research

Alcohol screening and intervention in clinical practice p 189

Effect of positioning in sedated adults p 192

Treatment of pruritus in patients receiving haemodialysis p 193

ADHD treatment and adverse outcomes p 194

Alcohol screening and brief intervention in clinical practice

ORIGINAL RESEARCH Pragmatic cluster randomised controlled trial

Effectiveness of screening and ultra-brief intervention for hazardous drinking in primary care

So R, Kariyama K, Oyamada S, et al

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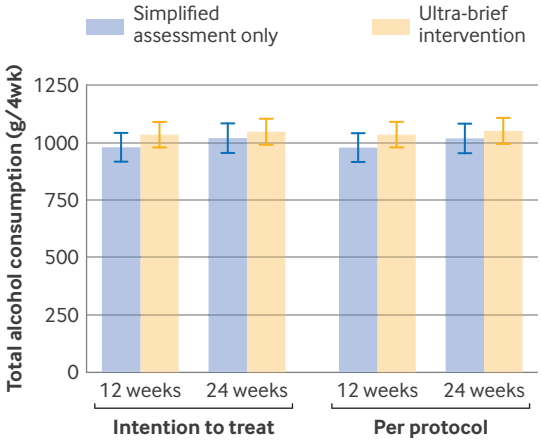
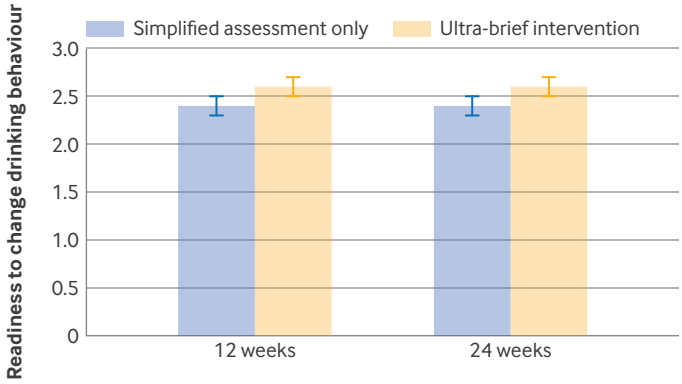
Study question Does a doctor delivered ultra-brief intervention reduce alcohol consumption in patients with hazardous drinking in primary care compared with simplified assessment alone?

Methods This pragmatic, cluster randomised controlled trial was conducted across 40 primary care clinics in Japan. 1133 patients aged 20-74 years with hazardous drinking (AUDIT-C (alcohol use disorders identification test-consumption) scores ≥5 for men and ≥4 for women) were randomly assigned to receive either ultra-brief intervention (<1 minute), comprising screening, brief oral feedback, and an alcohol information leaflet, or simplified assessment only, comprising a simplified assessment with AUDIT-C. The main outcome measures included total alcohol consumption in the four weeks preceding both the 24 week follow-up (primary outcome) and the 12 week follow-up (secondary outcome). Secondary outcomes also included readiness to change drinking behaviour, measured at 12 and 24 weeks.

Study answer and limitations At 24 weeks, the difference in total alcohol consumption between the ultra-brief intervention group (1046.9 g/4 weeks (g/4wk), 95% confidence interval (CI) 918.3 to 1175.4) and control group (1019.0 g/4wk, 893.5 to 1144.6) was 27.8 g/4wk (−149.7 to 205.4, P=0.75). At 12 weeks, the difference in total alcohol consumption between the intervention group (1034.1 g/4wk, 919.6 to 1148.7) and control group (979.3 g/4wk, 866.1 to 1092.4) was 54.9 g/4wk



Total alcohol consumption (grams in four weeks (g/4wk) preceding follow-up) at 12 and 24 weeks. Error bars represent standard errors



Readiness to change drinking behaviour, at 12 and 24 weeks. Error bars represent standard errors

(−104.1 to 213.9, P=0.49). Readiness to change drinking behaviour scores were higher in the intervention group than in the control group at both 12 weeks (difference 0.25, 95% CI 0.12 to 0.39) and 24 weeks (difference 0.19, 0.05 to 0.32). A limitation was that baseline alcohol consumption and readiness to change drinking behaviours were not collected for all participants.

What this study adds This trial found no evidence to support the effectiveness of a doctor delivered ultra-brief intervention for hazardous drinking compared with simplified assessment only in primary care in Japan.

Funding, competing interests, and data sharing The study was supported by a grant from the Japan Agency for Medical Research and Development awarded to authors RS, KN, and SM. RS and HN were employed by CureApp during the study. Some authors received personal fees from pharmaceutical companies or held patents outside the submitted work, as detailed in the full paper on bmj.com. Data and statistical codes are available at https://doi.org/10.5061/dryad.866t1g22m.

Trial registration UMIN Clinical Trials Registry UMIN000051388.

ANDY GIBSON/ALAMY

Screening has been a longstanding cornerstone of global public health strategies.[1] The seminal work of Edwards et al[2] facilitated the growth in alcohol screening and brief intervention (ASBI) research, resulting in numerous clinical trials and more than 40 systematic reviews across a variety of settings and modes of delivery, in addition to studies of cost effectiveness and implementation.

Interventions considered as brief typically range from 5-30 minutes and 1-5 sessions, making comparisons between studies difficult to interpret. In their study, So and colleagues present a well designed and conducted, pragmatic cluster randomised controlled trial on the effectiveness of alcohol screening and ultra-brief intervention, comprising an information leaflet and a verbal message, which was delivered in less than one minute by primary care doctors.[3] Participants included 1133 outpatients aged 20-74 years who scored ≥5 for men and ≥4 for women on the alcohol use disorders identification test–consumption (AUDIT-C) subscale, indicating hazardous/harmful drinking or alcohol dependence. The ultra-brief intervention did not reduce alcohol consumption compared with a simplified assessment. Given the size and rigour of this trial, it is important to consider the implications for ASBI as a public health measure to reduce harmful alcohol consumption.[4 5]

In a definitive Cochrane systematic review of ASBI in primary care and emergency departments, a meta-analysis included 34 studies (n=15 197).[6] Overall, participants who received brief intervention consumed less alcohol than those who received minimal or no intervention at 12 months. However, six out of 11 (55%) trials published between 1988 and 1999 reported positive outcomes, compared with just two out of 23 trials (9%) published between 2000 and 2014. The earlier trials reported considerably larger mean differences, with highly dispersed confidence intervals, compared with the later studies. The authors concluded that these changes over time may be due to wider inclusion criteria and increased intervention effects in control groups.

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Larger pragmatic trials may better reflect real world effectiveness

Another explanation for this finding might be the "decline effect" in systematic reviews of clinical interventions,[7] which may undermine the validity of meta-analyses.[8] The potential explanations for decline effects include publication bias, improvements in methodological rigour, and smaller early efficacy trials being superseded by larger effectiveness trials.[9] Also, pragmatic, multicentre effectiveness trials might achieve lower intervention fidelity than smaller single site trials.[10 11] This factor is important for clinical practice and policy, as larger pragmatic trials may better reflect real world effectiveness that could be expected in wider roll-out.

What the literature says

In longitudinal observational studies, people with less severe alcohol use disorders (AUDs) experience greater natural remission than those with more severe AUDs.[12] This effect is likely to be greater in risky drinkers, the primary target population in ASBI. As drinking fluctuates over time, selecting people who are consuming alcohol at a higher level at the point of screening and study enrolment may account for significant regression to the mean of drinking in both intervention and control groups.[11 13] Quality of life at entry to ASBI trials tends to be high, be similar to the general population mean, and show little change post-intervention, possibly owing to ceiling effects.[6] This means the potential for gains in quality of life years is limited compared with AUD populations with higher morbidity and lower quality of life.

Our large pragmatic clinical trials of ASBI in NHS primary care and emergency departments showed no difference in effectiveness between simple clinical feedback plus an information leaflet and longer ASBI (20 minutes of lifestyle counselling delivered by trained alcohol health workers).[11 13] So and colleagues' trial found no difference between the equivalent of our control condition and simplified assessment only.[3]

Clinical implications

In summary, the populations targeted by ASBI are mostly risky drinkers with a high regression to the mean effect, and they have low morbidity and a high quality of life at baseline. Therefore, what brief intervention might add to natural remission may be a relatively small effect of hastening a transition to lower alcohol intake, and that may be offset at a population level by increased intake in people who are temporarily consuming alcohol at a lower level who did not screen positive or receive an intervention. The early promise of ASBI has not been borne out in subsequent trials of real world effectiveness. Practitioners attribute the lack of widespread implementation of ASBI to a lack of time, training, and confidence to help patients reduce alcohol consumption.[14] Encouraging uptake of training by staff who do not specialise in alcohol disorders, as would pertain in widespread roll-out, is challenging.[10-15]

More value may be gained in screening and early detection of higher risk patients with AUD (eg, alcohol dependence) who have more substantial morbidity and a considerable gap in access to treatment.[16 17] Particularly so in higher prevalence populations (eg, acute hospitals and mental health services), with the purpose of facilitating earlier access to specialist alcohol treatments that are more likely to be clinically and cost effective.[18]

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Effect of lateral versus supine positioning on hypoxaemia in sedated adults

Ye H, Chu L-H, Xie G-H, et al

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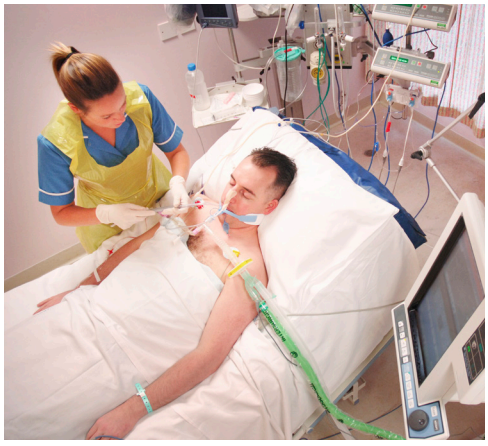
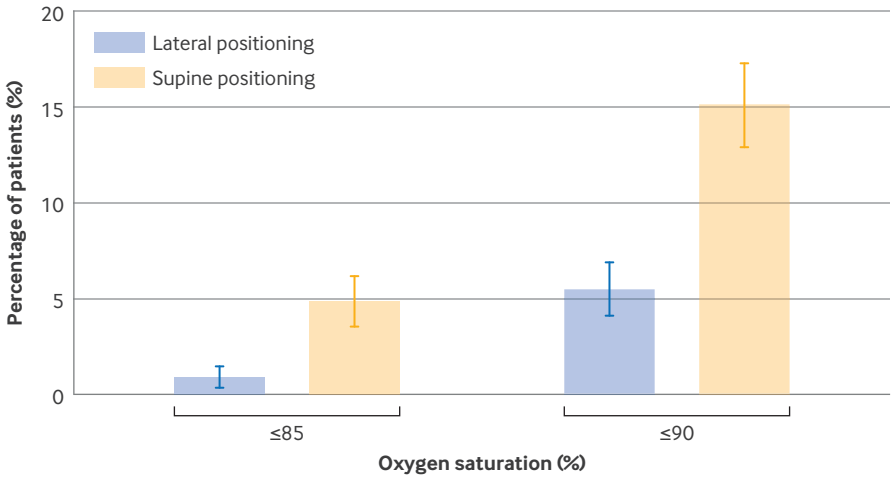
Study question Does lateral positioning reduce the incidence of hypoxaemia compared with supine positioning in sedated adults?

Methods In this multicentre randomised controlled trial conducted across 14 hospitals in China, 2159 sedated adults (≥18 years) in the post-anaesthetic care unit were randomly assigned (1:1) to receive either lateral positioning or supine positioning for 10 minutes. The primary outcome was the incidence of hypoxaemia, defined as peripheral oxygen saturation (SpO_2) ≤90% within the first 10 minutes after positioning. Secondary outcomes included the need for airway rescue interventions and the occurrence of severe hypoxaemia (SpO_2 ≤85%). Safety outcomes, including tachycardia and hypotension, were also monitored.





Percentage of patients with various degrees of hypoxaemia by randomised groups (lateral *v* supine positioning). Error bars represent 95% confidence intervals. Primary outcome was hypoxaemia, defined as oxygen saturation ≤90%; severe hypoxaemia, oxygen saturation ≤85%, was one of the secondary outcomes

Study answer and limitations Of 2159 patients randomised, 2143 were included in the primary analysis. The mean age of the patients was 53.1 years, mean body mass index was 23.9, and 53.7% (1150/2143) were women. The incidence of hypoxaemia was significantly lower in the lateral group compared with supine group (5.4% (58/1073) *v* 15.0% (161/1070); adjusted risk ratio 0.36, 95% confidence interval (CI) 0.27 to 0.49; P<0.001). Compared with patients in the supine group, patients in the lateral group required fewer airway rescue interventions (6.3% (68/1073) *v* 13.8% (148/1070); adjusted risk ratio 0.46, 0.34 to 0.61; P<0.001) and had a lower incidence of severe hypoxaemia (0.7% (8/1073) *v* 4.8% (51/1070); adjusted risk ratio 0.16, 0.07 to 0.33; P<0.001). Safety outcomes were comparable, but tachycardia occurred less frequently in the lateral group. Limitations included a patient population that was younger than western surgical populations and with a lower average body mass index, and lack of a semi-recumbent comparator.

What this study adds Lateral positioning substantially reduces both the incidence and the severity of hypoxaemia in sedated adults, decreasing the need for airway rescue interventions without compromising safety. The intervention represents a simple, cost effective respiratory management strategy suitable for widespread adoption, particularly in resource constrained settings.

Funding, competing interests, and data sharing
Funded by the National Natural Science Foundation of China. No competing interests declared. Data underlying the findings are available in Synapse.

Study registration ClinicalTrials.gov NCT06459167.

Efficacy and safety of anrikefon in patients with pruritus undergoing haemodialysis

Liu B-C, Li Z-L, Zhang P, et al

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Study question How efficacious and safe is anrikefon, a novel selective peripherally restricted kappa opioid receptor agonist, in patients with chronic kidney disease associated moderate to severe pruritus?

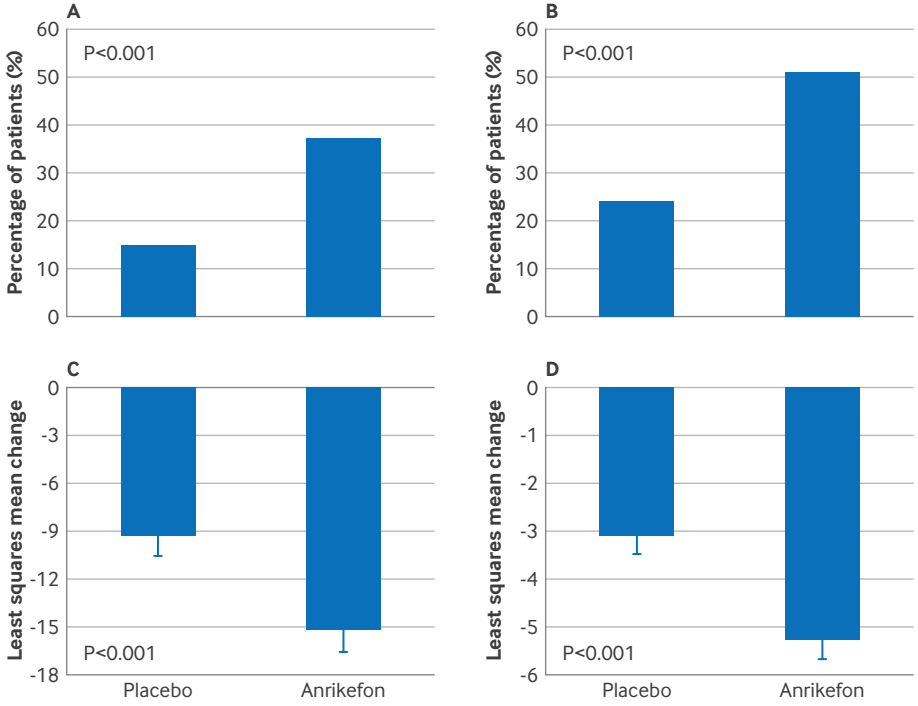
Methods This multicentre, double blind, randomised placebo controlled phase 3 trial was conducted at 50 centres in China. The trial comprised a double blind treatment phase for 12 weeks, followed by an open label extension of anrikefon treatment for 40 weeks. A total of 652 patients were screened, with 545 randomly assigned in a 1:1 ratio to receive either intravenous anrikefon (n=275) 0.3 µg/kg of body weight or placebo (n=270) three times weekly for 12 weeks, followed by an optional open label treatment phase with anrikefon for 40 weeks. The primary endpoint was the percentage of patients achieving at least a 4 point improvement from baseline to week 12 in the weekly mean 24 hour worst itching intensity numerical rating scale (WI-NRS) score. Secondary outcomes were the percentage of patients achieving at least a 3 point improvement in the weekly mean WI-NRS score, as well as changes in quality of life from baseline using the Skindex-10 and 5-D itch scales.

Study answer and limitations 243/275 (88%) patients in the anrikefon group and 254/270 (94%) in the placebo group completed the 12 week double blind treatment. 443 subsequently entered the 40 week open label extension phase. 37% of patients in the anrikefon group showed at least a 4 point reduction in WI-NRS score at week 12 compared with 15% in the placebo group (P<0.001). The percentage of patients with at least a 3 point reduction in WI-NRS score from baseline to week 12 was 51% in the anrikefon group compared with 24% in the placebo group (P<0.001).

The anrikefon group showed significant improvements in itch related quality of life (mean change from baseline in 5-D itch scale −5.3 *v* −3.1, P<0.001 and in Skindex-10 scale −15.2 *v* −9.3, P<0.001). Anrikefon also showed sustained long term efficacy during the open label extension phase at week 40, with persistent improvement in quality of life scores on the 5-D itch scale. Mild to moderate dizziness was more common in the anrikefon group than placebo group. As this trial exclusively enrolled patients with end stage renal disease requiring haemodialysis, the efficacy and safety of anrikefon in patients with chronic kidney disease who did not require dialysis remain to be investigated.

What this study adds In patients with moderate to severe pruritus undergoing haemodialysis, anrikefon was found to be safe and resulted in a noticeable reduction in itch intensity and an improvement in itch related quality of life. The continuous therapeutic effect and low incidence of central opioid adverse reactions suggest that anrikefon would be a promising new treatment option for patients with chronic kidney disease associated pruritus.

COSTFOTO/NURPHOTO/GETTY IMAGES



Proportion of patients in anrikefon and placebo groups at week 12 with at least a 4 point reduction from baseline in weekly mean 24 hour WI-NRS score (A) and at least a 3 point reduction from baseline in weekly mean WI-NRS score (B). Mean change from baseline in Skindex-10 scale (C) and 5-D itch scale (D) total score at 12 weeks. The Skindex-10 scale is a validated instrument designed to measure the impact of skin disease on patients' quality of life. The 5-D itch scale measures five dimensions of itch: degree, duration, direction, disability, and distribution. Error bars indicate standard errors. P values were calculated using χ^2 test (A and B) and analysis of covariance (C and D). WI-NRS=worst itching intensity numerical rating scale

Funding, competing interests, and data sharing
Funded by the Haisco Pharmaceutical Group. No competing interests declared. The data underlying the trial's findings are openly and publicly available at https://doi.org/10.5061/dryad.rr4xgxdk8.

Study registration ClinicalTrials.gov NCT05135390.

ADHD drug treatment and risk of suicidal behaviours, substance misuse, accidental injuries, transport accidents, and criminality

Zhang L, Zhu N, Sjölander A, et al

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Study question Does the use of drug treatment for attention deficit/hyperactivity disorder (ADHD) reduce the risk of suicidal behaviours, substance misuse, accidental injuries, transport accidents, and criminality in people with a new diagnosis of ADHD?

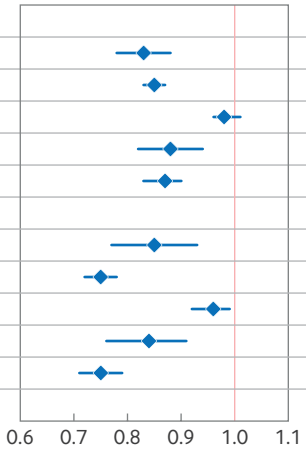
Methods This study used the target trial emulation design in 148 581 individuals aged 6-64 years with a new diagnosis of ADHD from Swedish national registers (2007-20) who either started or did not start drug treatment for ADHD within three months of diagnosis. Outcomes assessed over two years were first and recurrent events of suicidal behaviours, substance misuse, accidental injuries, transport accidents, and criminality. These outcomes were selected in consultation with people with lived experience of ADHD.

Study answer and limitations ADHD drug treatment was associated with significantly reduced rates of first occurrence of suicidal behaviours (adjusted incidence rate ratio 0.83, 95% confidence interval 0.78 to 0.88), substance misuse (0.85, 0.83 to 0.87), transport accidents (0.88, 0.82 to 0.94), and criminality (0.87, 0.83 to 0.90) but not accidental injuries (0.98, 0.96 to 1.01). Risk reductions were more pronounced for recurrent events, showing significant reductions for all five outcomes. A key limitation is the observational nature of the data. Despite use of methods to emulate a randomised trial, unmeasured confounding cannot be ruled out.

What this study adds This large national study provides evidence that drug treatment for ADHD is associated with reduced risks of suicidal behaviours, substance misuse, transport accidents, and criminality in people with ADHD. For recurrent events, ADHD drug treatment was associated with reduced rates of all five outcomes.

Funding, competing interests, and data sharing Funded by the Swedish Research Council for Health, Working Life and Welfare, the Swedish Research Council, and others (see full paper on bmj.com). See full paper for competing interests. Individual data cannot be shared publicly owing to Swedish law; code is available at Open Science Framework.

Initiation *v* non-initiation strategy	Initiation incidence rate	Non-initiation incidence rate	Incidence rate ratio (95% CI)
First events			
Suicidal behaviours	14.5	16.9	0.83 (0.78 to 0.88)
Substance misuse	58.7	69.1	0.85 (0.83 to 0.87)
Accidental injuries	88.5	90.1	0.98 (0.96 to 1.01)
Transport accidents	24.0	27.5	0.88 (0.82 to 0.94)
Criminality	65.1	76.1	0.87 (0.83 to 0.90)
Recurrent events			
Suicidal behaviours	22.7	24.3	0.85 (0.77 to 0.93)
Substance misuse	166.1	201.5	0.75 (0.72 to 0.78)
Accidental injuries	119.4	122.8	0.96 (0.92 to 0.99)
Transport accidents	31.6	37.2	0.84 (0.76 to 0.91)
Criminality	111.3	143.4	0.75 (0.71 to 0.79)



Attention deficit/hyperactivity disorder (ADHD) drug treatment and rates of first and recurrent outcome events over two year follow-up among people with ADHD. Incidence rates were calculated per 1000 person years. Numbers reported are weighted and account for follow-up censoring, including treatment discontinuation or switching. CI=confidence interval