Deutsch 2015

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Care Plan Usual Group Overall **Included criteria:** High-frequency ED users (4+ visits/year) with opiate addiction (opioid use disorder diagnosis) **Excluded criteria:** We excluded no eligible patients as candidates because of the following: 1) significant cardiac, renal, hepatic, endocrine, metabolic, neurologic or other systemic disease which, in the opinion of the principal investigator, would influence the results, or 2) hospice, end-of-life or comfort care only. **Pretreatment:** None of the differences were statistically significant
Interventions	**Intervention Characteristics** Care Plan • *This study evaluated the efficacy of electronic alerts to notify ED providers upon accessing the electronic medical record of an opiate use care plan for a patient.*: Use of electronic alerts to notify providers of an opioid-use care plan for high frequency ED patients. Usual Group • *This study evaluated the efficacy of electronic alerts to notify ED providers upon accessing the electronic medical record of an opiate use care plan for a patient.*: Care as usual.
Outcomes	*Change in Morphine Equivalents Given in Hospital* • **Outcome type**: Continuous Outcome • **Reporting**: Fully reported • **Scale**: Units • **Unit of measure**: Morphine Equivalents • **Direction**: Lower is better • **Data value**: Change from baseline *Change in Morphine Equivalents Given in Prescriptions* • **Outcome type**: Continuous Outcome • **Reporting**: Fully reported • **Direction**: Lower is better • **Data value**: Change from baseline *Change in Percent of Visits with Radiologic Imaging* • **Outcome type**: Continuous Outcome • **Unit of measure**: Percentage • **Direction**: Higher is better

	• **Data value**: Endpoint *Change in Total Charges Per Patient* • **Outcome type**: Continuous Outcome • **Reporting**: Fully reported • **Unit of measure**: Dollars • **Direction**: Lower is better • **Data value**: Endpoint *Change in Number of ED Visits* • **Outcome type**: Continuous Outcome • **Reporting**: Fully reported • **Unit of measure**: Number of Visits • **Direction**: Higher is better • **Data value**: Change from baseline *Change in the Percent of Visits with Labs Ordered* • **Outcome type**: Continuous Outcome • **Reporting**: Fully reported • **Unit of measure**: Percentage • **Direction**: Higher is better • **Data value**: Change from baseline
Identification	**Sponsorship source:** Not reported **Country:** USA **Setting:** Emergency Department **Comments:** This study revealed that a care plan for patients with a history of opiate abuse decreases the amount of opiates given to that patient and the percent of visits with advanced imaging. Total cost declined but was not statistically significant. The number of ED visits and percent of visits with lab tests were not reduced **Authors name:** Ashley Deutsch **Institution:** Baystate Medical Center, Springfield, MA **Email:** Not provided **Address:** Not provided
Notes	*Anees Bahji* on 06/10/2018 21:46 **Outcomes** This study revealed that a care plan for patients with a history of opiate abuse decreases the amount of opiates given to that patient and the percent of visits with advanced imaging. Total cost declined but was not statistically significant. The number of ED visits and percent of visits with lab tests were not reduced

Risk of bias table

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	High risk	

Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Study was explicitly non-blinded.
Blinding of outcome assessment (detection bias)	High risk	Judgement Comment: Study was explicitly non-blinded.

Andersen 1986

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Personalized Nursing Care as Usual Overall **Included criteria:** One hundred and fifty-five drug-dependent women in an urban hospital emergency room in Detroit, Michigan, were the subjects for this 3- year exploratory field study. Subjects were women who told the emergency room staff that while they wanted assistance with their presenting health problems, they wanted no assistance with their drug addiction. **Excluded criteria:** Not well described: however, anyone less than 18 years of age or male patients were not eligible. **Pretreatment:** It is important to note that the women referred to this study were drug dependent and refused referral to traditional treatment programs. In this sense they represented a reluctant treatment group. It became evident that these women had other drug treatment experiences and chose not to repeat those experiences.
Interventions	**Intervention Characteristics** Personalized Nursing • *Description*: The experimental women were treated using "Personalized Nursing," a nursing intervention model, which focused on providing assistance for client-identified concerns. Care as Usual • *Description*: Patients did not receive the individualized nursing appointments but were included in the pre and post assessment surveys.
Outcomes	*Daily Drug Cost* • **Outcome type**: Continuous Outcome • **Reporting**: Partially reported • **Data value**: Endpoint *Average Daily Heroin Cost* • **Outcome type**: Continuous Outcome • **Reporting**: Partially reported • **Unit of measure**: $ • **Data value**: Endpoint

	Change in Daily Drug Cost • **Outcome type**: Continuous Outcome • **Reporting**: Partially reported • **Unit of measure**: $ • **Data value**: Change from baseline
Identification	**Sponsorship source:** National Institute on Drug Abuse; DA-03059 **Country:** USA **Setting:** Emergency Room **Comments:** Results show that while there were no differences between the study groups at the pretest interview, the experimental group reported a lower daily drug cost (F(1, 95) = 2.90; p = 0.09), a lower daily heroin cost (U = 165; p = .01), less perceived stress (F(1, 84) = 3.00; p = .09) and emotional distress (F(1, 83) = 3.70; p = .06) than control subjects at the 8-week post-test. The experimental subjects also reported less perceived stress (t(65) = -2.35; p = .02) at 6-month follow-up than control subjects. It was found that results could be improved if members of the experimental clients' social networks were treated simultaneously and if project nurses were correctly utilizing the model. **Authors name:** Marcia D. Andersen **Institution:** College of Nursing, Wayne State University **Email:** Not provided **Address:** Not provided
Notes	*Anees Bahji* on 06/10/2018 22:05 **Outcomes** The experimental group reported a lower daily drug cost (F(1, 95) = 2.90; p = 0.09), a lower daily heroin cost (U = 165; p = .01), less perceived stress (F(1, 84) = 3.00; p = .09) and emotional distress (F(1, 83) = 3.70; p = .06) than control subjects at the 8-week post-test. The experimental subjects also reported less perceived stress (t(65) = -2.35; p = .02) at 6-month follow-up than control subjects. It was found that results could be improved if members of the experimental clients' social networks were treated simultaneously and if project nurses were correctly utilizing the model.

Risk of bias table

Blondell 2007

Methods	**Study design:** Prospective cohort study **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Buprenorphine Methadone Overall

	Included criteria: The study consisted of 662 consecutive admissions to a dedicated inpatient unit from May 1, 2004 to May 31, 2005, for medically man-aged detoxification from opioids. **Excluded criteria:** Patients treated with both medications (buprenorphine and methadone) and patients transferred to the psychiatric unit. **Pretreatment:** There was a significant difference (P 0.001) in the mean ages between those treated with methadone and those treated with buprenorphine (33±10 years vs. 36±11years, respectively). The mean age difference was 2.9 years and 95% CI of mean difference was 1.3-4.5. Those treated with buprenorphine were more likely (P= 0.025) to be under the age of 40 than those treated with methadone (70%vs. 62%). The insurance mix was significantly different between the two groups (P= 0.004).For example, as compared to those treated with methadone, those treated with buprenorphine were more likely to be uninsured (40% vs. 32%) and less likely to have Medicaid insurance (23% vs. 36%)
Interventions	**Intervention Characteristics** Buprenorphine • *Description*: Partial agonist of opioid receptor. Methadone • *Description*: Long-acting synthetic full agonist of the opioid receptor.
Outcomes	*Completion of Inpatient Detoxification (%)* • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Unit of measure**: % • **Direction**: Higher is better • **Data value**: Endpoint *Completion of Inpatient Detoxification (n)* • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Unit of measure**: number (n) • **Direction**: Higher is better • **Data value**: Endpoint
Identification	**Sponsorship source:** This study was supported, in part, by a grant from Research for Health in Erie County (RLS) and by GrantK23-AA015616 from the National Institute on Alcohol Abuse and Alcoholism (RDB). **Country:** USA **Setting:** Inpatient Detoxification

	Comments: Buprenorphine and methadone are both effective for the control of the acute signs and symptoms of opiate withdrawal, but it is not known if there are differences between these two medications for other important clinical outcomes. This observational, non-randomized study evaluated completion rates of patients over a 13-month period when buprenorphine replaced methadone as the medication used for short-term inpatient opiate detoxification. Of the 644 patients in the study, the 303 treated with buprenorphine were more likely to complete detoxification than the341 treated with methadone (89% vs. 78%;P .001). Improvement in completion rates coincided with the introduction of buprenorphine. We conclude that as compared to methadone, buprenorphine is associated with greater rates of completion of inpatient detoxification. **Authors name:** Richard D. Blondell **Institution:** Department of Family Medicine, The State University of New York, University at Buffalo, Buffalo, New York **Email:** blondell@buffalo.edu **Address:** Richard D. Blondell, MD, 462 Grider Street CC-175, Buffalo, NY
Notes	*Anees Bahji* on 06/10/2018 22:18 **Outcomes** Of the 644 patients in the study, the 303 treated with buprenorphine were more likely to complete detoxification than the 341 treated with methadone (89% vs. 78%;P .001). Improvement in completion rates coincided with the introduction of buprenorphine. We conclude that as compared to methadone, buprenorphine is associated with greater rates of completion of inpatient detoxification.

Risk of bias table

DeAtley 2017

Methods	**Study design:** Retrospective cohort study **Study grouping:** Parallel group
Participants	**Baseline Characteristics** morphine 0.04 mg/kg/dose administered orally every 4 hours morphine 0.06 mg/kg/dose administered orally every 3 hours Overall **Included criteria:** The study population consisted of all newborn patients admitted to the facility who were diagnosed with neonatal abstinence syndrome (NAS) and received morphine to treat signs and symptoms consistent with NAS during 2014 and 2015. 71 neonates were diagnosed with neonatal abstinence syndrome (NAS) and required morphine for treatment during the 2-year study time frame.

	Excluded criteria: 59 patients were included and 12 were excluded from the statistical analysis due to institutional transfer early during admission or because an agent other than morphine was used to treat NAS. **Pretreatment:** Of the 59 included neonates, 33 were included in the protocol 1 group, and 26 were included in the protocol 2 group. The authors present some tables of the characteristics of participants in the two groups, such as maternal drug exposures, neonatal comorbidities, and discharge disposition, however, they do not describe to what extent the groups are different.
Interventions	**Intervention Characteristics** morphine 0.04 mg/kg/dose administered orally every 4 hours • *Description*: Low dose morphine protocol. morphine 0.06 mg/kg/dose administered orally every 3 hours • *Description*: High dose morphine protocol.
Outcomes	*Length of Hospital Stay* • **Outcome type**: Continuous Outcome • **Reporting**: Partially reported • **Unit of measure**: Days • **Direction**: Lower is better • **Data value**: Change from baseline *Average Duration of Treatment* • **Outcome type**: Continuous Outcome • **Reporting**: Partially reported • **Unit of measure**: Days • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** N/R **Country:** USA **Setting:** Level 2 Nursery in a Community Hospital **Comments:** The authors sought to evaluate the impact on length of hospital stay and treatment duration of morphine after implementation of a change in the institutional protocol for managing neonatal abstinence syndrome (NAS) in an effort to improve patient outcomes. A single-center, retrospective chart review was conducted at a Level II nursery in a community hospital in Kentucky. Fifty-nine neonates born between January 1, 2014, and December 31, 2015, who were diagnosed with NAS and received morphine for treatment were included. The protocol 1 group consisted of 33 neonates who received an initial dose of morphine 0.04 mg/kg/dose administered orally every 4 hours (January 1–December 31,2014), and the protocol 2 group consisted of 26 neonates who received an initial dose of

	morphine0.06 mg/kg/dose administered orally every 3 hours (January 1–November 30, 2015), after a change in the protocol for managing NAS was implemented on January 1, 2015. Data were reviewed and com-pared between the two protocol groups to determine the impact that the dosage change had on length of hospital stay and morphine treatment duration. The average length of stay decreased by 7 days in the protocol 2 group compared with the protocol 1 group (21 vs 28.65 days). The average duration of treatment decreased by 7 days in the protocol 2 group compared with the protocol 1 group (18.3 vs 25.4 days). These differences between groups were not statistically significant, however, because the population size was not large enough to achieve adequate power. These results indicate that protocol 2 displayed the potential to decrease length of stay and duration of treatment compared with protocol 1 at this facility; however, balancing higher starting doses with the risk of over sedation will continue to challenge the health care team. Concern for over sedation when using the higher starting dose in protocol 2 has prompted further research (e.g., protocol 3, initial morphine 0.05 mg/kg/dose every 3 hrs). Continued research is also necessary with larger patient populations to enable generalizability to other institutions **Authors name:** Heather N. DeAtley **Institution:** Inpatient Pharmacy Department, Ephraim McDowell Regional Medical Center, Danville, Kentucky **Email:** hdeatley@emhealth.org **Address:** 217 South 3rd Street, Danville, KY 40422
Notes	

Risk of bias table

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	
Allocation concealment (selection bias)	High risk	
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	
Other bias	Unclear risk	

D'Onofrio 2015

Methods	**Study design:** Randomized controlled trial

	Study grouping: Parallel group
Participants	**Baseline Characteristics** Buprenorphine Referral Brief Intervention Overall **Included criteria:** All patients 18 years or older who were opioid-dependent who were treated at an urban university teaching hospital emergency department. **Excluded criteria:** Non–English speaking, critically ill, unable to communicate due to dementia or psychosis, suicidal, or in police custody. **Pretreatment:** There were no grossly observed significant differences in baseline characteristics, however, authors did not measure the statistical significance of differences in baseline characteristics.
Interventions	**Intervention Characteristics** Buprenorphine • *Description*: Screening, brief intervention, ED-initiated treatment with buprenorphine/naloxone, and referral to primary care for 10-week follow-up. Referral • *Description*: Screening and referral to treatment. Brief Intervention • *Description*: Screening, brief intervention, and facilitated referral to community-based treatment services.
Outcomes	*Enrolment in and Receiving Addiction Treatment 30 days After Randomization* • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Direction**: Higher is better • **Data value**: Endpoint *Number of days of illicit opioid use per week* • **Outcome type**: Continuous Outcome • **Reporting**: Fully reported • **Unit of measure**: Days • **Direction**: Lower is better • **Data value**: Endpoint *rates of urine samples that tested negative for opioids* • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Unit of measure**: % • **Direction**: Lower is better

	• **Data value**: Endpoint *Use of Inpatient Addictions Treatment* • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Unit of measure**: % • **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** Not reported **Country:** USA **Setting:** Emergency Department **Comments:** This study tested the efficacy of 3 interventions for opioid dependence: (1) screening and referral to treatment (referral); (2) screening, brief intervention, and facilitated referral to community-based treatment services (brief intervention); and (3) screening, brief intervention, ED-initiated treatment with buprenorphine/naloxone, and referral to primary care for 10-week follow-up (buprenorphine). Among opioid-dependent patients, ED-initiated buprenorphine treatment vs brief intervention and referral significantly increased engagement in addiction treatment, reduced self-reported illicit opioid use, and decreased use of inpatient addiction treatment services but did not significantly decrease the rates of urine samples that tested positive for opioids or of HIV risk. These findings require replication in other centers before widespread adoption. **Authors name:** Gail D'Onofrio **Institution:** Department of Emergency Medicine, Yale School of Medicine **Email:** gail.donofrio@yale.edu **Address:** Gail D'Onofrio, MD, MS, Department of Emergency Medicine, Yale School of Medicine, 464 Congress Ave, Ste 260, New Haven, CT 06159
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Low risk	
Incomplete outcome data (attrition bias)	Low risk	

Selective reporting (reporting bias)	Low risk	
Other bias	Unclear risk	

Favrat 2006

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Rapid Opiate Detoxification Under Anaesthesia Clonidine Detoxification Overall **Included criteria:** Enrolled patients admitted to the substance abuse detoxification unit of the psychiatric teaching hospital, Lausanne, Switzerland between May 2000 and May 2002. The inclusion criteria were opiate dependence diagnosed according to DSM IV (1994), age over 18 years and consent to be detoxified. **Excluded criteria:** The exclusion criteria were alcohol, cocaine, or benzodiazepine dependence, pregnancy, known idiosyncratic reactions, severe psychiatric comorbidity and other serious medical conditions. Positive urine toxicology result on day of procedure also caused exclusion of participant from study. **Pretreatment:** The groups are comparable as regards the baseline characteristics. The group of eligible patients declining to participate in the study did not differ statistically with respect to baseline variables from the group who agreed to take part in the study. The authors found no statistical differences for baseline variables. The proportions of patients involved in a methadone treatment programme on a regular daily basis were similar in both groups (14/26 in the anaesthesia group and 10/21 in the clonidine group). 7/26 (27%) in the anaesthesia group joined an inpatient therapeutic community after the procedure versus 8/21 (38%) in the clonidine group (p= 0.41).
Interventions	**Intervention Characteristics** Rapid Opiate Detoxification Under Anaesthesia • *Description*: An accelerated opioid detoxification performed using opioid antagonist medication under general anesthesia. Clonidine Detoxification • *Description*: Traditional detoxification.
Outcomes	*Successful Detoxification* • **Outcome type**: Dichotomous Outcome *Self-Reported Abstinence* • **Outcome type**: Dichotomous Outcome • **Unit of measure**: %

Identification	**Sponsorship source:** This study was supported by the Swiss Federal Office of Public Health. **Country:** Switzerland **Setting:** Specialized substance abuse unit in a psychiatric teaching hospital and an intensive care unit of a general hospital. **Comments:** Although the detoxification success rate and abstinence after 3 months were slightly better for the RODA procedure compared to clonidine treatment, these differences were not statistically significant and disappeared completely after 6 and 12 months. **Authors name:** Bernard Favrat **Institution:** Substance Abuse Division, Department of Psychiatry, University of Lausanne **Email:** Bernard.Favrat@hospvd.ch **Address:** Substance Abuse Division, Department of Psychiatry, University of Lausanne, Medical Outpatient Clinic, Bugnon 44,1011 Lausanne, Vaud, Switzerland
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	
Sequence Generation	Low risk	

Foy 1989

Methods	**Study design:** Prospective cohort study **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Methadone Maintenance Overall **Included criteria:** Adults consecutively admitted for methadone maintenance program as an inpatient to the hospital. **Excluded criteria:** N/A **Pretreatment:** N/A
Interventions	**Intervention Characteristics**

	Methadone Maintenance • *ad*: Long-acting synthetic opioid receptor agonist that can alleviate symptoms of opioid withdrawal.
Outcomes	*Stable State (Abstinence for 3+ Months)* • **Outcome type**: Dichotomous Outcome
Identification	**Sponsorship source:** Not described **Country:** Australia **Setting:** Royal Newcastle Hospital **Comments:** In a prospective study of 63 admissions to a methadone maintenance programme in a public hospital, 13 admissions were for less than two weeks. Of the remaining 50 such admissions, 35 admissions were terminated because of absenteeism, drug abuse, violence or drug-dealing. Twelve patients did not take intravenously administered drugs during the time that they were receiving methadone, but in 25 of the 50 admissions that lasted for more than two weeks, such drugs were abused at least fortnightly. Eight patients achieved a stable state without drugs that lasted at least three months. No improvements were note in patients' social situations, relationships, health or criminal activity, but compliant patients did improve their employment status. A significant minority of patients has benefited from methadone maintenance therapy, but most patients have continued their drug abuse and drug-related life-styles. **Authors name:** Aidan Foy **Institution:** University of Newcastle **Email:** aidan.foy@newcastle.edu.au **Address:** Callaghan, University Drive, Callaghan, NSW 2308, Australia
Notes	*Anees Bahji* on 05/10/2018 23:34 **Included** No full text *Anees Bahji* on 06/10/2018 23:27 **Included** Emailed author for full-text

Risk of bias table

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	High risk	

Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	
Sequence Generation	Low risk	

G 2013

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Group A: Lateral/Superior NAc Lesion Expansion Group B: Anterior/Superior NAc Lesion Expansion Group C: Lateral/Anterior NAc Lesion Expansion Group D: Lateral/Superior/Anterior NAc Lesion Expansion Overall **Included criteria:** Heroin abuse using 0.3-1.0g daily for at least three years by IV injection without concomitant IN use; failure of prior treatments with 5+ relapses; 18-50 years old; no surgical contraindication; completion of detox preoperatively with no withdrawal symptoms and negative urine toxicology screen. **Excluded criteria:** Inability to provide informed consent; HIV/HBC/HCV carriers; developmental/cognitive delay; personality disorders; neuropsychiatric diseases (other than addiction); no other additional treatment of opioid addiction postoperatively. **Pretreatment:** Groups were fairly similar in terms of their baseline characteristics.
Interventions	**Intervention Characteristics** Group A: Lateral/Superior NAc Lesion Expansion • *Description*: Lateral superior lesion expansion. Group B: Anterior/Superior NAc Lesion Expansion • *Description*: Anterior superior lesion expansion. Group C: Lateral/Anterior NAc Lesion Expansion • *Description*: Lateral anterior lesion expansion. Group D: Lateral/Superior/Anterior NAc Lesion Expansion • *Description*: Lateral, superior anterior lesion expansion.
Outcomes	*Abstinence Rate at Fourth Post-Operative Year* • **Outcome type**: Dichotomous Outcome • **Reporting**: Fully reported • **Unit of measure**: % • **Direction**: Higher is better • **Data value**: Endpoint *Long Term Neuropsychiatric Adverse Events* • **Outcome type**: Adverse Event • **Unit of measure**: %

	• **Direction**: Lower is better • **Data value**: Endpoint
Identification	**Sponsorship source:** China National 11th Five Years Scientific Support Plan, among other sources (listed). **Country:** China **Setting:** Tangdu Hospital Fourth Military Medical University **Comments:** Stereotactic ablation of the nucleus accumbens (NAc) has the potential to effectively treat opioid use disorder, however, there are concerning neuropsychiatric adverse effects; this study was prematurely stopped due to government intervention. **Authors name:** Xuelian Wang **Institution:** Department of Neurosurgery, Tangdu Hospital ,Xi'an, Chin **Email:** tdwxlian@126.com **Address:** Department of Neurosurgery, Tangdu Hospital, Xi'an, China
Notes	

Risk of bias table

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	Low risk	
Blinding of outcome assessment (detection bias)	Low risk	
Incomplete outcome data (attrition bias)	High risk	
Selective reporting (reporting bias)	High risk	
Other bias	High risk	
Sequence Generation	Unclear risk	

J 2013

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** 5-day buprenorphine detoxification Buprenorphine induction, intra-hospital dose stabilization, and post-discharge transition to maintenance buprenorphine OAT Overall **Included criteria:** Eligible (not alcohol dependent, no benzodiazepine misuse), and consenting patients to be in the study. Opioid dependency diagnosis was confirmed with the Structured Clinical interview for DSM Disorders. **Excluded criteria:** Not listed.

	Pretreatment: Among 119 participants, the mean age was 40.1 (±11.8) years, 85 (71.4 %) were male, 50 (42.0 %) were non-Hispanic Caucasian, 35 (29.4 %) were African-American, and 25 (21.0 %) were Latino. Control and intervention arms did not differ significantly (all p values >.4) on demographic characteristic.
Interventions	**Intervention Characteristics** 5-day buprenorphine detoxification • *Description*: Traditional opioid detoxification using buprenorphine to manage withdrawal symptoms. Buprenorphine induction, intra-hospital dose stabilization, and post-discharge transition to maintenance buprenorphine OAT • *Description*: Patients are connected with maintenance therapy with buprenorphine initiated in the hospital.
Outcomes	*Entry into outpatient buprenorphine OAT* • **Outcome type**: Dichotomous Outcome • **Data value**: Endpoint *Days receiving OAT* • **Outcome type**: Continuous Outcome • **Data value**: Endpoint *OAT Retention* • **Outcome type**: Dichotomous Outcome • **Data value**: Endpoint
Identification	**Sponsorship source:** Not specified **Country:** USA **Setting:** Hospitalized Patients **Comments:** LINKAGE was able to enrol 74 % of out-of-treatment, opiate-dependent hospitalized persons in buprenorphine OAT. Compared to standard inpatient detox, initiation of and linkage to buprenorphine treatment is an effective mean for engaging medically hospitalized patients who are not actively seeking care for their substance dependence in long-term addiction treatment. Integrating OAT into inpatient medical care is a promising avenue to reach persons with opioid dependence. **Authors name:** Jane M. Liebschutz **Institution:** Boston University School of Medicine, Boston, MA **Email:** Not provided **Address:** Not provided
Notes	

Risk of bias table

Bias	**Authors' judgement**	**Support for judgement**

Allocation concealment (selection bias)	High risk	
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	
Other bias	Unclear risk	
Sequence Generation	Unclear risk	

Lawal 1998

Methods	**Study design:** Prospective cohort study **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Full Assessment, Detoxification, and Treatment Overall **Included criteria:** Eighty patients, managed primarily for heroin and cocaine dependence on an inpatient detoxification unit of the hospital. **Excluded criteria:** N/A **Pretreatment:** N/A
Interventions	**Intervention Characteristics** Full Assessment, Detoxification, and Treatment • *What does it include?* The management package included full assessment, detoxification, treatment of associated physical conditions, group therapy sessions, occupational and vocational rehabilitation.
Outcomes	*Completion of Inpatient Detoxification (%)* • **Outcome type**: Dichotomous Outcome *Attendance at Outpatient Follow-up* • **Outcome type**: Dichotomous Outcome
Identification	**Sponsorship source:** Not reported **Country:** Nigeria **Setting:** Hospital **Comments:** Eighty patients, managed primarily for heroin and cocaine dependence at the Drug Rehabilitation Unit of Psychiatric Hospital, Yaba, Lagos, were followed up monthly for a period of 12 months post-discharge and assessed with regard to continued substance use, employment status and illegal activities. The management package included full assessment, detoxification, treatment of associated physical conditions, group therapy sessions, occupational and vocational rehabilitation. The sample was predominantly male (91%),

	young adults (mean age 29.1 years; SD 5.99) and single (58%). Although 95% had some formal education, many were school drop-outs, and only 31.3% were gainfully employed. The majority (84%), used a combination of heroin and cocaine, almost all on a daily basis, mainly by smoking and "chasing the dragon" (95%). Other substances reportedly used preadmission were alcohol (22.5%), cannabis (76.3%) and tobacco (97.5%). Less than one half (43.8%) completed the minimum one month required for inpatient treatment. Only seven (8.7%) attended the follow-up clinic regularly, but all defaulters were assessed in their homes. The level of heroin, cocaine and cannabis use, as well as report of illegal activities, dropped sharply from the first month post-discharge, but started to rise again (albeit slowly) by the second half of the follow-up period. There was only a slight insignificant gain in employment status of patients during the follow-up period. The community-based management approach is strongly advocated as a way of addressing the several factors identified in this study as militating against the successful management of substance abusers. **Authors name:** R.A. Lawal **Institution:** Drug Rehabilitation Unit of Psychiatric Hospital, Yaba, Lagos **Email:** Not supplied **Address:** Not supplied
Notes	*Anees Bahji* on 06/10/2018 05:02 **Included** No full text available *Anees Bahji* on 07/10/2018 23:57 **Included** Not an intervention study!

Risk of bias table

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	

Sequence Generation	Low risk	

Lintzeris 2008

Methods	**Study design:** Retrospective Case File Audit **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Naltrexone Implant Overall **Included criteria:** Patients who had received a naltrexone implant for the treatment of heroin dependence (an unlicensed product for this indication in Australia). Identified through referrals to Drug and Alcohol Consultation–Liaison services over a 12-month period, August 2006 to July 2007. **Excluded criteria:** N/A **Pretreatment:** N/A
Interventions	**Intervention Characteristics** Naltrexone Implant • *Description*: Naltrexone is a long-acting opioid antagonist that is theorized to have efficacy in the treatment of heroin dependence.
Outcomes	*Severe opiate withdrawal and dehydration* • **Outcome type**: Adverse Event • **Reporting**: Fully reported • **Unit of measure**: n • **Direction**: Lower is better • **Data value**: Endpoint *Average hospital stay* • **Outcome type**: Continuous Outcome • **Unit of measure**: Days • **Direction**: Lower is better • **Data value**: Endpoint *Severe Infection* • **Outcome type**: Adverse Event • **Data value**: Endpoint *Anxiety* • **Outcome type**: Adverse Event • **Data value**: Endpoint *Analgesia Complications* • **Outcome type**: Adverse Event *Cardiac Arrhythmia* • **Outcome type**: Adverse Event • **Data value**: Endpoint
Identification	**Sponsorship source:** Not described

	Country: Australia **Setting:** 2 Sydney Teaching Hospitals **Comments:** Objective: To describe hospital presentations related to the use of naltrexone implants, an unlicensed product used in Australia for treating heroin dependence. Design: Retrospective case file audit. Setting: Two Sydney teaching hospitals. Patients: Identified through referrals to Drug and Alcohol Consultation–Liaison services over a 12-month period, August 2006 to July 2007.Main outcome measures: Diagnosis, management and duration of admission. Results: Twelve cases were identified: eight were definitely or probably related to naltrexone implants or the implantation procedure (rapid detoxification). Of these, six patients had severe opiate withdrawal and dehydration, with an average hospital stay of 2.3 days. One patient had an infection at the implant site, and one an underlying anxiety disorder requiring psychiatric admission. Three patients had analgesia complications, and one had unrelated cardiac arrhythmia. Conclusions: These severe adverse events challenge the notion that naltrexone implants are a safe procedure and suggest a need for careful case selection and clinical management, and for closer regulatory monitoring to protect this marginalized and vulnerable population. **Authors name:** Nicholas Lintzeris **Institution:** Drug Health Services, Sydney South West Area Health Service, Sydney, NSW **Email:** nicholas.lintzeris@sswahs.nsw.gov.au **Address:** Not Provided
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	High risk	
Other bias	High risk	Judgement Comment: Did not look at potential benefits.

Sequence Generation	Unclear risk	Judgement Comment: N/A

M 2013

Methods	**Study design:** Prospective cohort study **Study grouping:** Parallel
Participants	**Baseline Characteristics** 6-week Inpatient Opiate Detoxification Overall **Included criteria:** A group of 113 patients consecutively admitted to a closed detoxification unit between October 2011 and September 2012 were assessed at the beginning of the treatment, after three and six months using a variety of semi structured research scales. **Excluded criteria:** N/A **Pretreatment:** N/A
Interventions	**Intervention Characteristics** 6-week Inpatient Opiate Detoxification • *Description*: Traditional multidisciplinary rehabilitation performed on an inpatient unit.
Outcomes	*Complete abstinence in the 28 days before review* • **Outcome type**: Dichotomous Outcome *Heroin use* • **Outcome type**: Dichotomous Outcome *Other drug use* • **Outcome type**: Dichotomous Outcome
Identification	**Sponsorship source:** Not described **Country:** Slovenia **Setting:** Centre for treatment of drug addiction (an inpatient closed-ward hospital detoxification program) **Comments:** Introduction: In the field of drug abuse treatment, non-completion and negative outcome is a general problem. Objectives: Outcome of hospital treatment of opioid dependence was examined. Aims: The purpose of the present study was examination of a cohort of patients treated at Centre for treatment of drug addiction at the beginning of the treatment, after three and six months. Methods: A group of 113 patients consecutively admitted to a closed detoxification unit between October 2011 and September 2012 were assessed. Positive outcome of the treatment is defined as complete abstinence in the 28 days before review. Baseline data were obtained using The Treatment Outcomes Profile (TOP), The Drug Addiction Treatment Efficacy Scale (DATES), and a semi structured research interview for obtaining information on patient's sociodemographic characteristics. Follow up scores of TOP and DATES have been recorded after three and six months. Results: Fifty-two patients

	completed 6 weeks of detoxification program. After 3 months 45 of 84 evaluated subjects (53%)had a positive outcome, 14 patients (12%) abused heroin and 36 patients (32%) abused other drugs. After 6 months 14 of 52evaluated patients (27%) had a positive outcome and 9 patients (8%) used heroin. Conclusion: The share of patients with positive outcome peaked at 3 months, however the decreased use of heroin was sustained throughout the observation period. **Authors name:** M. Delic **Institution:** Centre for Treatment of Drug Addiction Ljubljana **Email:** Not provided **Address:** Not provided
Notes	

Risk of bias table

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	High risk	
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	
Sequence Generation	Unclear risk	

McKnight 2016

Methods	**Study design:** Retrospective cohort study **Study grouping:** Parallel group
Participants	**Baseline Characteristics** NICU Rooming In Overall **Included criteria:** Infants at risk of neonatal abstinence syndrome (NAS) who were either admitted to the neonatal intensive care unit (NICU) or to the rooming-in program over a 13-month period. **Excluded criteria:** N/A **Pretreatment:** N/A
Interventions	**Intervention Characteristics** NICU • *Some centers have instituted a policy of rooming-in for infants at risk of NAS, where infants are observed for signs of*

	withdrawal while staying in the same room with their mothers.: Traditional observation provided for neonates at risk for neonatal abstinence syndrome. Rooming In • *Some centers have instituted a policy of rooming-in for infants at risk of NAS, where infants are observed for signs of withdrawal while staying in the same room with their mothers.*: Some centers have instituted a policy of rooming-in for infants at risk of NAS, where infants are observed for signs of withdrawal while staying in the same room with their mothers.
Outcomes	*Needed pharmacologic treatment of NAS* • **Outcome type**: Dichotomous Outcome • **Data value**: Endpoint *Median Days in Hospital* • **Outcome type**: Continuous Outcome • **Unit of measure**: Days • **Direction**: Lower is better • **Data value**: Endpoint *Median days treated with morphine* • **Outcome type**: Continuous Outcome • **Unit of measure**: Days • **Data value**: Endpoint *Median maximum daily dose of 1st line medication in mg/kg/day* • **Outcome type**: Continuous Outcome • **Unit of measure**: mg/kg/day • **Direction**: Lower is better • **Data value**: Change from baseline *Number who needed adjunctive clonidine* • **Outcome type**: Dichotomous Outcome
Identification	**Sponsorship source:** Philanthropic contributions (not a research grant or formal sponsorship source). **Country:** Canada **Setting:** General Hospital **Comments:** Objective: to examine the impact of a rooming-in program for infants at risk of neonatal abstinence syndrome (NAS) on the need for pharmacologic treatment and length of hospitalization. Study Design: our hospital implemented a rooming-in program for newborns at risk of NAS in June 2013. Previously, standard care was to admit these infants to the neonatal intensive care unit (NICU). Charts were reviewed to abstract data on at-risk infants born in the13-month periods prior and subsequent to implementation of rooming-in (n = 24 and n = 20, respectively) and the groups were compared with the

	outcomes of interest. Result: rooming-in was associated with a reduced need for pharmacologic treatment and shorter length of stay. Conclusion: these findings add to an emerging body of evidence on the health care resource utilization benefits associated with rooming-in for infants at risk of NAS. Future studies should evaluate a broader range of outcomes for this model of care. **Authors name:** Kimberly Dow **Institution:** Department of Pediatrics, Queen's University, Kingston, Ontario, Canada **Email:** dowk@queensu.ca **Address:** Department of Pediatrics, Kingston General Hospital, 76 Stuart Street, Kingston, Ontario, K7L 2V7, Canada
Notes	*Anees Bahji* on 08/10/2018 00:45 **Outcomes** All values were the same for the rooming-in group for the dose of the 1st line medication that could be given; accordingly, the median and IQR could not be calculated.

Risk of bias table

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	
Sequence Generation	Low risk	

Ochoa 2008

Methods	**Study design:** Prospective cohort study **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Inpatient Detoxication Overall **Included criteria:** Inpatients who underwent detoxification from methadone without requesting a maximum-limit dose at the start of their treatment. **Excluded criteria:** N/A **Pretreatment:** N/A

Interventions	**Intervention Characteristics** Inpatient Detoxication • *Description*: During the detoxification they are given treatment with clonidine and benzodiazepines (dosage being adjusted according to concomitant use of alcohol, benzodiazepines and cocaine) and non-opiate-based painkillers. On the seventh day they are given 50 mg of naltrexone.
Outcomes	*Completion of Detoxification* • **Outcome type**: Dichotomous Outcome • **Reporting**: Partially reported
Identification	**Sponsorship source:** Not described **Country:** Spain **Setting:** Hospital Inpatient Unit **Comments:** The increase in opiate addicts in treatment with methadone, coupled with improved survival of HIV patients, has meant an increase in the demand for detoxification from this substance in our environment. It is common practice in hospital detoxification units to request a maximum dose of methadone (around 40 mg) on beginning detoxification treatment. However, this is not always possible, due to the time needed for a gradual decrease for outpatients making daily visits to the methadone dispensing centres, due to the appearance of withdrawal symptoms, or because the patient starts out from very high doses of methadone. Reported here is an experience with 22 inpatients who over the last two years underwent detoxification from methadone without requesting from their treatment centres a maximum-limit dose at the start of their treatment. During the detoxification they are given treatment with clonidine and benzodiazepines (dosage being adjusted according to concomitant use of alcohol, benzodiazepines and cocaine) and non-opiate-based painkillers. On the seventh day they are given 50 mg of naltrexone. Of these addicts, 21 completed the detoxification adequately. **Authors name:** Enriqueta Ochoa **Institution:** Servicio de Psiquiatría, Hospital Universitario Ramón y Cajal, Madrid **Email:** eochoa.hrc@salud.madrid.org **Address:** Enriqueta Ochoa. Servicio de Psiquiatría. Hospital Universitario Ramón y Cajal. Ctra Colmenar Km 9,100. 28034 Madrid
Notes	

Risk of bias table

Bias	**Authors' judgement**	**Support for judgement**

Allocation concealment (selection bias)	High risk	
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	
Sequence Generation	Unclear risk	

P 2003

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Rapid Detoxification Under General Anesthesia Standard Methadone Tapering Overall **Included criteria:** Candidates for this study were opiate-dependent with a clear wish to attain abstinence. They were referred by an outpatient addiction clinic in Eindhoven, the Netherlands and by external counsellors in the outpatient addiction circuit. The staff at the Novadic addiction centre, St Oedenrode, the Netherlands made a further selection of the candidates using the following inclusion criteria: opiate addiction according to DSM-IV, 18 – 40 years of age, documented failed efforts of standard methadone tapering, definite desire for sustained abstinence and a good understanding of the Dutch language. **Excluded criteria:** Exclusion criteria were dependent on other drugs, severe physical illness that contraindicated general anaesthesia, severe psychiatric illness and pregnancy. **Pretreatment:** The baseline characteristics showed no significant differences between the SMT group and the group that was treated with RD-GA, except for the duration of methadone use. The duration of methadone use was statistically significant longer in the RD-GA group [9.4 years (SD 6.7) vs. 3.5 years (SD 5.2) in the SMT group. The average dose of methadone received prior to detoxification was higher for the RD-GA group, but not statistically significant. Subjects from the SMT group were on average younger than subjects from the RD-GA group (31.1 years vs. 34.9 years, respectively). More men than women participated in this study (24 and six, respectively). Only one opiate-dependent participant had received higher education.
Interventions	**Intervention Characteristics**

	Rapid Detoxification Under General Anesthesia • *Description*: Accelerated detoxification using opioid antagonist given under anesthesia. Standard Methadone Tapering • *Description*: Traditional detoxification using methadone to alleviate withdrawal symptoms.
Outcomes	*Opiate-free urine samples during follow-up (measure of abstinence)* • **Outcome type**: Dichotomous Outcome
Identification	**Sponsorship source:** Not described **Country:** Netherlands **Setting:** Inpatient Addictions Centre **Comments:** The aim of this work was to study abstinence rates and withdrawal effects of rapid detoxification of opioid-dependents under general anaesthesia (RD-GA) compared to standard methadone tapering (SMT) using a prospective clinical trial with a follow-up of 3 months, as a preliminary study at the Novadic Addiction Centre in St. Oedenrode and St. Joseph Hospital in Veghel, the Netherlands. Thirty opioid-dependent patients took part. Outcome measures included urine toxicology screening for opiates to determine abstinence and presence of objective and subjective opioid withdrawal distress symptoms. Statistically significant differences in abstinence rate between RD-GA and SMT were present after one (RD-GA 100% vs. SMT 40%, p0.01) and 2 months (RD-GA 93% vs. SMT 33%, p0.01). After 3 months the difference in abstinence was still substantial, but no longer statistically significant (RD-GA 67% vs. SMT 33%, p= 0.14). Objective and subjective withdrawal symptoms showed largely identical outcomes and were equally low in the two groups for those who remained in the study. There was a considerably higher percentage of abstinence in the RD-GA group after 1, 2 and 3 months of follow-up accompanied by relatively mild withdrawal symptoms of shorter duration. However, if one completes SMT the data suggest a greater chance of staying clean in the long term than those completing RD-GA. **Authors name:** Paul Krabbe **Institution:** Department of Medical Technology Assessment (253),University Medical Centre Nijmegen **Email:** p.krabbe@mta.umcn.nl **Address:** Paul F. M. Krabbe PhD, Department of Medical Technology Assessment (253),University Medical Centre Nijmegen, PO Box 9101, 6500 HB Nijmegen, The Netherlands.
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	
Sequence Generation	High risk	

R 2011

Methods	**Study design:** Prospective cohort study **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Biopsychosocial Intervention Overall **Included criteria:** High frequency users of the ED (e.g., >10 visits in a one-year period). This included a broad range of diagnoses, including opioid users. **Excluded criteria:** N/A **Pretreatment:** N/A
Interventions	**Intervention Characteristics** Biopsychosocial Intervention • *Decryption*: The patients were evaluated in an independent clinic setting, given intensive medical and case management interventions with care being transferred to a primary care physician after 6 months. The patients had a1-hour preliminary physician evaluation followed by 5 to 6 30-minute follow-up visits. The patients were also seen by medical social work at least 1 time and an average 3 times.
Outcomes	*Number of ED Visits* • **Outcome type**: Continuous Outcome *Decrease in ED Visits (%)* • **Outcome type**: Continuous Outcome • **Scale**: % • **Direction**: Higher is better • **Data value**: Change from baseline *Total Costs ($)* • **Outcome type**: Continuous Outcome • **Unit of measure**: $

	• **Direction**: Lower is better
Identification	**Sponsorship source:** Not described **Country:** USA **Setting:** Emergency Department **Comments:** High intensity biopsychosocial evaluation and treatment of patients who are high frequency users of the ED has a significant effect on total visits, diagnostic accuracy and overall cost. As opposed to conventional thought, most of these patients were not opiate addicts, but rather were victims of the health care system as well as their own inability to effectively explain their medical issues. The personalized biopsychosocial approach not only yields better patient care, but given the future of health care would also significantly decrease the cost of managing these patients. **Authors name:** RC Waller **Institution:** Spectrum Health Medical Group **Email:** Not provided **Address:** Not provided
Notes	

Risk of bias table

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	High risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	
Other bias	High risk	Judgement Comment: Funding source not provided.
Sequence Generation	High risk	

R 2013

Methods	**Study design:** Retrospective cohort study **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Extended release naltrexone (XR-NTX) Treatment as Usual Overall

	Included criteria: Opioid dependent patients treated with (or without) extended release naltrexone (XR-NTX). **Excluded criteria:** N/A **Pretreatment:** Not described
Interventions	**Intervention Characteristics** Extended release naltrexone (XR-NTX) • *Description*: XR-NTX is a long acting opioid receptor antagonist that can help alleviate symptoms of opioid use disorder (e.g., cravings). Treatment as Usual • *Description*: No injection given.
Outcomes	*Proportion of patients leaving against medical advice (%)* • **Outcome type**: Dichotomous Outcome • **Reporting**: Partially reported
Identification	**Sponsorship source:** This analysis was conducted under a research services agreement with Penn State University from Alkermes, Inc. XR-NTX (VIVITROL) was developed with support from NIDA Grant R43DA013531 NIAAA Grant N43AA001002. Dr. Herschman and Mr. Bird are employees of CRC Health Group, Inc. Dr. Gastfriend is a full-time employee of Alkermes. **Country:** USA **Setting:** Hospitalized patients with opioid use disorder. **Comments:** XR-NTX patients had an 84% Relative Risk Reduction for against medical advice departure in early recovery, which suggests implications for opioid residential treatment. **Authors name:** David Gastrfriend **Institution:** CRC Health Group **Email:** David.Gastfriend@alkermes.com **Address:** Not provided
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	High risk	

Incomplete outcome data (attrition bias)	High risk	Judgement Comment: Did not describe group differences between those who did and did not receive Vivitrol.
Selective reporting (reporting bias)	High risk	
Other bias	High risk	Judgement Comment: Writers work for Alkermes - creator of the intervention for which this study was based around.
Sequence Generation	Low risk	

Razani 1975

Methods	**Study design:** Historically controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Self-Regulated Methadone Detoxification Overall **Included criteria:** Individuals with heroin addiction who were trialed on a self-regulated schedule of methadone hydrochloride detoxification in an inpatient unit. **Excluded criteria:** N/A **Pretreatment:** N/A
Interventions	**Intervention Characteristics** Self-Regulated Methadone Detoxification • *Description*: The patient is included in the methadone detoxification tapering (rather than using the traditional authoritarian approach). The patient can request "as needed" methadone dosing within a set of guidelines.
Outcomes	*Satisfaction with Withdrawal Regimen* • **Outcome type**: Dichotomous Outcome *Completion of Inpatient Detoxification (n)* • **Outcome type**: Dichotomous Outcome *Mean Length of Stay (days)* • **Outcome type**: Continuous Outcome • **Unit of measure**: Days *Mean Total Dose of Methadone (mg)* • **Outcome type**: Continuous Outcome • **Unit of measure**: mg *Attendance at Outpatient Follow-up* • **Outcome type**: Dichotomous Outcome
Identification	**Sponsorship source:** Not described **Country:** USA **Setting:** Inpatient Detoxification Unit

	Comments: We used a method of detoxifying heroin addicts involving a self-regulated schedule of methadone hydrochloride detoxification in an inpatient setting. This method allows the addict to receive methadone on an "as needed" basis within specified guidelines, thus permitting him to regulate his own detoxification. For this study, 30 chronic heroin addicts were detoxified using this self-regulated detoxification procedure. Measures of length of stay, amount of methadone required, and degree of patient satisfaction indicate that this is a practical means of withdrawing chronic heroin addicts that may have advantages over fixed withdrawal schedules. **Authors name:** Javad Razani **Institution:** Department of Psychiatry, University of Southern California School of Medicine, Los Angeles **Email:** Not provided **Address:** Psychiatric Hospital, 1934 Hospital Place, Los Angeles, CA 90033 (Dr.Chisholm)
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	High risk	
Blinding of outcome assessment (detection bias)	High risk	
Incomplete outcome data (attrition bias)	High risk	
Selective reporting (reporting bias)	Low risk	
Other bias	High risk	Judgement Comment: Did not disclose funding source!
Sequence Generation	Unclear risk	

Singh 2012

Methods	**Study design:** Prospective cohort study **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Opioid Substitution Treatment Overall **Included criteria:** People who inject drugs, specifically opioids.

	Excluded criteria: Not described; not relevant as this is a prospective study of uptake of OST based out of hospitals as a public health intervention for addictions. **Pretreatment:** Not reported (not applicable).
Interventions	**Intervention Characteristics** Opioid Substitution Treatment • *Description*: OST is a public health intervention that can reduce morbidity and mortality associated with injection opioid use.
Outcomes	*Number of clients engaging with OST* • **Outcome type**: Continuous Outcome • **Data value**: Endpoint *Retention Rate (%)* • **Outcome type**: Continuous Outcome *Average Buprenorphine Dose (mg)* • **Outcome type**: Continuous Outcome
Identification	**Sponsorship source:** Not reported (likely Public Health Association of Punjab funded this study) **Country:** India **Setting:** Hospitals in the Punjab **Comments:** In this large-scale hospital-based public health intervention, the initiation of opioid substitution therapy (OST) in 5 hospitals over the course of a year led to improve retention and uptake of OST by over 300 individuals. **Authors name:** Rana Ranbir Singh **Institution:** Opioid Substitution Treatment Centre, District Hospital, Tan Taran, Punjab, India **Email:** ranaforyou2002@yahoo.co.in **Address:** Not provided
Notes	*Anees Bahji* on 08/10/2018 02:20 **Included** This is a public health intervention provided through a hospital.

Risk of bias table

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Unclear risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Unclear risk	

Other bias	Unclear risk	
Sequence Generation	Unclear risk	

Strang 1997

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Specialist Inpatient Unit General Psychiatric Ward Overall **Included criteria:** The study cohort was a consecutive series of opiate addicts who had been referred to the DDU for in-patient detoxification from opiates and who entered the cue exposure study; 186 subjects (143 men and 43 women) met that study's inclusion criteria including: opiate dependent; no other psychiatric or AIDS-related illness, or pregnancy; suitable for standard in-patient admission (excluded subjects who also needed benzodiazepine detoxification from more than 30 mg diazepam daily). **Excluded criteria:** Participants who also need benzodiazepine detox (from more than 30 mg diazepam daily). **Pretreatment:** At baseline, DDU and GEN subjects were similar on these features apart from a significantly higher (more severe) score on one of the seven scales of the Addiction Severity Index (ASI; McLellan et a! 1980) among DDU subjects.
Interventions	**Intervention Characteristics** Specialist Inpatient Unit • *Description*: Comparison was made to a specialized inpatient detoxification for opioids. General Psychiatric Ward • *Description*: Usual care - involves seeing a general psychiatrist for treatment as usual.
Outcomes	*Completion of Inpatient Detoxification (%)* • **Outcome type**: Dichotomous Outcome *Opiate Free Status in Follow-Up* • **Outcome type**: Dichotomous Outcome
Identification	**Sponsorship source:** Not described **Country:** UK **Setting:** Hospital Inpatient **Comments:** Referral to a specialized inpatient detoxification ward was associated with greater rates of completion of inpatient detoxification and better follow-up outcomes (e.g., rates of opioid use in follow-up were lower in those referred to the specialized unit).

	Authors name: John Strang **Institution:** National Addiction Centre, Institute of Psychiatry, The Maudsley **Email:** john.strang@kcl.ac.uk **Address:** Addiction Sciences Building, 4 Windsor Walk, Denmark Hill, London, SE5 8AF
Notes	

Risk of bias table

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	Unclear risk	
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	
Sequence Generation	Low risk	

T 2014

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Naltrexone Implant + Placebo Pill Placebo Implant + Naltrexone Pill Double Placebo Overall **Included criteria:** 306 heroin addicts who recently completed detoxification at addiction treatment hospital in St. Petersburg, Russia and gave informed consent were randomized to a 24-week course of biweekly drug counselling and one of three treatment conditions: naltrexone (oral), naltrexone (injection), and placebo (or combinations thereof). **Excluded criteria:** Not described. **Pretreatment:** Patients in all three groups had similar ASI pro-files at baseline.
Interventions	**Intervention Characteristics** Naltrexone Implant + Placebo Pill • *Dosing*: 1000mg, 3 times − every 8 weeks) Placebo Implant + Naltrexone Pill

	• *Dosing*: Dose not provided Double Placebo • *Dosing*: Fake placebo injection
Outcomes	*Employability Score (on Addictions Severity Index)* • **Outcome type**: Continuous Outcome • **Direction**: Lower is better • **Data value**: Endpoint *Global Assessment of Function Score* • **Outcome type**: Continuous Outcome • **Data value**: Endpoint
Identification	**Sponsorship source:** Not reported **Country:** Russia **Setting:** Recent Hospital-Based Inpatient Detoxification **Comments:** The study showed that improvements in overall functioning and social adjustment were significantly better in the naltrexone implant group ASI (employment section) and GAF scale. This improvement in overall functioning and social adjustment might be related to the higher efficacy of treatment with naltrexone implant which contributes to social re-adaptation(employment, improvement of the quality of life and social functioning). The improvements in overall adjustment, psychiatric symptoms, and social functioning among those who remained in treatment and did not relapse are the most likely the effect of treatment success which is not specific to naltrexone because it was found regardless of the group treatment. **Authors name:** T. Yaroslavtseva **Institution:** First Pavlov State Medical University, Valdman Institute of Pharmacology, St. Petersburg, Russia **Email:** Not provided **Address:** Not provided
Notes	

Risk of bias table

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	Low risk	
Blinding of outcome assessment (detection bias)	Low risk	
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	

Sequence Generation	Low risk	

V 2012

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Naltrexone + Guanfacine Naltrexone + Placebo Guanfacine + Placebo Double Placebo Overall **Included criteria:** Adults with heroin addiction who recently completed inpatient detoxification in hospital. Patients were randomized to one of four treatments: naltrexone + guanfacine; naltrexone + placebo; placebo + guanfacine; double placebo. **Excluded criteria:** Patients were excluded if they had clinically significant cognitive impairment; schizophrenia; major depression, bipolar or seizure disorder; advanced neurological, cardiovascular, renal, or hepatic disease; active tuberculosis or current febrile illness; a significant laboratory abnormality such as severe anemia, unstable diabetes, or liver function tests > 3× above normal; legal charges with impending incarceration; current participation in another treatment study; or concurrent treatment in another substance abuse program. **Pretreatment:** There were no significant baseline differences between groups in demographics or clinical variables.
Interventions	**Intervention Characteristics** Naltrexone + Guanfacine • *Dosage*: 50 mg/day + 1 mg/day Naltrexone + Placebo • *Dosage*: 50 mg/day + placebo Guanfacine + Placebo • *Dosage*: 1 mg/day + placebo Double Placebo • *Dosage*: Double placebo
Outcomes	*Retention in Treatment (weeks)* • **Outcome type**: Continuous Outcome • **Unit of measure**: Weeks
Identification	**Sponsorship source:** None reported **Country:** Russia **Setting:** Recent Inpatient Hospital Detoxification **Comments:** The efficacy of combination of naltrexone and guanfacine was comparable with efficacy of naltrexone alone. Usage of

	combination of opioid receptor antagonist with alpha adrenergic receptor blocker was safe and noted to have few adverse effects. **Authors name:** V. Palatkin **Institution:** Pavlov State Medical University, Valdman Institute of Pharmacology, St. Petersburg, Russia **Email:** Not reported **Address:** Not reported
Notes	

Risk of bias table

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	Low risk	
Blinding of outcome assessment (detection bias)	Low risk	
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	
Other bias	Low risk	
Sequence Generation	Low risk	