Appendix Table 1. Inclusion and exclusion criteria

| **PICOTS** | **Inclusion and Exclusion Criteria** |
| --- | --- |
| **Population**  | **Include:** Adults over 18 years enrolled in medications for opioid use disorder (MOUD) program for opioid use disorder, persons soon to be released from incarceration (e.g., released to the community during the study)**Exclude:** Special populations (e.g., people younger than 18 years of age, pregnant persons, palliative care/end-of-life, HIV, persons incarcerated for the duration of the study) |
| **Intervention**  | **Include:** Medication formulation (e.g., extended-release), psychosocial adjuncts (e.g., counseling, Cognitive Behavioral Therapy [CBT], peer support, 12-step programs, mindfulness therapy), contingency management, care settings/logistical support (e.g., MOUD setting, low-threshold models), financial support (e.g., MOUD medication/program reimbursement), and health information technology (IT)  |
| **Comparator** | **Include:** Comparator groups, (e.g., treatment as usual [TAU]) must also consist of individuals with access to MOUD, including usual referral and enrollment in outpatient in-person treatment programs, daily MOUD formulations, XR formulations) |
| **Outcomes** | **Include\***Primary:  Treatment retentionSecondary:  Mortality Harms |
| **Timing** | **Include:** Retention in MOUD was evaluated for at least 3 months. |
| **Setting** | **Include:** Only studies conducted in countries ranked as Very High Human Development by the United Nations’ Development Programme’s 2018 Statistical Update “Human Development Indices and Indicators.” Outpatient MOUD only. |
| **Study design** | **Include:** High quality systematic reviews, randomized control trials, observational studies (non-randomized studies with control groups) |
| **Language** | **Include:** English |

\* Systematic reviews and primary studies were included only if they report the primary or secondary outcomes of interest. PICOTS= population, intervention, comparator, outcomes, timing, setting; MOUD= medications for opioid use disorder; CBT= cognitive behavioral therapy; IT= information technology; TAU = treatment as usual; XR = extended-release; HIV= human immunodeficiency virus

Table 2. Published literature on care settings, services, and logistical support

| **Author, Year,****Study Design****Country** | **Number of Participants****Participant Characteristics** | **MOUD Medications** | **Timing & Outcome** | **Interventions** | **Results** | **Quality Rating** |
| --- | --- | --- | --- | --- | --- | --- |
| **Pre-release MOUD settings** |
| **Hedrich, 2012,1****SR** | 27 articles | Methadone, buprenorphine and methadone, buprenorphine-naloxone, levo-alpha acetyl methadol (LAAM) | 6 months after release Retention: % participants remaining in MOUD  | Intervention: MOUD in prison vsControl: No MOUD in prison  | KQ1: More than 50% [range 27-75%] retained in intervention group vs fewer than 5% [range 0-9%] retained in control groupKQ2: Not reportedKQ3: Not reported | Good |
| **Friedmann, 20182****RCT****USA** | 15Pre-release v Post-releasen=9 vs 5Mean Age= 38.9 vs 33.6Gender: 7% female Race/Ethnicity: 17% non-WhiteYears education: 11.6 vs 11.0Employed: 14.1 vs 33.3ASI drug risk: 1.9 vs 1.0 | Naltrexone (XR and injection) | 6 monthsRetention:1. Injections received2. Percentage who received all 6 monthly injections3. Treatment appointments attended | Pre-release intervention: Participants received 1 XR-naltrexone injection 1-2 weeks prior to release from prison plus up to 5 monthly injections in communityvsPost-release: No pre-release injection. Up to 6 post-release injections in community | KQ1: Mean (SD) number of injections received (p-values not reported): 2.8(1.9) pre-release vs 1.3(1.9) post-release Received all 6 injections: 2/9 (22%) in pre-release group vs 0/6 (0%) in post-release groupTreatment appointments attended: 46% pre-release group vs 22% post-release groupKQ2: Not reportedKQ3: Not reported | Poor |
| **Gordon, 2017**3**2 x 2 factorial design RCT****USA** | 213Mean Age: 39.08(8.8) yearsGender: 29.9% female Race/Ethnicity: 70.1% African American; 25.6% WhitePrior drug treatment: 81.9%Prior buprenorphine treatment: 15.2%# heroin use days prior to incarceration: 24.45(10.1) | Buprenorphine | 12 monthsRetention: Days in treatment program post-release up to 12 months | 2 (Pre-release Treatment Condition: Buprenorphine Treatment Vs. Counseling Only) x 2 (Post-Release Service Setting: OTP vs. CHC)Buprenorphine began either (1) in prison and continue care in an OTP or in (2) an outpatient substance abuse program within a CHC; or to begin buprenorphine after release from prison (3) in an OTP or (4) in the CHC Post-release: titrated dose to 8 mg/day, then 16 mg 3x/week. | KQ1: Mean (SE) number of days retained in treatment: 65.9(12.2) pre-release vs 21.8(7.6) post-release (p=0.005)KQ2: Not reportedKQ3: No differences in retention outcomes by gender | Fair |
| **Integrated MOUD into Psychiatric and Primary Care** |
| **Brooner, 20134****RCT****USA** | 316A vs B:n= 160 vs 156Mean Age: 40.2(0.71) vs 39.4(0.68)Gender: 62.5% vs 62.2% femaleRace/Ethnicity: 42.5% vs 40.4% minority raceEducation: 11.14 vs 10.88Employed: 12.5% vs 16.7%Cocaine: 31.9% vs 26.3% | Methadone | 12 monthsRetention:1. % participants remaining in substance abuse treatment at 12 months2. Treatment days over 12 months | On-site and integrated substance abuse and psychiatric care with methadonevs. Off-site and non-integrated substance abuse and psychiatric care. Traditional specialty methadone outpatient treatment program | KQ1: Completed 12-month substance abuse treatment: 41.3% on-site vs 41.0% off-site (p=0.96)Mean (SE) treatment days: 226.0 (10.8) on-site vs 228.7(10.7) off-site (p=0.89)KQ2: Not reportedKQ3: Not reported | Fair |
| **Carrieri, 20145****RCT****France** | 195Primary care (PC) vs Specialized care (SC): n=147 vs 48Mean Age: 32[27-38] vs 30[27-39]Gender: 14% vs 21% female | Methadone | 12 monthsRetention: % participants retained in methadone treatment  | Integration of methadone into primary care (PC)vs. Methadone received in specialty clinic setting (SC) | KQ1: Retention: 33/48 (69%) in SC vs 129/147 (88%) in PC were still in treatment. pLog rank=0.13 (per protocol analysis)KQ2: Not reportedKQ3: Not reported | Fair |
| **Miotto, 20126****RCT****USA** | 94Opioid-treatment program (OTP) vs psychiatrist’s private practice (PCS) vs manualized matrix model (MMM):Mean Age: 34.51(10.47) vs 36.46(9.76) vs 35.24(9.88)Gender: 32.14% vs 48.48% vs 42.42% femaleRace/Ethnicity: 42.86% vs 57.58% vs 69.70% WhiteUnemployed: 17.86% vs 21.21% vs 27.27% | Buprenorphine | 12 monthsRetention:1. Weeks retained: Number of weeks between induction and the last day the participant was assessed during treatment period 2. % of group who were present at week 20 | PCS: physician provided supportive and educational counseling about drug abuse and recovery; vsBehaviorally oriented psychosocial treatment (MMM) using matrix recovery-relapse prevention modelvsUsual care: Outpatient OTP  | KQ1: Mean number of weeks retained: 18.52(21.77) PCS vs 24.85(22.09) MMM vs 13.96(14.96) OTP (p=0.11)Present at week 20: 33.3% PCS vs 51.52% MMM vs 21.43% OTP (p=0.05)KQ2: Not reportedKQ3: Not reported | Fair |
| **MOUD in ED/Hospital Settings** |
| **Liebschutz, 20147****RCT****USA** | 139Mean Age: 40.5(11.8) Gender: 18.8% femaleRace/Ethnicity: 43.2% Non-Hispanic WhiteMean Rate of Opioid Use: 20.8(9.7) daysPrior OAT 57(41.0) | Buprenorphine | 6 month outcomes from enrollment assessedRetention:1. Engagement in outpatient buprenorphine treatment at 6 months 2. Opioid agonist treatment (OAT) days -self-reported in the 30 days before 3-, 6-month interviews using standard 30-day timeline follow-back | Linkage group: received 12 mg buprenorphine/naloxone on day 2 and 16 mg on day 3 and remainder of hospitalization. Linked to hospital associated primary care buprenorphine OAT with initial intake within 7 days of dischargevs Treatment as usual (TAU) | KQ1: Engaged in OAT at 6 months: 12(16.7%) linkage group vs 2(3%) TAU group (p=0.007)Self-report days of OAT use per 30 follow-up days: 16.4 linkage group vs 6.4 TAU group, P<.01. KQ2: Not reportedKQ3: Not reported | Fair |
| **D’Onofrio, 20178****RCT****USA** | 290Mean Age: 31.5Gender: 24.1% femaleRace/Ethnicity: 75.5% White Married: 11.0%Unemployed: 22.4%Unstable Housing: 8.3%Primary Opioid Heroin: 75.9% | Buprenorphine | 6 months and 12 monthsRetention:self-reported formal engagement in addiction treatment using Treatment Services Review instrument | ED initiated buprenorphine with linkage to outpatient primary carevsReferral (TAU)vsBrief Intervention of 10-15 minute manual-driven audio taped Brief Negotiation Interview conducted by study RA | KQ1: 6-month retention: 49/92 (53%) 95% CI 43–64 vs B. 42/70 (60%) 95% CI 48–72 vs C. 39/76 (51%) 95% CI 40– 63, p=0.54612 months retention: A. 42/86 (49%) 95% CI 38–60 vs B. 36/73 (49%) 95% CI 38–61 vs. C 49/78 (63%) 95% CI 52–74, p = 0.136KQ2: Not reportedKQ3: Not reported | Fair |
| **Logistical Support** |
| **Schwartz, 20179****RCT****USA** | 300Mean Age: 42.7(10.1) Gender: 41% femaleRace/Ethnicity: 42% African American;41% White | Methadone | 12 months Retention:1. Treatment retention in original OTP at 12 months2. Enrollment at any MOUD program at 12 months\*Treatment retention in original OTP was measured from program records and in any other OTP or buprenorphine treatment from self-report | Patient-centered methadone treatment (PCM): Encouraged but not required to attend individual/group counseling. Counselors served solely as therapists. Modified clinic rules. No administrative discharge.vsTreatment as usual (TAU) | KQ1: Retention at 12 months: 48.6% PCM group vs 46.3% TAU group, OR=0.91(0.58,1.44) Risk diff 0.02(-0.09,0.14) p=0.69 % enrolled in any OTP or buprenorphine treatment at 12 months: 78.9% PCM group vs 76.7% TAU group, OR= 0.88(0.48,1.62), p=0.68KQ2: 4 non-study related deaths in TAU. 2 overdoses in TAU. PCM had 2 non-study related deaths, 1 from methadone overdose; 59 non-study related hospitalizations in TAU and 67 in PCM.KQ3: Not reported | Good |
| **Beattie, 201610****RCT****UK** | 100Gender: 16% femaleRace/Ethnicity: 93.4% White; 6.1% Caribbean/Asian/Other Had GP: 69%Prior Treatment SUD: 90%Current Mental Health Care: 12%Homeless: 26% | Methadone | 3 monthsRetention: Percentage of patients on opioid substitution treatment (OST) at 3-months after randomization | Treatment intervention at a syringe exchange program (SEP)Intervention group: Script in a day" Offers immediate access to OST through referral to local specialist primary care center. Peer support volunteer accompanied participant to office, initiated on 30-40 mL methadone, and script for 6 days for 21 days, then transfer to GP practicevsTreatment as usual (TAU) | KQ1: In OST at 3-months: 51% intervention group vs 47% TAU group (OR 1.17 95% CI 0.54-2.57)KQ2: Not reportedKQ3: Not reported | Fair |
| **Kidorf, 201811****3 arm RCT****USA** | 212Standard care intervention (SCI) vs Voucher reinforcement intervention (VRI) vs Low threshold intervention (LTI):Mean Age: 40.3(10.9) vs 40.3(10.0) vs 38.8(9.4)Gender: 54% vs 47% vs 65% maleRace/Ethnicity: 34 vs 43 vs 36% WhiteEducation: 11.2(2.1) vs 11.5 (2.3) vs 11.3 (2.0)Employed: 6% vs 13% vs 6%HIV+: 3% vs 6% vs 9% | Methadone | 6 monthsRetention: % retained at 90 days and 180 days  | Treatment intervention at a syringe exchange program (SEP) Voucher reinforcement intervention (VRI): SCI supplemented with contingency management - contingent on adherence to daily schedules of dosing and counseling. One time per week based on adherence the prior week. Initial value $12, maximum $174, $30 bonus for 3 weeks of adherence, earnings were exchanged for goods/services from local communityvsLow threshold intervention (LTI): Participants excluded from adaptive treatment. Only required to attend 1 counseling session/month.vsStandard care intervention (SCI): Routine program, evidenced-based adaptive treatment model | KQ1: 90 day retention: 34% VRI vs 35% LTI vs 31% SCI (p=0.28)180 day retention: 34% VRI vs 37% LTI vs 29% SCI (p=0.36)KQ2: Not reportedKQ3: Not reported | Fair |
| **Parpouchi, 201812****RCT****Canada** | 97Mean Age: 39.1(8.9)Gender: 36.5% femaleRace/Ethnicity: 56.7% White; 20.6% Indigenous; 22.7% Other Unemployed:94.8% | Methadone | Retention: Medication possession ratio (MPR): Proportion of days during an observation period for which a person has been dispensed medication between randomization and end of study period (March 31, 2013) or date of death. | Housing first (HF) model: 3 interventions:1) market rental apartments with associated assertive community treatment (ACT) teams; 2) market rental + intensive case management; 3) dedicated building with integrated health and social service providers on-site.vs Treatment as usual (TAU) referral to housing | KQ1: Mean MPR: 0.52 HF group vs 0.57 TAU group (p=0.559)KQ2: Not reportedKQ3: Not reported | Fair |

MOUD= medications for opioid use disorder; SR= systematic review; RCT= randomized controlled trial; n=number of participants; LAAM= levo-alpha acetyl methadol; KQ= key question; XR= extended-release; NTX= naltrexone; SD= standard deviation; OTP= opioid treatment program; CHC= community health center; SE= standard error; PC= primary care; SC= specialized care; PCS= psychiatrist’s private practice; MMM= manualized matrix model; OAT= opioid agonist treatment; TAU= treatment as usual; ED= emergency department; PCM= patient-centered methadone treatment; OST= opioid substitution treatment; SEP= syringe exchange program; SCI= standard care intervention; VRI= voucher reinforcement intervention; LTI= low threshold intervention; MPR= medication possession ratio; HF= housing first; ACT= assertive community treatment

Table 3. Published literature on contingency management

| **Author, Year****Study Design****Country** | **Number of Participants****Participant Characteristics** | **MOUD Medications** | **Timing & Outcome** |  **Intervention**  | **Results** | **Quality Rating** |
| --- | --- | --- | --- | --- | --- | --- |
| **Amato,** **201113****SR** | 4319 | Methadone Buprenorphine Levo-alpha acetyl methadol (LAAM) | Timing variable (6 - 48 weeks)Retention: # participants in treatment at the end of the study | Any psychosocial / behavioral + any agonist maintenance treatmentvsStandard agonist treatment | KQ1: Results do not show benefit for retention in treatment (26 studies, 2582 participants)KQ2: Not reportedKQ3: Not reported | Good |
| **DeFulio, 201214****RCT****USA** | 38Contingency group:Gender: 58% femaleRace/Ethnicity: 84% African AmericanUnemployed over past 3 years: 74%Control group:Gender: 26% femaleRace/Ethnicity: 95% WhiteUnemployed over past 3 years: 58%  | Naltrexone injections  | 6 monthsRetention: % of participants who completed entire course of naltrexone injections  | CM: Access to therapeutic workplace contingent upon acceptance of naltrexone injectionvsPrescription: Access to therapeutic workplace noncontingent upon acceptance of naltrexone injection | KQ1: 74% CM group vs 25% prescription group,χ2 (1) = 8.53, *p* = .004KQ2: Not reportedKQ3: Not reported | Fair |
| **Dunn,** **201315****RCT** **&** **Dunn,** **201516****RCT****USA** | 67Mean Age: 45 Gender: 39% femaleRace/Ethnicity: 86% African American | Oral naltrexone | Retention:1. % of participants who completed course of medication. 26 weeks.2. % of participants who had naltrexone-positive urine screens at 100% of 30-day check-points.3. Self-reported drug treatment in 30 days before 12 month assessment16 | CM: Access to therapeutic workplace contingent upon supervised ingestion of medicationvsPrescription: Access to therapeutic workplace noncontingent upon medication ingestion. | KQ1: Completed course of medication: 54% CM group vs 16% prescription group (p<0.01) Naltrexone-positive urine screens at 100% of 30-day check-points: 43% CM group vs 3% prescription group (p<0.01)Drug treatment at 12 months: 17% CM group vs 31% prescription group (p=0.45)KQ2: 1/67 deaths in contingency, 1 month after studyKQ3: Not reported | Fair |
| **Epstein, 200917****RCT****USA** | 252Gender: 52% femaleRace/Ethnicity: 66% African AmericanUnemployed: 18%  | Methadone | 20 weeksRetention: % of participants retained in study through study completion  | CM: Vouchers for goods and services provided for submitting opioid-negative urine samplesvsNon-CM: Vouchers awarded independent of urine screen results on a schedule yoked to the performance of another participant | KQ1: No group differences in retentionLog-rank χ2 = 2.51, df=2, p=0.29KQ2: Not reportedKQ3: Not reported | Good |
| **Everly,** **201118****RCT****USA** | 35Mean Age: 42.5%Contingency group:Gender: 42.5% femaleControl group:Gender: 53% female | Naltrexone injections  | 26 weeksRetention: % of participants who accepted all scheduled naltrexone injections | CM: Access to therapeutic workplace contingent upon acceptance of naltrexone injectionsvsPrescription: Access to therapeutic workplace not contingent upon acceptance of naltrexone injections | KQ1: Received all injections: 66% CM group vs 35% prescription groupχ2 (1) = 4.94*,* p=0.026; HR = 0.32; 95% CI = 0.117 - 0.874KQ2: Not reportedKQ3: Not reported | Fair |
| **Holtyn,** **201419****RCT****USA** | 98Work reinforcement group:Gender: 33% femaleRace/Ethnicity: 63% African AmericanAbstinence, methadone, and work reinforcement:Gender: 45% femaleRace/Ethnicity: 73% African American | Methadone | 26 weeksRetention: % of participants enrolled in MOUD at 30-day assessments | CM: Access to therapeutic workplace contingent upon verified enrollment in outside MOUD programNon-CM: Access to workplace independent of MOUD enrollment status | KQ1: 30-day retention: 81% CM group vs 82% non-CM groupOR (95% CI) 1.40 (0.40-4.83), p=0.60KQ2: Not reportedKQ3: Not reported | Fair |
| **Kidorf,** **201811****RCT****USA** | 212(Standard care intervention) vs (Voucher reinforcement intervention) vs (Low threshold intervention):Mean Age: 40.3(10.9) vs 40.3(10.0) vs 38.8(9.4)Gender: 54% vs 47% vs 65% maleRace/Ethnicity: 34 vs 43 vs 36% WhiteEducation: 11.2(2.1) vs 11.5 (2.3) vs 11.3 (2.0)Employed: 6% vs 13% vs 6%HIV+: 3% vs 6% vs 9% | Methadone | 6-monthsRetention: % retained at 90 days and 180 days  | Treatment intervention at a syringe exchange program (SEP) Voucher reinforcement intervention (VRI): SCI supplemented with contingency management - contingent on adherence to daily schedules of dosing and counseling. One time per week based on adherence the prior week. Initial value $12, maximum $174, $30 bonus for 3 weeks of adherence, earnings were exchanged for goods/services from local communityvsLow threshold intervention (LTI): Participants excluded from adaptive treatment. Only required to attend 1 counseling session/month.vsStandard care intervention (SCI): Routine program, evidenced-based adaptive treatment model | KQ1: 90 day retention: 34% VRI vs 35% LTI vs 31% SCI (p=0.28)180 day retention: 34% VRI vs 37% LTI vs 29% SCI (p=0.36)KQ2: Not reportedKQ3: Not reported | Fair |
| **Specka, 201320****RCT****Germany** | 136Gender: 67% maleUnemployed: 72% | Methadone Buprenorphine | 26 weeksRetention: % of participants who completed the study | CM: Received escalating number of take-home dosages of medication contingent upon increasing number of opioid-free urine samplesvsTreatment as usual (TAU): Received 4 days of medication dosages for 12 consecutive opioid-free weekly urine screens | KQ1: 62.5% CM group vs 64.1% TAU group (p=0.85)KQ2: Not reportedKQ3: Not reported | Fair |

MOUD= medications for opioid use disorder; SR= systematic review; RCT= randomized controlled trial; LAAM= levo-alpha acetyl methadol; KQ= key question; CM= contingency management; SEP= syringe exchange program; SCI= standard care intervention; VRI= voucher reinforcement intervention; LTI= low threshold intervention; TAU= treatment as usual

Table 4. Published literature on health IT for MOUD

| **Author, Year****Study Design****Country** | **Number of Participants****Participant Characteristics** | **MOUD Medications** | **Timing & Outcome**  | **Interventions** | **Results** | **Quality Rating** |
| --- | --- | --- | --- | --- | --- | --- |
| **Marsch, 201421****RCT****USA** | 160 Mean Age: 40.7Gender: 25% femaleRace/Ethnicity: 27.4% Hispanic Married: 9.4%Unemployed: 46.8% | Methadone | 12 monthsRetention: % retained in treatment over duration of treatment | Computer-based education & supportIntervention: 50%/50% in-person/Therapeutic Education System (TES) vsTreatment as usual (TAU): MOUD + clinic resources (In-person counseling & group therapy) | KQ1: Retention: 31/80 (39%) intervention group vs 31/80 (39%) TAU groupp=0.56, OR CI (0.5-1.2) KQ2: Not reported KQ3: Not reported | Fair |
| **Moore,** **201822** **RCT** **USA** | 82 Treatment arm (n=40): Mean Age: 43.6Gender: 60% maleRace/Ethnicity: 65% WhiteMarried: 60%Unemployed: 63% | Methadone | 3-monthsRetention: % of days of medication adherence | Computer-based education & supportIntervention: Automated, computer-based, cognitive behavioral therapy (CBT) interactive voice response (IVR) systemvsTAU: Methadone + clinic resources (In-person counseling & group therapy) | KQ1: 94% p=0.60 (retention only reported for entire study population, not individual groups) KQ2: 12 Adverse Events not described (7 of 40 [17%] Intervention, 5 Control of 42 [12%]); 1 Control removed from study due to medical issuesKQ3: Not reportedGreater IVR use, more days abstinent.IVR group requested continued access to IVR post study.Qualitative interviews patients reported just knowing resource was available was beneficial. | Poor |
| **Ruetsch,****201223****RCT****USA** | 1426 Participant characteristics not reported | Buprenorphine | 12 monthsRetention: Medication taken at the prescribed dose on at least 80% of days (22/28 days) based on participant self-report of the previous 28 days | Computer-based education & supportIntervention: Here to Help: online educational materials, treatment calendar, peer stories, telephone coaching + MOUDvsTAU: MOUD + clinic resources (In-person counseling & group therapy) | KQ1: 55% intervention group vs 56.1% TAU group (p= not reported)KQ2: Not reported KQ3: Not reported | Fair  |
| **Shi,** **201924****RCT****USA** | 20Mean Age: 18+Gender: Predominantly maleRace/Ethnicity: Predominantly WhiteEducation: Most completed high schoolEmployment: “About half” | Buprenorphine | 3-monthsRetention: Mean number of days in 12-week protocol  | Computer-based education & supportIntervention: Web-based CBT vsTAU: MOUD + clinic resources (In-person counseling & group therapy) | KQ1: Mean days in 12-week protocol: 83 days intervention group vs 69 days TAU group (p=0.19)KQ2: Not reportedKQ3: Not reported | Fair |
| **Eibl,** **201725****Retrospective cohort****Entire Province of Canada** | 3733 | Methadone, Buprenorphine | 12-months Retention: At least 1- year consecutive MOUD  | TelehealthPatients stratified by primary treatment modality:>75% telehealth vs.25-75% mixedvs.<25% in-person | KQ1:50%; aOR 1.27 (1.14-1.41)47% aOR 1.27 (1.08-1.47)39% (reference)KQ2: Not reportedKQ3: Receiving care in Northern clinics was positively associated with retention. Significant associations were also detected for sex, clinic region, age, and peak methadone dose, but not for clinic rurality. | Fair |
| **Weintraub, 201826****Retrospective chart review** **USA** | 177Mean Age: 35.1 Gender: 89% maleRace/Ethnicity: 82% White Insurance: 96% Medicaid Self-reported abstinence at initial evaluation: 72% | Buprenorphine | 3-months Retention: % retained in treatment  | TelehealthTelehealth (to patient), teleconsult (to provider) not specified; connection of academic medical center to rural treatment centerPatients were detoxified prior to study | KQ1: 57.4% KQ2: Not reportedKQ3: Not reported | Fair |
| **Zheng,** **201727****Retrospective chart review****USA** | 55\* Mean Age: 37.2 and 34.4 Race/Ethnicity: mostly WhiteUnemployed: mostly unemployed\*study n= 100, 55 followed for 12 months | Buprenorphine | 12 monthsRetention: % of patients in program at 12 months | TelehealthIntervention: Telehealth psychiatryvsIn-person psychiatry  | KQ1: 41.7% 35.5% p = 0.55KQ2: Not reportedKQ3: Not reported | Fair |

IT= informational technology; MOUD= medications for opioid use disorder; RCT= randomized controlled trial; TES= Therapeutic Education System; TAU= treatment as usual; KQ= key question; CBT= cognitive behavioral therapy; IVR= interactive voice response

Table 5. Published literature on extended-release medication based treatments

| **Author, Year****Study Design****Country****Funder** | **Number of participants****Participant characteristics** | **MOUD Medications** | **Timing & Outcome** | **Interventions** | **Results** | **Quality Rating** |
| --- | --- | --- | --- | --- | --- | --- |
| **Tanum, 201728****RCT****Norway** | 159Mean Age: 35.1Gender: 72.3% maleRace/Ethnicity: 89.2% WhiteIV drug users: 85.5% Only participants who successfully completed medically supervised withdrawal were randomized into the study | XR NTX monthly injectionDaily SL buprenorphine/ naloxone | 3 monthsRetention: number of days until dropout from study medication and by the number of patients completing the study at week 12. | XR NTX monthly injectionvsDaily SL buprenorphine/ naloxone | KQ1: Retention, mean (SD) time: 69.3 (25.9) XR NTX vs 63.7 (29.9) days daily buprenorphine / naloxone. At 12 weeks 66% participants had attended all scheduled follow-up and taken their medications as prescribed.KQ2: Serious adverse events not different between the two groups (8.5% vs 4.2%, p=0.33).10 participants (4 in the XR NTX group and 6 in the buprenorphine/ naloxone group) exited the study due to adverse events: KQ3: Not reported | Good |
| **Lee, 201829****RCT****USA** | 570Age: 18+Gender: 70.5% maleRace/Ethnicity: 74% White Heroin Users: 81% Prescription Opioid Users: 15.5%Participants were randomized into the study either prior to or following successful completion of medically supervised withdrawal | XR NTX monthly injectionDaily SL buprenorphine/ naloxone | 6 months Retention: % study participants who completed 6 months of the study | XR NTX monthly injectionvsDaily SL buprenorphine/ naloxone  | KQ1: Retention at 6 months: 96/283 (33.9%) XR NTX vs 115/287 (40%) daily buprenorphine/ naloxone (p value not reported)KQ2: serious adverse events not different between groups (14% and 11%). 28 overdose events, 18 (64%) in the XR NTX group, including 8 among induction failures and 10 among those who received at least a single XR NTX injection. 5 overdoses were fatal, including 2 in the XR NTX group and 3 in the daily buprenorphine/naloxone group.KQ3: Not reported | Fair |
| **Sullivan, 201930****RCT****USA****NIDA** | 60Mean Age: 39.5 Gender: 83.3% maleRace/Ethnicity: 63.3% White Heroin Users: 26.7% Prescription Opioid Users: 85.0%Participants were randomized after successfully completing medically supervised opioid withdrawal  | XR NTX monthly injectionDaily naltrexone | 6 monthsRetention: % study participants who completed 6 months of the study. | XR NTX monthly injectionvsDaily naltrexone | KQ1: Retention at 6 months: 57.1% XR NTX vs 28.1% daily naltrexone (HR=2.18, 95% CI=1.07, 4.43) KQ2: 9 serious adverse events, including 5 in the XR NTX and 3 in the daily naltrexone group. 5 participants were from the study which included 1 participant who developed hives after an XR NTX injection.KQ3: Not reported | Fair |
| **Rosenthal, 201631****RCT****USA****Braeburn Pharmaceuticals** | 177Age: 18+ Gender: 59.1% maleRace/Ethnicity: 94.9% White, Heroin Users: 21.0% Prescription Opioid Users: 74.4% | XR Buprenorphine 6-month implantDaily SL buprenorphine | 6 monthsRetention: % study participants who completed 6 months of the study. | Clinically stable on daily buprenorphine for 6 months before enrollment:XR Buprenorphine 6-month implantvsDaily SL buprenorphine | KQ1: Retention: 81/87 (93.1%) implant vs 84/90 (94.3%) daily buprenorphine (p-value not reported) KQ2: 5 serious adverse events reported, 3 in the daily buprenorphine and 2 in the buprenorphine implant group. 1 participant in the buprenorphine implant exited the study.KQ3: Not reported | Good |
| **Lofwall, 201832****RCT****USA****Braeburn Pharmaceuticals****University of Kentucky** | 428Age: 18+ Gender: 61.4% maleRace/Ethnicity: 74.2% White Heroin Users: 70.8% Prescription Opioid Users: 29.2%  | XR Buprenorphine monthly injectionDaily SL buprenorphine /naloxone | 24 weeksRetention: % participants retained on the study medication regimen at 24 weeks of treatment | XR Buprenorphine injections (weekly during weeks 1 – 11, monthly during weeks 12 – 24) + daily SL placebovsPlacebo injections (weekly during weeks 1 – 11, monthly during weeks 12 – 24) + daily SL buprenorphine/ naloxone | KQ1: Retention: 56.8% XR buprenorphine vs 58.1% daily buprenorphine/naloxone (p-value not reported)KQ2: 18 participants reported at least 1 serious non-fatal adverse event; which lead to study disenrollment among 3.3% buprenorphine injection and 1.4% daily buprenorphine participants. only 1 serious adverse event was related to the buprenorphine injection. 5 daily buprenorphine/ naloxone participants reported nonfatal overdoses. KQ3: Not reported | Fair |

MOUD= medications for opioid use disorder; RCT= randomized controlled trial; IV= intravenous; XR= extended-release; NTX= naltrexone; SL= sublingual; KQ= key question; CI= confidence interval; KCL= King’s College London; SLaM= South London and Maudsley; NHS= National Health Service

Table 6. Published literature on psychosocial support interventions

| **Author, Year****Study Design****Country** | **Number of participants****Participant characteristics** | **MOUD Medications** | **Timing & Outcome** | **Interventions** | **Results** | **Quality Rating** |
| --- | --- | --- | --- | --- | --- | --- |
| **Amato,** **201113****SR** | 4319Age: 18+, average 35, range: 27-45 yearsGender: 73% maleNon-pregnantNaïve/stable in treatment: varies at individual study level | Methadone Buprenorphine Levo-alpha acetyl methadol (LAAM) | Timing variable (6 - 48 weeks)Retention: # participants in treatment at the end of the study | Any psychosocial / behavioral + any agonist maintenance treatmentvsStandard agonist treatment | KQ1: Results do not show benefit for retention in treatment (26 studies, 2582 participants)KQ2: Not reportedKQ3: Not reported | Quality of included studies for outcome of retention assessed as ‘high’ using GRADE |
| **Christensen, 201433****RCT****USA** | 170Mean Age: 20-63Non-pregnantNot incarcerated Naïve/stable in treatment: naïve, but unclear of if any patients had previous MOUD | Buprenorphine induction Buprenorphine-naloxone tablet maintenance | 3-monthsRetention: % participants completed all 3-months  | Web-based community reinforcement approach (CRA) + contingency management (CM) + minimal therapist counseling + MOUDvsCM + minimal therapist counseling + MOUD | KQ1: Retention: 80% CRA+CM vs 64% CM+ counsellingOR =2.30 (1.15, 4.60)KQ2: Not reportedKQ3: when stratified by prior treatment the hazard of dropping out for CM-alone participants was 6.57 times (χ2(1) = 9.01, p=0.003) that for CRA+ participants. For treatment-naïve participants, the hazard for CM-alone participants was 1.15 times (χ2(1) = 0.13, p=0.718) that for CRA+ participants | Poor |
| **Fiellin, 201334****RCT****USA** | 141Mean Age: 33Gender: <70% maleRace/Ethnicity: <80% WhitePrescription drug use: 36% Prior detox attempt: 49%  | BuprenorphineNaloxone | 6 monthsRetention: % participants completed all 6 months  | Physician management + cognitive behavioral therapy (CBT)vsPhysician management alone | KQ1: Retention: 39% CBT vs 45% physician management alone(p=0.43)KQ2: Not reportedKQ3: Not reported | Good |
| **Jaffray, 201435****RCT****Scotland** | 542Mean Age: 32 Gender: 64% maleUnemployed: 91% Naïve/stable in treatment: "initiated in the last 24 months" - stable | Methadone | 6 months in study; baseline mean 9 months in methadoneRetention: % participants still receiving treatment at 6 months | Motivational interviewing + resource pack (with area-specific information on available services for pharmacists) + normal practice methadone treatmentvsNormal practice methadone treatment | KQ1: Retention:88% intervention vs 81% usual care(Adjustedp=0.34)OR = 1.76 (0.55, 5.64)KQ2: Physical and psychological health of the intervention group significantly deteriorated between baseline and follow-up, whilst the control group remained relatively unchangedKQ3: Not reported | Poor |
| **Marsden, 201936****RCT****UK** | 273Age: 18+All participants were treatment resistant (i.e., had used illicit or non-prescribed opioids or cocaine on one or more days in the past 28 days at study screening, which was verified by positive urine drug screen) | BuprenorphineMethadone | 18 weeksRetention: # days from randomization to the endpoint or exit | Personalized psychosocial intervention + treatment as usualvsTreatment as usual (TAU) | KQ1: No between-group difference in retention in eitherunadjusted or adjusted analyses.KQ2: The number of adverse events was similar between groups, and no severe adverse events in either group were judged to be treatment related.KQ3: Not reported | Fair |
| **Mitchell, 201337****RCT****USA** | 300Age: 18+Race/Ethnicity: African American populationNewly admitted to buprenorphine treatment at one of the participating treatment programs | Buprenorphine | 6 monthsRetention: % participants in buprenorphine treatment at 6 months | Intensive outpatient (IOP)vsStandard outpatient (OP) | KQ1: Retention: 56.6% IOP vs 58.7% OPKQ2: Controlling for # of days in treatment, greater counseling exposure was associated with significantly less improvement for three outcomes: days of heroin use, days of cocaine use, and days of criminal activity (however authors suggest the association is not causal)KQ3: Not reported | Poor |
| **Schwartz, 201238****RCT****USA** | 230Mean Age: 43.2 Gender: 70% maleRace/Ethnicity: 77.4% African AmericanMarried: 13.5% Employed During 30 Days Prior to Baseline: 32.6%Non-pregnantOpioid dependent for 1 year+ | Methadone | 12 monthsRetention: % participants retained in original MTP | Interim methadone (IM; supervised methadone with emergency counseling only for the first 4 months of treatment)vsRestored methadone (RM; routine counseling with smaller case loadsvsStandard methadone (SM; with routine counseling) | KQ1: Retention: 60.6% IM vs 37% RM vs 54.8% SMχ2(2) = 4.8(p>0.05)KQ2: Not reportedKQ3: Not reported | Fair |
| **Stein,** **201539****RCT****USA** | 49Mean Age: 41 Gender: 65.3% maleRace/Ethnicity: 85.7% Non-Latino WhiteReported they had ever received prescribed buprenorphine: 28.6% | Buprenorphine-naloxone inductionBuprenorphine maintenance | 3-monthsRetention: % participants retained in treatment | DT (distress tolerance) intervention + buprenorphine-naloxone induction then 3-months buprenorphine maintenancevsHE (health education) control + buprenorphine-naloxone induction then 3-months buprenorphine maintenance | KQ1: Retention: 75% DT vs 76% controlBetween group mean difference (95% CI) −1.0 (−25.1; 23.1)KQ2: Not reportedKQ3: Not reported | Good |
| **Sullivan, 2015****RCT****USA** | 125Mean Age: 38 Gender: 21% femaleRace/Ethnicity: 43% WhiteHeavy use (>6 bags heroin/day): 34% | XR NaltrexoneOral Naltrexone | 6 monthsRetention: % of participants retained in treatment | Behavioral Naltrexone Therapy (BNT) + standard (oral and injectable naltrexone) treatmentvsCompliance Enhancement (CE) + standard (oral and injectable naltrexone) treatmentvsBehavioral Naltrexone Therapy (BNT) + placebo injection and oral naltrexonevsCompliance Enhancement (CE) + placebo injection and oral naltrexone | KQ1: Retention: 47.8% BNT + standard Naltrexone vs 16.7% CE +standard naltrexone vs 23.8% BNT + placebo vs 14.3% CE+placeboKQ2: Not reportedKQ3: For low-severity opioid users, retention was highest (60% at 6 months) in Behavioral Naltrexone Therapy with a single administration of injection naltrexone (XR-naltrexone) post-detoxification.For high-severity opioid users, BNT-XR-naltrexone + oral naltrexone did not perform as well. | Fair |
| **Weiss,** **201140****RCT****UK** | 653Mean Age: 32.9Gender: 38% femaleRace/Ethnicity: 91.5% WhiteUnmarried: 49.2% Employment: 63.8% FTEMet DSM IV criteria for current opioid dependence on prescription opioids | Buprenorphine-naloxone | Phase 1: 4 weeks (2 week stabilization, 2 week taper)Retention: # of SMM (standard medical management) visitsPhase 2: 16 weeks (12 week treatment, 4 week taper) | SMM + ODC (opioid drug counseling)vsSMM alone | KQ1: Mean (SD) visits Phase 1: 4.4 (1.5) ODC vs4.5 (1.5) SMM alone(z=1.24, p=0.39)Phase 2: 14.1 (4.4) ODC vs 13.9 (4.0) SMM alone(z=0.86, p=0.21)KQ2: Psychiatric symptoms were the most common serious adverse events (7 of 36), particularly depression leading to hospitalization (n=5); all of these occurred soon after completion of the Phase 1 (n=2) or Phase 2 (n=3) taper.KQ3: A history of ever using heroin was associated with lower Phase 2 success rates while taking buprenorphine-naloxoneChronic pain at baseline was not related to outcomes either in Phase 1 or during Phase 2 while taking buprenorphine-naloxone | Fair |

MOUD= medications for opioid use disorder; SR= systematic review; LAAM= levo-alpha acetyl methadol; KQ= key question; GRADE= Grading of Recommendations Assessment, Development and Evaluation; RCT= randomized controlled trial; CRA= community reinforcement approach; CM= contingency management; CBT= cognitive behavioral therapy; TAU= treatment as usual; IOP= Intensive outpatient; OP= standard outpatient; MTP= methadone treatment program; IM= interim methadone; RM= restored methadone; SM= standard methadone; DT= distress tolerance; HE= health education; XR= extended-release; BNT= Behavioral Naltrexone Therapy; CE= compliance enhancement; SMM= standard medical management; ODC= opioid drug counseling; SD= standard deviation

Table 7. Quality ratings for care settings, services, logistical support

| **Author, Year** | **Randomization** | **Allocation Concealment** | **Groups Similar at Baseline** | **Blinded Outcome Assessors** | **Blinded Care Provider** | **Blinded Patient** | **Intention-To-Treat (ITT) Analysis** | **Acceptable Levels of Overall Attrition** | **Avoidance of Selective Outcomes Reporting** | **Final Quality Rating** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Pre-Release MOUD Models** |
| **Friedmann, 20182** | Unclear | Unclear | Yes | No | No | No | Yes | Yes | No | Poor |
| **Gordon, 20173** | Yes | Yes | Yes | Unclear | No | No | Yes | Yes | Yes | Fair |
| **MOUD Integrated into Primary Care** |
| **Brooner, 20134** | Yes | Unclear | Yes | Unclear | No | No | Yes | Unclear | Yes | Fair |
| **Carrieri, 20145** | Yes | Unclear | Yes | Unclear | No | No | Yes | Yes | Yes | Fair |
| **Miotto,** **20126** | Yes | Yes | No | No | No | No | Yes | Unclear | Yes | Fair |
| **MOUD in ED/Hospital Settings** |
| **Liebschutz,** **20147** | Yes | Unclear | Yes | No | No | No | Yes | Yes | Yes | Fair |
| **D’Onofrio8** | Yes | Yes | Yes | Unclear | No | No | No | Yes | Yes | Fair |
| **MOUD in Community Settings/Social Services** |
| **Schwartz,** **20179** | Yes | Yes | Yes | No | No | No | No | Yes | Yes | Good |
| **Beattie,** **201610** | Yes | Yes | Yes | No | No | No | Yes | Yes | Yes | Fair |
| **Kidorf,** **201811** | Yes | Unclear | Unclear | Unclear | No | No | Yes | Yes | No | Fair |
| **Parpouchi,** **201812** | Yes | Unclear | Yes | Unclear | No | No | No | Unclear | Yes | Fair |

Table 8. Quality ratings for contingency management

| **Author, Year** | **Randomization** | **Allocation Concealment** | **Groups Similar at Baseline** | **Blinded Outcome Assessors** | **Blinded Care Provider** | **Blinded Patient** | **Intention-To-Treat (ITT) Analysis** | **Acceptable Levels of Overall Attrition** | **Avoidance of Selective Outcomes Reporting** | **Final Quality Rating** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **DeFulio, 201214** | Yes | Unclear | Yes | Unclear | No | No | Yes | Yes | Yes | Fair |
| **Dunn,** **201315** | Yes | Unclear | Yes | Unclear | No | No | Yes | Yes | Yes | Fair |
| **Dunn,** **201516** | Yes | Unclear | No | Unclear | No | No | Yes | Yes | Yes | Fair |
| **Epstein,** **200917** | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Good |
| **Everly,** **201118** | Yes | Unclear | Yes | Unclear | Unclear | No | Yes | Yes | Yes | Fair |
| **Holtyn,** **201419** | Yes | No | Unclear | Unclear | No | No | Yes | Yes | No | Fair |
| **Kidorf,** **2018 11** | Yes | Unclear | Unclear | Unclear | No | No | Yes | Yes | No | Fair |
| **Specka,** **201320** | Unclear | Unclear | Unclear | No | No | No | Yes | Yes | Yes | Fair |

Table 9. Quality ratings for health IT

| **Author, Year** | **Randomization** | **Allocation Concealment** | **Groups Similar at Baseline** | **Blinded Outcome Assessors** | **Blinded Care Provider** | **Blinded Patient** | **Intention-To-Treat (ITT) Analysis** | **Acceptable Levels of Overall Attrition** | **Avoidance of Selective Outcomes Reporting** | **Final Quality Rating** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Marsch, 201421** | Yes | No | Yes | Yes | No | No | Yes | Yes | Unclear | Fair |
| **Moore,** **201922**  | Unclear | No | Unclear | No | No | No | Yes | Yes | Unclear | Poor |
| **Reutsch, 201223**  | Yes | Unclear | Yes | Unclear | Unclear | Unclear | Unclear | Yes | Yes | Fair |
| **Shi,** **201924** | Yes | Unclear | Yes | Unclear | No | No | Yes | Yes | Yes | Fair |

|  |
| --- |
| **Cohort studies** |
| **Author, Year** | **Randomization** | **Allocation Concealment** | **Groups Similar at Baseline** | **Blinded Outcome Assessors** | **Blinded Care Provider** | **Blinded Patient** | **Intention-To-Treat (ITT) Analysis** | **Acceptable Levels of Overall Attrition** | **Avoidance of Selective Outcomes Reporting** | **Final Quality Rating** |
| **Eibl,** **201725** | N/A | Yes | Yes | No | No | No | No | Unclear | Yes | Fair |
| **Weintraub, 201826** | N/A | Yes | Yes | No | No | No | No | Unclear | Yes | Fair |
| **Zheng,** **201727** | N/A | Yes | Yes | No | No | No | Yes | Unclear | Yes | Fair |

Table 10. Quality ratings for extended-release medication based treatments

| **Author, Year** | **Randomization** | **Allocation Concealment** | **Groups Similar at Baseline** | **Blinded Outcome Assessors** | **Blinded Care Provider** | **Blinded Patient** | **Intention-To-Treat (ITT) Analysis** | **Acceptable Levels of Overall Attrition** | **Avoidance of Selective Outcomes Reporting** | **Final Quality Rating** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Tanum, 201728** | Yes | Yes | Yes | Yes | No | No | Yes | Yes | Yes | Good |
| **Lee,** **201829** | Yes | Yes | Yes | Unclear | Unclear | Unclear | Yes | No | Yes | Fair |
| **Sullivan, 201930** | Yes | Unclear | Yes | No | No | No | Yes | Yes | Yes | Fair |
| **Rosenthal, 201631** | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Good |
| **Lofwall, 201832** | Yes | Yes | Yes | Unclear | Unclear | Unclear | Yes | No | Yes | Fair |

Table 11. Quality ratings for psychosocial

| **Author,** **Year** | **Randomization** | **Allocation Concealment** | **Groups Similar at Baseline** | **Blinded Outcome Assessors** | **Blinded Care Provider** | **Blinded Patient** | **Intention-To-Treat (ITT) Analysis** | **Acceptable Levels of Overall Attrition** | **Avoidance of Selective Outcomes Reporting** | **Final Quality Rating** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Christensen, 201433** | No | No | No | No | No | No | Unclear | No | Yes | Poor |
| **Fiellin,** **201334** | Yes | Yes | Yes | Unclear | No | No | Yes | Yes | Yes | Good |
| **Jaffray,** **201435** | Unclear | Unclear | Yes | Unclear | No | Yes | Yes | No | Yes | Poor |
| **Marsden, 201936** | Yes | No | Yes | No | No | No | Yes | Yes | Yes | Fair |
| **Mitchell, 201337** | Yes | Yes | No | Unclear | No | No | Yes | No | Unclear | Poor |
| **Schwartz, 201238** | Yes | Unclear | Yes | Unclear | No | No | Yes | No | Yes | Fair |
| **Stein,** **201539** | Yes | Yes | Yes | Yes | No | No | Yes | Yes | Yes | Good |
| **Sullivan, 2015** | Unclear | Yes | Yes | Unclear | No | Yes | Unclear | No | Yes | Fair |
| **Weiss,** **201140** | Unclear | Unclear | Yes | No | No | No | Yes | Yes | Yes | Fair |

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