrawal problem Univariate analysis (confirmed by multivariate analysis) There was a significant difference between the number of people who had withdrawal problems and those who did not with respect to: Previous alcohol-specific hospitalisation days (10.01 vs 7.13; p&lt;0.05)</p> <p>There was no significant difference between people who had withdrawal problems and those who did not with respect to: The number of previous alcohol-specific hospitalisations (0.95 vs 0.82;ns)</p> <p>There was a significant difference between those patients with unspecified seizures and those without with respect to: Previous alcohol-specific hospitalisations (1.48 vs 0.81; p&lt;0.01) Previous alcohol-specific hospital days (14.52 vs 7.12; p&lt;0.01)</p>								
<p>Lukan JK, Reed DN, Jr., Looney SW et al. Risk factors for delirium tremens in trauma patients. <i>Journal of Trauma-Injury Infection &amp; Critical Care</i>.</p>	<p>Retrospective cohort 2+</p>	<p>N=1856</p>	<p>Patients admitted for trauma who developed DT whilst in hospital or presenting with a positive blood alcohol concentration (BAC) on admission.</p> <p>Setting: General hospital</p> <p>Patient population: DT group – 90% male, 92% white, 63% &gt; 40</p>	<p>Patients with DT N=104 (one patient excluded)</p> <p>Treatment regimen: Various but mainly administration of benzodiazepines</p>	<p>Non-DT group N=1751</p>	<p>NA</p>	<p>Association between Statistical analysis: univariate and logistic regression</p>	<p>None reported</p>

DRAFT FOR CONSULTATION

<p>2002; 53(5):901-906. Ref ID: 1139</p>			<p> yrs*, BAC mean 43 mmol/L*, BAC ≥ 200 mg dL 60%*, 32% car accident*, 17% fall*, assault 10%, stab wound 12%, Glasgow Coma Score ≤ 7 9%</p> <p>Non-DT – 85% male, 77% white, age &gt; 40 yrs 32%*, BAC mean 41.2 mmol/L, BAC ≥ 200 mg dL 48%*, 50% car accident*, 8% fall, assault 10%, stab wound 8%, Glasgow Coma Score ≤ 7 15%</p> <p>Denotes significant difference</p>					
<p>Effect Univariate analysis The following were significant predictors of whether a patient developed DT or not: The following were age &gt; 40 yrs (OR 3.21, 95%CI 2.14 to 4.81; p&lt;0.001) blood alcohol concentration ≥ 43 mmol/L (200 mg/dL) (OR 1.69, 95%CI 1.08 to 2.62; p&lt;0.05)</p> <p>The following were not significant predictors of whether a patient developed DT or not: mean blood alcohol concentration on admission (ns)</p> <p>Regression analysis Age &gt; 40 yrs but not blood alcohol concentration ≥ 43 mmol/L (200 mg/dL) remained a significant predictor of DT in the multiple regression model (OR adjusted age &gt; 40 yrs 2.98; 95%CI 1.97 to 4.51; p&lt;0.001)</p>								
<p>F Ferguson JA, Suelzer CJ, Eckert GJ et al. Risk factors for delirium</p>	<p>Retrospective cohort 2+</p>	<p>N=200</p>	<p>Patients with alcohol withdrawal or detoxification</p> <p>Setting: Internal medicine hospital at general hospital</p>	<p>Delirium tremens N=48</p> <p>Treatment regimen: Scheduled and as needed</p>	<p>No delirium tremens N=152</p>	<p>NA</p>	<p>Association between delirium tremens and the number of days since the last drink and</p>	<p>Bureau of health professions, health resources and services administration</p>

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<p>tremens development. <i>Journal of General Internal Medicine.</i> 1996; 11(7):410-414. Ref ID: 1101</p>			<p>Exclusion: Presence of DT on admission</p> <p>Patient population: mean age 42 yrs, 85% male</p>	<p>benzodiazepines</p>			<p>the number of previous withdrawal episodes (obtained from medical records but not further defined)</p> <p>Statistical analysis: Univariate and logistic regression</p>	
<p>Effect Incidence of DT 48/200 (24%) developed delirium tremens, of these 4/48 (8%) died Univariate analysis The development of delirium tremens was significantly associated with: More days since the last drink (p&lt;0.10)</p> <p>There was no significant association between the development of delirium tremens and:</p> <p>History of previous withdrawal events (ns)</p> <p>In the multiple regression analysis more days since the last drink was an independent predictors of the development of delirium tremens (OR 1.3; 95%CI 1.09 to 1.61)</p>								
<p>Vinson DC, Menezes M. Admission alcohol level: a predictor of the course of alcohol withdrawal. <i>Journal of Family Practice.</i> 1991; 33(2):161-167. Ref ID:</p>	<p>Retrospective cohort 2+</p>	<p>N=233</p> <p>N=119 non-medical unit</p> <p>N=113 medical unit</p>	<p>Patients admitted for alcohol withdrawal</p> <p>Setting: 1) nonmedical social detoxification setting. Patients with severe withdrawal and transferred elsewhere. 2) medical detoxification unit</p> <p>Patient population: Non-medical: mean age 37 yrs, male:female 99:2,</p>	<p>Non-medical social detoxification setting.</p> <p>N=119</p> <p>Patients with severe withdrawal and transferred elsewhere.</p> <p>Treatment regimen:</p>	<p>Medical detoxification unit</p> <p>N=114</p> <p>Treatment regimen as for intervention</p>	<p>NA</p>	<p>Alcohol level on admission and: Amount of chlordiazepoxide used during withdrawal</p>	<p>None reported</p>

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1011			<p>mean daily alcohol consumption 377 g/d</p> <p>Medical: mean age 45 yrs, all male, mean daily alcohol consumption 361 g/d</p>	<p>chloridazepoxide prn</p>				
<p>Effect</p> <p>Non-medical setting                  Linear regression analysis showed a significant relationship between breath alcohol levels on admission and severity of withdrawal (amount of chlordiazepoxide used in first 48 hrs) (<math>R^2=0.26;p&lt;0.0001</math>). This reduced to <math>p=0.002</math> when AST was entered in to the equation. When patients were classified in to two groups based on the median level of alcohol on admission (<math>\leq 33</math> mmol/L (150 mg/dL vs <math>&gt; 33</math> mmol/L) higher levels were associated with more severe adverse outcomes, including transfer to acute care hospital for medical detoxification and a maximum withdrawal assessment score of greater than 6 (indicating medical consultation is required). When the same threshold was applied to the medical setting, the threshold distinguished between those patients who required a total of 50 mg chlordiazepoxide or less and those who required more.</p> <p>Medical setting                  Linear regression analysis showed a significant relationship between breath alcohol levels on admission and severity of withdrawal (<math>R^2=0.41;p&lt;0.0001</math>). This level of significance remained the unaltered when AST was entered in to the equation.</p>								
<p>Kraemer KL, Mayo SM, Calkins DR. Impact of age on the severity, course, and complications of alcohol withdrawal. <i>Archives of Internal Medicine.</i> 1997; 157(19):2234-2241. Ref ID: 50</p>	<p>Retrospective case series 3</p>	<p>N=284                  Stratified random sampling to ensure equal samples across age groups</p>	<p>Patients with alcohol withdrawal                  Setting: alcohol detoxification unit                  Exclusion: comorbid drug abuse                  Patient population: Almost 100% male population</p>	<p>Comparison across the following age groups:                  &lt;40 (N=56), 40 to 49 (N=70), 50 to 59 (N=74), 60 to 69 (N=63), <math>\geq 70</math> (N=21)                  Treatment regimen: Symptom-triggered chlordiazepoxide</p>	<p>See intervention</p>	<p>NA</p>	<p>Statistical analysis: univariate and regression (adjusted for limited variables). P values adjusted for multiple outcomes</p>	<p>None reported</p>
<p>Effect                  Incidence</p>								

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The incidence of current DT was 1% (N=3)  
 The incidence of past DT ranged from 3/21 (14.3%) (≥ 70 yrs) to 28/74 38% (50 to 59 yrs)  
 The incidence of past withdrawal seizures ranged from 1/21 (5%) (≥ 70 yrs) to 17/74 (23%) (50 to 59 yrs)  
 The association between past DT, past withdrawal seizures and age were reported in the univariate analysis only  
 There was no significant difference between the age groups (<40 vs 40 to 49 vs 50 to 59 vs 60 to 69 vs ≥ 70) with respect to:  
 Mean severity of alcohol withdrawal (maximal CIWA-Ar score) (ns)  
 Mean initial CIWA-Ar score (ns)

Kraemer KL, Mayo SM, Calkins DR. Independent clinical correlates of severe alcohol withdrawal. <i>Substance Abuse</i> . 2003; 24(4):197-209. Ref ID: 86	Retrospective case review 3	N=284	Patients admitted to an acute inpatients detoxification unit  Mean age 51 yrs, 99%male, 20% employed, 19% homeless, mean duration of drinking 25 yrs  Setting: Inpatient detoxification unit	Treatment regimen: Fixed and symptom triggered	Severity of alcohol withdrawal (600 mg or more, total, cumulative benzodiazepine (expressed in chloridazepoxide equivalents))	NA	Use of an early morning eye opener, initial CIWA-Ar score, admission serum AST ≥ 80 U/L, past benzodiazepine use, history of delirium tremens, participation in two or more prior alcohol treatment programs, daily alcohol intake, no. of drinking days over past month, no. of past withdrawal episodes  Statistical analysis: multivariate logistic regression	None reported
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Effect  
 The incidence of severe withdrawal was 25%  
 Multivariate logistic regression

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Predictors of severe withdrawal (600 mg or more, total, cumulative benzodiazepine (expressed in chloridazepoxide equivalents)):  
 history of delirium tremens (OR 2.9; p=0.007)  
 participation in two or more prior alcohol treatment programs (OR 2.6; p=0.01)

There was no significant association (all were significant in the univariate but not the multivariate analysis) between severity of withdrawal (600 mg or more, total, cumulative benzodiazepine (expressed in chloridazepoxide equivalents) and:  
 daily alcohol intake (ns)  
 no. of drinking days over past month (ns)  
 no. of past withdrawal episodes (ns)  
 history of withdrawal seizure (ns)

<p>Lechtenberg R, Worner TM. Total ethanol consumption as a seizure risk factor in alcoholics. <i>Acta Neurologica Scandinavica</i>. 1992; 85(2):90-94. Ref ID: 207</p>	<p>Prospective case series 3</p>	<p>N=500</p>	<p>Patients with alcoholism who were at potential risk of:                   Dangerous or disabling withdrawal, high risks of seizures, DT or hallucinations, failure of previous outpatient detoxification, unstable social situation (admission criteria)                   Setting: Alcohol detoxification unit                   Patient population: mean age 41 yrs, mean no. of admission 2, mean alcohol use duration 25 yrs, mean alcohol consumption 293 g/day, male:female 81:17</p>	<p>Association between ethanol consumption and seizure risk                  Treatment regimen: not stated</p>	<p>NA</p>	<p>NA</p>	<p>Detoxifications (from patient reported and hospital records, no further definition provided), seizure history, alcohol use history                   Statistical analysis: Univariate and discriminant function analysis</p>	<p>None reported</p>
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Effect  
 There were no seizures during the current episode of withdrawal  
 55/98 patients reported a history of alcohol withdrawal seizures  
 Mean number of previous detoxification admissions 2

Discriminant function analysis

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<p>The following were not correlated with prevalence of seizure history:          Years of alcoholism (<math>R^2</math>-Ad 0.007, <math>F=2.6</math>; ns)          Age (ns, no further details reported)</p>								
<p>Detoxification admission was correlated with prevalence of seizure history (<math>R^2</math>-Ad 0.041, <math>F=15.1</math>; <math>p&lt;0.0001</math>)</p>								
<p>Lechtenberg R, Worner TM. Relative kindling effect of detoxification and non-detoxification admissions in alcoholics. <i>Alcohol &amp; Alcoholism</i>. 1991; 26(2):221-225. Ref ID: 1126</p>	<p>Retrospective case series 3</p>	<p>N=400</p>	<p>Patients requesting admission for alcohol detoxification</p> <p>Inclusion criteria:          Alcoholism service accepts patients with potentially dangerous or disabling symptoms. Patients were eligible if they had failed outpatient detoxification or were in unstable social situations</p> <p>Setting: Alcoholism service</p> <p>Patient population:          male:female 340:60          mean age 41 yrs, mean number of previous detoxification 2, mean number of years of alcohol consumption 25</p>	<p>History of seizure</p> <p>N=84          Treatment regimen not specified</p>	<p>No history of seizure</p> <p>N=316</p>	<p>Na</p>	<p>Seizure prevalence (associated with alcohol withdrawal but not in all cases) and detoxification admission (not defined),</p> <p>Statistical analysis:          univariate and discriminant function analysis</p>	<p>None reported</p>
<p>Effect          Incidence of seizures          84/400 (21%) of patients had a history of a seizure. No seizures were reported in the current hospital admission for detoxification.</p> <p>There was a significant association between a history of a seizures and the total number of previous detoxification admissions (mean 2, <math>R^2</math>-Ad 0.035, <math>F=13.2</math>; <math>p&lt;0.001</math>).</p> <p>The following were not significantly associated with a history of seizures and:          Age (ns)          Years of alcoholism (ns)</p>								

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<p>Palmstierna T. A model for predicting alcohol withdrawal delirium. <i>Psychiatric Services</i>. 2001; 52(6):820-823. Ref ID: 1099</p>	<p>Prospective case series 3</p>	<p>N=334</p>	<p>Patients seeking treatment for alcohol withdrawal</p> <p>Setting: Psychiatric and dependency emergency unit</p> <p>Patient population: male:female 251:83 Recent consumption of more than 250 g pure alcohol/daily for at least three weeks 132/334 (40%)</p>	<p>Risk of developing alcohol withdrawal delirium (DSM-IV)</p> <p>Treatment regimen: fixed dose oxazepam and diazepam prn</p>		<p>NA</p>	<p>Risk of DT and: Previous DT, previous epileptic seizure, epileptic seizure within past 48 hrs, recent consumption of &gt; 250 grams pure alcohol daily for at least three weeks, alcohol concentration of more than 1 g/litre of body fluid regardless of withdrawal symptoms, more than 24 hrs since the last drink, duration of current episode of current drinking</p> <p>Statistics: univariate and multivariate</p>	<p>None reported</p>
<p>Effect Incidence of delirium 145/334 (43%) had previously experienced alcohol withdrawal delirium 139/334 (42%) had a previous epileptic seizure 23/334 (7%) had a epileptic seizure in the past 48 hrs Univariate analysis Risk of developing DT is significantly associated with: Previous epileptic seizure (p&lt;0.001) Previous alcohol withdrawal delirium (p&lt;0.001)</p>								

DRAFT FOR CONSULTATION

The risk of developing DT was not significantly associated with:  
 Epileptic seizure within the past 48 hrs (ns)  
 recent consumption of > 250 grams pure alcohol daily for at least three weeks (ns)  
 alcohol concentration of more than 1 g/litre of body fluid regardless of withdrawal symptoms (ns)  
 more than 24 hrs since the last drink (ns)  
 duration of current episode of current drinking (ns)

Multiple regression  
 Risk of developing DT was significantly associated with  
 Previous epileptic seizure (p<0.05)  
 Previous delirious episode (p<0.05)

A previous history of alcohol withdrawal delirium and of epileptic seizures independently contributed only 6% and 6.8%, respectively, to the risk of developing delirium

<p>Daryanani HE, Santolaria FJ, Reimers EG et al. Alcoholic withdrawal syndrome and seizures. <i>Alcohol &amp; Alcoholism</i>. 1994; 29(3):323-328. Ref ID: 469</p>	<p>Prospective cohort 2-</p>	<p>N=72  N=68 could describe previous withdrawal episodes</p>	<p>Patients with alcohol withdrawal syndrome (tremour, hallucinations, DT or seizure)  Inclusion criteria: under 65 yrs and daily ethanol intake of at least 80 g/day  Setting: Internal medical unit  Patient population: 93% male, mean age 45 yrs, mean duration of chronic alcohol use 20 yrs</p>	<p>Treatment regimen: diazepam prn</p>		<p>NA</p>	<p>Association between seizure on admission and: Prior history of seizure Mean alcohol intake/day Mean duration of alcohol use  Statistics: univariate analysis for outcomes reported here</p>	<p>None reported</p>
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Effect  
 Incidence of a history of DT and seizure  
 26/68 (38%) described a past history of seizures  
 39/68 (57%) had a past history of DT  
 Incidence of DT and seizure on admission  
 33/72 patients had a seizure on admission  
 18/33 developed DT

There was a significant association between a seizure on admission and a prior history of a seizure (p=0.0001)  
 There was no significant association between the presence of seizures and:

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Mean alcohol intake/day (ns) Mean duration of alcohol misuse (ns)								
Fiellin DA, O'Connor PG, Holmboe ES et al. Risk for delirium tremens in patients with alcohol withdrawal syndrome. <i>Substance Abuse</i> . 2002; 23(2):83-94. Ref ID: 486	Case control 2-	N=60	Patients undergoing detoxification  Setting: Inpatient detoxification unit  Exclusion criteria: Signs and symptoms that may indicate early manifestations of DT, no alcohol use in the prior 72 hrs (and were therefore at risk of alcohol withdrawal), discharge within 24 hrs  Patient population: 100% male, 80% white, mean age 49 yrs  There were no significant differences at baseline	Patients with delirium tremens (DSM-IV)  N=15	Patients without DT  N=45	NA	History of DT and prior seizure, or DT  Univariate statistics	None reported
Effect Cases with a history of delirium tremens were significantly more likely than controls with out a history to have experienced: a prior alcohol withdrawal seizure (33 vs 20%, OR 1.9, 95%CI 0.43 to 8.3) a prior DT (47 vs 24%, OR 2.6, 95%CI 0.64 to 10.5) a prior complicated alcohol withdrawal syndrome (alcohol withdrawal seizure or DT) (53 vs 27%, OR 3.1, 95%CI 0.94 to 1.05)  There was no significant difference between case with a history of delirium tremens and those control without a history on: Number of previous alcohol detoxifications at a medical centre (ns)								
Mayo SM, Bernard D. Late-onset seizures in alcohol withdrawal.	Prospective cohort 2-	N=1044 (cohort)  From the cohort N=10 patients	Patients admitted for alcohol detoxification  Setting: Alcohol detoxification unit, Medical Centre	N=10 patients with seizure  Treatment Regimen: Fixed-dose and prn oxazepam	N=30 control patients without a seizure	NA	Association between seizure status and: age, history of withdrawal seizures, prior	None reported

DRAFT FOR CONSULTATION

<p><i>Alcoholism: Clinical &amp; Experimental Research.</i> 1995; 19(3):656-659. Ref ID: 181</p>		<p>with seizure matched with N=30 control patients without a seizure</p>	<p>Patient population:</p>				<p>detoxifications (no definition provided), history of DT</p> <p>Statistical analysis: univariate</p>	
<p>Effect</p> <p>The incidence of seizures (witnessed) was 11/1044 (1.1%). The seizures occurred 52 to 306 hrs after admission. A significantly greater proportion of those patients who had a seizure in the current admission had a history of withdrawal seizures compared with patients with a history (50 vs 13%; p&lt;0.05)</p> <p>There was no significant difference between the proportion of patients who had a seizures and those who did not with respect to:</p> <p>Age (ns)                  Previous detoxifications (ns)                  History of DT (ns)</p>								
<p>Shaw GK, Waller S, Latham CJ et al. The detoxification experience of alcoholic in-patients and predictors of outcome. <i>Alcohol &amp; Alcoholism.</i> 1998; 33(3):291-303. Ref ID: 1014</p>	<p>Prospective cohort 2-</p>	<p>N=160</p>	<p>Patients with alcohol dependence requiring medically assisted withdrawal</p> <p>Mean age 44 yrs, 59% socially unstable, 33% regular employment, male:female 131:29</p> <p>Setting Detoxification unit in psychiatric hospital</p>	<p>Treatment regimen: Fixed schedule chlomethiazole</p>	<p>Severity of alcohol withdrawal (8 items score 3 to 89)                  High grade 36 to 89                  Medium 5 to 35                  Low 3 to 15</p>	<p>NA</p>	<p>No. of previous detoxifications                  Severity of dependence (see text)                  Previous experience of withdrawal symptoms, family history of alcoholism</p> <p>Statistical analysis: stepwise multiple regression</p>	<p>None reported</p>
<p>Effect</p>								

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Predictors of severity of withdrawal  
 The proportion of patients experiencing high, medium and low grade withdrawal was 41/160, 77/160 and 42/160 respectively  
 Incidence of seizures 5/160 (3%) but two patients were epileptic

There was a significant difference between high vs. the medium and low scores of the severity of withdrawal scale for:  
 Alcohol dependence (SADQ) (high vs . medium and low) (41 vs 33 and 31; p<0.05)  
 Daily intake (U) on heavy drinking day (42 vs 33 and 31; p<0.05)  
 No. of detoxifications (7 vs. 2 and 1; p<0.05)  
 No. of years of heavy drinking (5 vs. 11 and 11; p<0.05)

In a stepwise multiple regression model, the following were predictors of severity of alcohol withdrawal:  
 Number of previous detoxifications (partial regression coefficient B=0.943)  
 Severity of alcohol dependence (SADQ) (B=0.327)  
 Previous experience of alcohol withdrawal symptoms (B=6.100)  
 Family history of withdrawal (B=2.069)  
 Multiple  $r^2 = 0.342$

<p>Worner TM. Relative kindling effect of readmissions in alcoholics. <i>Alcohol &amp; Alcoholism</i>. 1996; 31(4):375-380. Ref ID: 168</p>	<p>Retrospective cohort 2-  Unable to identify where discriminant function analysis or regression analysis has been performed</p>	<p>N=360</p>	<p>Patients admitted to alcohol detoxification  Setting: Detoxification unit in a hospital  Patient population: Seizure-positive male 55/68, mean age 40 yrs, mean duration of alcohol use 24 yrs, mean amount of alcohol 315 g/day  Seizure-negative: male 236/292, mean age 40 yrs, mean duration of alcohol use 24 yrs, mean amount of alcohol 316 g/day  There were no significant differences</p>	<p>Seizure-positive N=68  Treatment regimen: Chlordiazepoxide based on signs and symptoms or fixed dose (patient with seizure history)  Seizure history based on self or carer report and medical records</p>	<p>Seizure-negative N=292</p>	<p>Admissions over 5 yr period</p>	<p>Number of previous detoxifications Breath ethanol on admission  Statistical analysis: t-tests and regression analysis</p>	<p>None reported</p>
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DRAFT FOR CONSULTATION

			at baseline					
<p>Effect</p> <p>Seizure-positive vs seizure-negative:                  At the initial admission a history of seizures (positive N=16 vs negative N=44) was associated with the number of previous detoxifications:                  Mean number of detoxifications (2.78 vs 1.45; p&lt;0.01)                  On re-admission patients a history of seizures (positive N=26 and negative N=49) was associated with the number of previous detoxifications:                  Mean number of detoxifications (4.50 vs 2.83; p=0.0001)</p> <p>There was no association between a history of seizures and breath ethanol on admission or re-admission(ns)</p>								
Wright T, Myrick H, Henderson S et al. Risk factors for delirium tremens: a retrospective chart review. <i>American Journal on Addictions</i> . 2006; 15(3):213-219. Ref ID: 1027	Retrospective case-control 2-	N=56	Patients (cases) with alcohol withdrawal delirium (ICD-9) and controls with alcohol withdrawal (ICD-9)  Exclusion: females  Setting: Medical centre (including medicine department, ICU, psychiatry and surgery)  Patient population: mean age 54 yrs, 66% Caucasian, 23% employed  No significant differences were reported at baseline	Delirium tremens N=28  Treatment regimen: benzodiazepines but schedule not specified	No delirium tremens  N=28	NA	Risk of DT and: History of DT (documented in medical notes), no. of previous detoxifications (from medical records but not further definition given), drinking history  Statistics: univariate	National Institute for Alcohol Abuse and Alcoholism
<p>Effect</p> <p>DT vs no DT                  Patients who developed DT compared with those who did not were significantly:                  More likely to have a prior history of DT (56 vs 20%; p=0.05)</p> <p>There were no significant differences between patients with a history of DT and those without on:                  Standard drinks per drinking day (ns)                  Drinking days in previous week (ns)                  Previous inpatient detoxification (ns)</p>								
Brown ME, Anton RF,	Retrospective case series 3-	N=50	Patients with documented alcohol	Alcohol withdrawal	Without alcohol withdrawal	NA	Seizures and: multiple	None reported

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<p>Malcolm R et al. Alcohol detoxification and withdrawal seizures: clinical support for a kindling hypothesis. <i>Biological Psychiatry</i>. 1988; 23(5):507-514. Ref ID: 251</p>			<p>withdrawal seizures</p> <p>Setting: Alcohol detoxification unit, psychiatry unit, medical/surgical unit</p> <p>Compared with patients admitted to an alcohol treatment program without seizure or neurological disorder</p> <p>Patient population: The mean age of the withdrawal seizure group was significantly lower than the mean age of the control group (43 vs 49, <math>p &lt; 0.05</math>). There were significantly more white patients in the control group compared to the seizure group (76 vs 52%, <math>p &lt; 0.05</math>)</p>	<p>seizures N=25</p> <p>Treatment regimen: Oxazepam (64%). Schedule not specified</p>	<p>seizures N=25</p>		<p>detoxifications History of drinking</p> <p>Statistical analysis: Chi-square, t-tests, ANOVA</p>	
<p>Effect</p> <p>Seizure history vs no seizure history (control)</p> <p>Significantly more patients with a history of withdrawal seizures had undergone five or more detoxifications compared to patients in the control group (12/25(48%) vs 3/25 (12%); <math>p &lt; 0.05</math>)</p> <p>There was no significant difference between those patients with a history of seizures and the control patients on:</p> <p>Alcohol use in the month prior to admission (ns)</p> <p>Years of significant use (ns)</p> <p>Age at which they first started drinking (ns)</p>								
<p>Glenn SW, Parsons OA, Sinha R et al. The effects of repeated</p>	<p>Prospective case series 3-</p>	<p>N=143</p>	<p>Patients with alcohol dependence/alcoholism who undergone detoxification three to six weeks prior to</p>	<p>Treatment regimen: no details provided</p>	<p>NA</p>	<p>NA</p>	<p>Association between number of withdrawals and performance on</p>	<p>None reported</p>

DRAFT FOR CONSULTATION

<p>withdrawals from alcohol on the memory of male and female alcoholics. <i>Alcohol &amp; Alcoholism</i>. 1988; 23(5):337-342. Ref ID: 240</p>			<p>testing</p> <p>Setting: Hospital affiliated and private treatment settings</p> <p>Patient population: mean age 35 yrs, mean yrs of drinking 10, mean days drinking 239, mean typical quantity 367 g/day, mean typical quantity 0.06 g/kg</p>				<p>memory and learning tests</p>	
<p><b>Effect</b></p> <p>There was a significant effect of the number of withdrawals on tests of immediate and delayed semantic and figural memory but not learning tasks (ns). The number of withdrawals was significantly correlated with:</p> <ul style="list-style-type: none"> <li>• Weschler Sematic Memory Test (Story B) immediate (0.221; p&lt;0.01) and delayed (0.204; p&lt;0.01)</li> <li>• Figural Memory sub-test I immediate (-0.181; p&lt;0.05) Figural II immediate (-0.171; p&lt;0.05)</li> <li>• Figural Memory sub-test II delayed (-0.144; p&lt;0.01)</li> </ul> <p>Level 2++</p> <p>There was no significant correlation between the number of withdrawals and:</p> <ul style="list-style-type: none"> <li>• Story A immediate and delayed (ns)</li> <li>• Figural delayed (ns)</li> <li>• Symbol-Digit paired associated (learning test) (ns)</li> <li>• Face-Name (learning test) (ns)</li> </ul>								
<p>Lechtenberg R, Worner TM. Seizure risk with recurrent alcohol detoxification. <i>Arch Neurol</i>. 1990; 47(5):535-</p>	<p>Retrospective case series 3-  Univariate analysis</p>	<p>N=301</p>	<p>Patients admitted for alcohol detoxification</p> <p>Setting: Structured inpatient detoxification program</p> <p>Exclusion critiera included: acute medical problems</p> <p>Patient population:</p>	<p>Seizure history</p> <p>Treatment regimen: chlodiazepoxide based on signs and symptoms</p>		<p>NA</p>	<p>Seizure history and previous detoxifications (documented in hospital records and by patient/carer report, no further definition supplied)</p> <p>Statistical</p>	<p>None reported</p>

DRAFT FOR CONSULTATION

538. Ref ID: 1133			mean age 41 yrs, 64/301 antecedent seizure, mean alcohol consumption 292 g/daily, duration of alcohol use 24 yrs				analysis: univariate	
<p>Effect Incidence of seizures There were no seizures in the current detoxification period</p> <p>There was no significant association between a history of seizures and: Age (ns) Duration of alcohol abuse (ns) Quantity of alcohol consumed (ns)</p>								
Wojnar M, Bizon Z, Wasilewski D. Assessment of the role of kindling in the pathogenesis of alcohol withdrawal seizures and delirium tremens. <i>Alcoholism: Clinical &amp; Experimental Research.</i> 1999; 23(2):204- 208. Ref ID: 1016	Retrospective (N=892) and prospective (N=321) case series 3-	N=1213	Patients with alcohol withdrawal or delirium tremens (DSM-IV)  Setting: general psychiatric hospital  Exclusion: patients with concomitant substance dependence  Patient population: 82.9% male, aged 18 to 75 yrs mean 41 yrs		Treatment: Not reported	NA	Severity of withdrawal (CIWA-A), incidence of delirium tremens, incidence of seizures  Statistics: ANOVA or non parametric equivalent (no covariates or regression analysis)	None reported
<p>Effect The proportion of patients according to age was: &lt; 30 yrs N=140, 30 to 39 yrs N=437, 40 to 49 yrs N=394, 50 to 59 yrs N=192, ≥ 60 N=50.</p>								

## DRAFT FOR CONSULTATION

There was a significant difference in the age of onset of drinking ( $p < 0.0001$ ), duration of harmful drinking ( $p < 0.0001$ ) and average alcohol intake during the last drinking bout ( $p < 0.05$ ), according to age group. Older adults ( $\geq 60$  yrs) started intensive drinking on average 11 yrs later than younger patients ( $< 30$  yrs), but had drunk harmfully for a lot longer period of time (mean 18 yrs). The amount of alcohol consumed in the last drinking bout was significantly lower as the patients' age increased.

The mean CIWA-A score was 27

The mean incidence of delirium tremens was 26%

The mean incidence of withdrawal seizures was 4%

The mean daily dose of BZ was 51 mg (equivalent mg of diazepam)

The mean length of stay was 10 days

Factors associated with several withdrawal:

No significant associations were reported between age ( $< 30$ , 30 to 39, 40 to 49, 50 to 59 and  $\geq 60$  yrs) and:

The severity of alcohol withdrawal (CIWA-A score) (ns)

Incidence of delirium tremens (ns)

Incidence of withdrawal seizures (ns)

Mean daily BZ dose (ns)

Mean length of stay (ns)