Appendix F. Details of Trials for Guiding Question 3

| **Model name Author, year** | **Comparators** | **Duration of Followup** | **N** | **Population Characteristics** | **Specifics of Model Components/ Implementation** | **Setting/ Provider Type/ Staffing** | **Types of Outcomes and Harms Examined and How They Were Measured** | **Findings** |
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| ***MAT Models of Care*** |  |  |  |  |  |  |  |  |
| D'Onofrio, 20151 | Screening and referral to treatment (referral) vs. screening, brief intervention, and facilitated referral to community-based treatment services (brief intervention) vs. screening, brief intervention, ED-initiated treatment with buprenorphine/naloxone, and referral to primary care for 10-week followup (buprenorphine) | 30 days | 329 | USA; 76.3% male; 75.4% white; mean age 31.4 years (SD 10.6); study done in USA; 34.3% use alcohol to intoxication; 47.4% used sedatives in past month; 52.9% used cannabis in past month; 55.3% used cocaine in past month; 88.1% used cigarettes in past month; 51.1% had received psychiatric treatment in the past; 26.1% had received in-patient psychiatric treatment; 41.9% had received out-patient psychiatric treatment; 12.2% had received treatment for depression in the past month; 24.9% used prescription opioids; 75.1% used heroin; 52.9% were IV drug users | Buprenorphine group given treatment for 10 weeks before transferred to community program or detoxification for 2 weeks; Referral group received information for treatment programs only; brief intervention program received a brief 10- to 15-minute manual-driven audio-taped brief negotiation interview from a research associate who linked them with a referral; buprenorphine group received a Brief Negotiation Interview and if they exhibited moderate to severe opioid withdrawal received ED-initiated treatment and sufficient take-home daily doses to get through to next appointment, those without opioid withdrawal were given unobserved inducted with detailed self-medication guide, then office based buprenorphine treatment, and ongoing opioid agonist maintenance treatment or detoxification | Urban teaching hospital; Research associate performed ED visits, interviews, and referrals. Physicians and nurses managed buprenorphine dosages | Engagement in treatment assessed by direct contact with the facility, clinicians, or both; self-reported number of days of illicit opioids use in the past 7 days; urine toxicology for illicit opioid use; HIV risk-taking behavior using an 11-item validated scale for drug use and sexual behavior; and use of addiction treatment services. | 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. |
| Fiellin, 20022 | Buprenorphine and medication management (thrice-weekly sessions with a nurse and a monthly meeting with a physician) vs. buprenorphine and medication management plus drug counseling (not described) | 13 weeks | 14 | USA; 71% male; 93% white, mean age 36 years; 50% current IV drug user; mean 7 years heroin use; 79% with history/current alcohol dependence; 79% with history/current cocaine dependence | Buprenorphine given 3 times per week following one week induction with dose escalation as needed for positive urine screen or withdrawal.  Medication management group had brief monthly counseling sessions with physicians and 3 times per week manual-guided counseling sessions with nurses covering recent drug use, abstinence efforts, attendance at self-help groups with support and advice for efforts to reduce drug use or remain abstinent.  Medication management plus manual-guided drug counseling sessions met weekly (no details provided) | Urban academically affiliated medical center; primary care; medical management provided by nurses and physicians (counseling issues reviewed weekly with physician and clinical psychologist) | Illicit drug use: urine toxicology and self report  Retention/adherence: attendance at visits  Overall health:SF-36  Patient satisfaction | Overall, patients reduced opioid-positive urine toxicology tests and good retention through maintenance; less patients in medication management group vs. medication management plus counseling group achieved greater than or equal to one week of opioid-free urine screens, though this difference was not statistically significant; A greater proportion of the medication management plus counseling group had opioid-free urine screens compared with the medication management alone group, though this difference was not statistically significant |
| Fiellin, 20063 | Standard medical management (20 minutes with a nurse) and once-weekly medication dispensing (buprenorphine-naloxone) vs. standard medical management and thrice-weekly medication dispensing vs. enhanced (45 minutes with a nurse) medical management and thrice-weekly medication dispensing  All groups met monthly with a physician | 24 weeks | 166 | USA; 78% male; 77% white; mean age 36 years; mean duration of opioid dependence 8 years; 17% prescription drug use; 31% history of intravenous drug use; 20% cocaine-positive urine specimen at treatment entry; 66% previously attempted detoxification; 32% history of participation in methadone-maintenance program | Nurses dispensed buprenorphine-naloxone and provided standard (20 minutes; sessions covered recent drug use or efforts to achieve or maintain abstinence, attendance in self-help groups, support for efforts to reduce drug use or remain abstinent, advice for the achievement or maintenance of abstinence, and the results of analysis of weekly urine specimens) or enhanced (45 minutes; sessions covered similar issues but provided more in-depth drug counseling) medical management Physicians met with patients monthly (20 minutes; sessions paralleled that of the standard sessions, with the addition of an assessment of employment, legal, family or social, medical, and psychiatric problems related to addiction)  The nurses, a physician, and a psychologist met weekly to review the counseling | Trained primary care nurses without previous addiction treatment, physician, psychologist  Primary care center | Illicit opioid use: urine toxicology and self-report Abstinence: measured in consecutive weeks | The efficacy of brief weekly counseling and once-weekly medication dispensing did not differ significantly from that of extended weekly counseling and thrice-weekly dispensing |
| Liebschutz, 20144 | Detoxification plus referral vs. induction plus contact from long-term opioid agonist treatment staff that facilitated linkage to hospital-associated primary care buprenorphine treatment | 6 months | 139 | USA; 71.2% male; mean age 40.5 (SD 11.8); mean illicit opioid use per 30 followup days 20.8 (SD 9.7) | Both groups received buprenorphine and naloxone up to 4 times for the first day in the hospital. Detoxification group received 4 additional days of tapering buprenorphine and naloxone, then treatment referral information; linkage group received buprenorphine and naloxone for hospitalization with enough given at discharge to get through to clinic appointment, before discharge research staff facilitated linkage to hospital-associated primary care buprenorphine treatment | Hospital and medical center; Research staff, which included an addiction nurse specialist, hospital nursing staff administered medication in hospital | Entry into opioid agonist treatment program, length of illicit opioid use defined as number of days of reported opioid use in the 30 days before visits, time to entry into buprenorphine program, number of self-reported prescribed opioid agonist treatment in the 30 days before visits, mortality. | Compared with an inpatient detoxification protocol, initiation of and linkage to buprenorphine treatment is an effective means for engaging medically hospitalized patients who are not seeking addiction treatment and reduces illicit opioid use 6 months after hospitalization. However, maintaining engagement in treatment remains a challenge. |
| Lucas, 20105 | Clinic-based, nurse-administered treatment with buprenorphine-naloxone vs. case management and referral to an intensive opioid treatment program (referred treatment) | 12 months | 93 | USA; 72% male; 98% black; median ages 45-46 years; median years of opioid use 18-20 years; 96% heroin used in previous month; 27% prescription opioid used in previous month; 72% used cocaine in previous month; 60% injection drug use in previous month; 73% positive for hepatitis C antibody; 10% AIDS-defining opportunistic condition in previous 3 months; 53% receiving ART | Clinic-based group was managed and seen weekly by a nurse (10-40 minutes; sessions included unstructured individual counseling, urine samples, observed buprenorphine doses, and provision of take-home supplies of buprenorphine to last until their next visit), and met with a physician 4-6 weeks after initiation of therapy and at other times as indicated. A treatment team, comprising the nurse and 2 to 5 buprenorphine prescribing physicians, met weekly to discuss participants’ progress in treatment. The treatment team set reporting frequencies, which ranged from 3 times weekly to monthly, according to drug test results and other factors.  Participants assigned to referred treatment were enrolled in an intensive case management program that has operated in the same clinic. A social worker or registered nurse in the case management program met with referred treatment participants shortly after randomization and made treatment plans that were primarily focused on linking participants to opioid treatment programs, but may have included such issues as food and housing needs | Licensed practical nurse with training and experience as a substance counselor, buprenorphine prescribing physicians HIV clinic | Drug use: urine toxicology Participation in opioid agonist therapy at study visits: self-reported   Also, visits with primary HIV providers, months of ART use, changes in HIV RNA levels and CD4 cell counts, and proportion of participants with emergency department visits or hospitalizations (methods NR) | Participation in opioid agonist therapy was significantly higher in clinic-based buprenorphine than for referred treatment. Positive test results for opioids and cocaine were significantly less frequent in clinic-based buprenorphine than in referred treatment, and study participants receiving clinic-based buprenorphine attended significantly more HIV primary care visits than those receiving referred treatment. Use of antiretroviral therapy and changes in HIV RNA levels and CD4 cell counts did not differ between the 2 groups. |
| Sullivan, 20066 | Buprenorphine/ naloxone and physician management (brief, biweekly) vs. buprenorphine/ naloxone and physician management plus once-weekly drug counseling and adherence management | 12 weeks | 16 | USA; 94% male; 31% white, 44% Black, 25% Hispanic; mean age 47 years; mean 17 years opioid dependence; 56% with injection drug use; 29% reported one or more days of alcohol use in past 30 days; 36% reported one or more days of cocaine use in past 30 days; 100% HIV positive; mean 13 years since HIV diagnosis; 63% currently on ART; 81% HCV positive | Buprenorphine/naloxone stabilization over 2-weeks with clinic visits 3 times per week and 1 and 2-day take home doses then 10-week maintenance period with once weekly clinic visits and 6 take home doses then offered 2-week taper or extension phase; all patients received brief, bi-weekly, manual-guided physician management that focused on symptoms, drug use, and progress; half of patients received physician management plus once-weekly drug counseling and adherence management focused on addiction-specific topics like triggers, relationships, and craving and strategies to increased adherence to antiretroviral treatment | HIV clinics; Buprenorphine and physician management provided by physician specialized in addiction medicine and experienced in HIV care; drug counseling and adherence management provided by trained nursing staff (issues reviewed with supervising physician and clinical psychologist) | Treatment retention Illicit drug use: urine toxicology and self-report Laboratory parameters: CD4 count, viral load, and liver function tests Adherence to MAT and ART: Medication Event Monitoring System (caps that record the date and time the pill bottle was opened) HIV transmission risk behaviors: HIV/AIDS Risk Inventory Health status: SF-36 Patient satisfaction: 5-point Likert scale questionnaire | There was no difference in treatment retention or illicit drug use by counseling group; Overall, the proportion of opioid-positive weekly urine screens decreased substantially over trial; CD4 counts remained stable; viral load declined significantly; demonstrated feasibility of integrating buprenorphine into HIV clinical care for treatment of opioid dependence |
| ***Psychosocial Interventions*** |  |  |  |  |  |  |  |  |
| Christensen, 20147 | Buprenorphine and individual counseling plus contingency management (based on urine results linked to points for gift cards or money) vs. buprenorphine and individual counseling and contingency management plus internet-based community reinforcement approach  Both groups had individual counseling every 2 weeks | 12 weeks | 170 | USA; 54% male, 95% white, mean age 34 years; 13% with concurrent alcohol dependence, 5% with concurrent cocaine dependence, 12% with concurrent sedative dependence, 29% with concurrent cannabis dependence; 46% had prior treatment; 14% with injection drug use | Buprenorphine given 3 times per week with extra dose for days in between; contingency management based on urine results linked to points for gift cards or money; community reinforcement approach completed set of topics on community reinforcement approach at each clinic visit; both groups had individual counseling every 2 weeks | Clinic setting at university research center; Buprenorphine from study physician; therapist for community reinforcement approach and counseling | Retention: number of days from start of intervention until participant left trial or completed trial  Abstinence: number of negative urine specimens overall and over longest continuous period with missed visits equal to positive result  Addiction-related severity: ASI | Compared to those receiving contingency management-alone, community reinforcement approach recipients had more total days of abstinence and were less likely to drop out of treatment; prior treatment for opioid dependence moderated the additional improvement of community reinforcement approach for longest continuous days of abstinence |
| Fiellin, 20022  (also a model of care | Buprenorphine and medication management (thrice-weekly sessions with a nurse and a monthly meeting with a physician) vs. buprenorphine and medication management plus drug counseling (not described) | 13 weeks | 14 | USA; 71% male; 93% white, mean age 36 years; 50% current IV drug user; mean 7 years heroin use; 79% with history/current alcohol dependence; 79% with history/current cocaine dependence | Buprenorphine given 3 times per week following one week induction with dose escalation as needed for positive urine screen or withdrawal.  Medication management group had brief monthly counseling sessions with physicians and 3 times per week manual-guided counseling sessions with nurses covering recent drug use, abstinence efforts, attendance at self-help groups with support and advice for efforts to reduce drug use or remain abstinent.  Medication management plus manual-guided drug counseling sessions met weekly (no details provided) | Urban academically affiliated medical center; primary care; medical management provided by nurses and physicians (counseling issues reviewed weekly with physician and clinical psychologist) | Illicit drug use: urine toxicology and self report  Retention/adherence: attendance at visits  Overall health:SF-36  Patient satisfaction | Overall, patients reduced opioid-positive urine toxicology tests and good retention through maintenance; less patients in medication management group vs. medication management plus counseling group achieved greater than or equal to one week of opioid-free urine screens, though this difference was not statistically significant; A greater proportion of the medication management plus counseling group had opioid-free urine screens compared with the medication management alone group, though this difference was not statistically significant |
| Fiellin, 20063  (also a model of care) | Standard medical management (20 minutes with a nurse) and once-weekly medication dispensing (buprenorphine-naloxone) vs. standard medical management and thrice-weekly medication dispensing vs. enhanced (45 minutes with a nurse) medical management and thrice-weekly medication dispensing  All groups met monthly with a physician | 24 weeks | 166 | USA; 78% male; 77% white; mean age 36 years; mean duration of opioid dependence 8 years; 17% prescription drug use; 31% history of intravenous drug use; 20% cocaine-positive urine specimen at treatment entry; 66% previously attempted detoxification; 32% history of participation in methadone-maintenance program | Nurses dispensed buprenorphine-naloxone and provided standard (20 minutes; sessions covered recent drug use or efforts to achieve or maintain abstinence, attendance in self-help groups, support for efforts to reduce drug use or remain abstinent, advice for the achievement or maintenance of abstinence, and the results of analysis of weekly urine specimens) or enhanced (45 minutes; sessions covered similar issues but provided more in-depth drug counseling) medical management Physicians met with patients monthly (20 minutes; sessions paralleled that of the standard sessions, with the addition of an assessment of employment, legal, family or social, medical, and psychiatric problems related to addiction)  The nurses, a physician, and a psychologist met weekly to review the counseling | Trained primary care nurses without previous addiction treatment, physician, psychologist  Primary care center | Illicit opioid use: urine toxicology and self-report Abstinence: measured in consecutive weeks | The efficacy of brief weekly counseling and once-weekly medication dispensing did not differ significantly from that of extended weekly counseling and thrice-weekly dispensing |
| Fiellin, 20138 | Physician management (15-20 minutes weekly for the first 2 weeks, every 2 weeks for the next 4 weeks, and then monthly) with buprenorphine-naloxone or physician management with buprenorphine-naloxone plus CBT (up to 12 50-minute weekly sessions during the first 12 weeks of treatment) | 24 weeks | 141 | USA; 74% male; 90% white; mean age 34 years; mean time opioid dependent 8 years; 35% prescription drug use; 32% current injection drug use; 45% prior attempted detoxification; 59% prior substance abuse treatment; mean 1.3 days of use of cocaine in previous 30 days | Physician management (15-20 minutes; sessions occurred weekly for the first 2 weeks, every 2 weeks for the next 4 weeks, and then monthly). The physician followed a structured note that reviewed the patient’s recent drug use; provided brief advice on how to achieve or maintain abstinence; supported efforts to reduce drug use or remain abstinent; reviewed medical and psychiatric symptoms; assessed social, work, and legal function; discussed weekly urine toxicology results; and reviewed attendance at self-help groups.CBT was provided using a CBT manual adapted for cocaine dependence. Fidelity measures were taken and supervision provided. Patients were offered up to 12 50-minute weekly sessions during the first 12 weeks of treatment. The main components of counseling focused on performing a functional analysis of behavior, promoting behavioral activation, identifying and coping with drug cravings, enhancing drug-refusal skills, enhancing decision-making about high-risk situations, and improving problem-solving skills. | Internal medicine physicians with experience providing buprenorphine, trained masters and doctoral-level clinicians  Primary care clinic | Frequency of illicit opioid use: self-report  Maximum number ofconsecutive weeks of abstinence from illicit opioids: urine toxicology and self-report  Also, the proportion of patients remaining in the study (the percentage of patients who did not meet the criteria for protective transfer, did not miss medication for 7 days, or did not miss 3 physician management sessions), the number of days of the study that were completed, and self-reported abstinence from cocaine use (verifiedby urinalysis) | The effectiveness of physician management did not differ significantly from that of physician management plus CBT. |
| Galanter, 20049 | Buprenorphine plus medication management (2 individual sessions per week) vs. buprenorphine plus network therapy (1 individual and 1 group counseling session per week) | 18 weeks | 66 | USA; 76% male; 59% white, 24% Hispanic, 12% Black, 5% Asian/other; mean age 36 years; mean 12 years of heroin use; 33% had injection drug use in past 30 days; 73% had history of treatment for heroin addiction, 30% had history of methadone maintenance treatment | Patients underwent induction on buprenorphine/naloxone, maintenance phase, and taper off over 15 weeks, doses given daily aside for weekend take-home dosing  Network therapy had one group and one individual session per week; Network therapy trains network members to provide supportive environment for patient's adherence to avoidance of illicit drug use, joint sessions with support network members as well as individual sessions organized;  Medication management had two individual sessions per week; medication management focused on medication response and adherence monitoring and the establishment of therapeutic relationship | Office-based; Therapies provided by psychiatry resident physicians | Illicit drug use: urine toxicologies, percentage of negative screens (goal of adherence to abstinence expectation) and whether or not last 3 scheduled urines in study were negative (goal of opiate-free state by end of treatment) | Network therapy led to significantly more negative urine toxicologies and more network therapy than medication management patients had positive outcome relative to secondary heroin use by the end of treatment |
| Moore, 201210 | Buprenorphine and physician management (15 minute sessions weekly) vs. buprenorphine and physician management plus CBT (45 minute sessions weekly, depending on therapist availability) | 12 weeks | 55 | France; 74% male; mean age 39 years; 72% white; mean opioid dependence 9 years; 45% prescription drug use; 16% history of IV drug use; 41% prior attempted detoxification | Physician management included weekly buprenorphine dispensing, 15 minutes per session Other arm included physician management and thrice weekly directly observed buprenorphine therapy plus weekly CBT, 45 minutes per session, based on therapist availability | Adult primary care center of an urban teaching hospital; Physician management provided by primary care internal medicine physician with experience in office-based buprenorphine treatment.  CBT provided by trained therapists (2 master's level and 3 doctoral-level) with at least 3 years of experience.  Induction performed by trained nursing staff. | Drug use: urine toxicology and self-report  Treatment completion: continued participation through the 14th week; Treatment retention: number of weeks;  Patient satisfaction: Primary Care Buprenorphine Satisfaction Scale | Analyses adjusting for baseline characteristics showed no significant differences between groups on retention or drug use based on self-report or urines. Patient satisfaction was high across conditions, indicating acceptability of CBT counseling with observed medication. The number of CBT sessions attended was significantly associated with improved outcome, and session attendance was associated with a greater abstinence the following week. |
| Sullivan, 20066 (also a model of care) | Buprenorphine/naloxone and physician management (brief, biweekly) vs. buprenorphine/naloxone and physician management plus once-weekly drug counseling and adherence management | 12 weeks | 16 | USA; 94% male; 31% white, 44% Black, 25% Hispanic; mean age 47 years; mean 17 years opioid dependence; 56% with injection drug use; 29% reported one or more days of alcohol use in past 30 days; 36% reported one or more days of cocaine use in past 30 days; 100% HIV positive; mean 13 years since HIV diagnosis; 63% currently on ART; 81% HCV positive | Buprenorphine/naloxone stabilization over 2-weeks with clinic visits 3 times per week and 1 and 2-day take home doses then 10-week maintenance period with once weekly clinic visits and 6 take home doses then offered 2-week taper or extension phase; all patients received brief, bi-weekly, manual-guided physician management that focused on symptoms, drug use, and progress; half of patients received physician management plus once-weekly drug counseling and adherence management focused on addiction-specific topics like triggers, relationships, and craving and strategies to increased adherence to antiretroviral treatment | HIV clinics; Buprenorphine and physician management provided by physician specialized in addiction medicine and experienced in HIV care; drug counseling and adherence management provided by trained nursing staff (issues reviewed with supervising physician and clinical psychologist) | Treatment retention Illicit drug use: urine toxicology and self-report Laboratory parameters: CD4 count, viral load, and liver function tests Adherence to MAT and ART: Medication Event Monitoring System (caps that record the date and time the pill bottle was opened) HIV transmission risk behaviors: HIV/AIDS Risk Inventory Health status: SF-36 Patient satisfaction: 5-point Likert scale questionnaire | There was no difference in treatment retention or illicit drug use by counseling group; Overall, the proportion of opioid-positive weekly urine screens decreased substantially over trial; CD4 counts remained stable; viral load declined significantly; demonstrated feasibility of integrating buprenorphine into HIV clinical care for treatment of opioid dependence |
| Tetrault, 201211 | Physician management (brief, once every 2 weeks) vs. physician management plus enhanced medical management (45 minutes weekly; focused on drug counseling and adherence to anti-retroviral treatment) | 12 weeks | 47 | USA; 39% male; 29% white; mean age 47 years; mean 4 days of alcohol use in past 30 days; mean 5 days of cocaine use in past 30 days; mean 17 years of opioid dependence; 87% with primary heroin use; 49% with injection drug use; mean 12 years duration of HIV diagnosis; 61% receiving ART, 26% HCV positive | Physician management group had physician visit once every 2 weeks where they took medication under observation and were given a supply to take-home; physician management was brief, manual-guided, medically focused counseling intervention that focused on drug use, symptoms, side effects. Enhanced medical management group had clinic weekly, took medication under observation, and given supply to take home; enhanced medical management was a manual-guided counseling intervention lasting 45 minutes focused on drug counseling and adherence to ART | HIV clinic; Physicians for medication and physician management; nurses delivered enhanced medical management | Illicit drug use: percentage of opioid-negative urine specimens, drug urine screen; and self-report Abstinence: self-report  Study completion: not meeting criteria for protective transfer (3 consecutive positive urine tests after buprenorphine dose increased), continued research visits and medication dispensing through week 12  MAT and ART adherence: computerized bottle caps  HIV clinical data: CD-4 and viral load HIV risk behaviors: AIDS Risk InventoryImpact of opioid treatment and counseling into HIV setting: buprenorphine/naloxone dose, number of sessions attended, length of visits, number of sessions missed | At end of trial, no difference between groups in percentage of opioid negative urines, maximum duration of continuous abstinence, or retention; the percentage of subjects with detectable viral loads decreased from baseline across both groups similarly; overall, providing extended counseling in this setting is feasible but does not provide detectable improvement in outcomes |
| Weiss, 201112 Prescription Opioid Addiction Treatment Study (POATS) | Phase 1: Standard medication management (after initial session,15-20 minute s weekly, then biweekly sessions with a physician) with buprenorphine/ naloxone vs. standard medication management with buprenorphine/ naloxone plus opioid dependence counseling (45-60 minute sessions with a counselor, twice weekly then biweekly)  Phase 2 (extended treatment for those who relapsed): Standard medication management (2 visits first week, then weekly) with buprenorphine/ naloxone vs. standard medication management with buprenorphine/ naloxone plus opioid dependence counseling (twice weekly then biweekly) | Phase 1: 12 weeks  Phase 2 (for patients with unsuccessful outcomes): 24 weeks | 653 | USA; 60% male; 91% white; mean age 33 years; 27% alcohol dependence during lifetime; 18% cocaine dependence during lifetime; 5 mean years of opioid use; 23% used heroin ever; 32% previous treatment for OUD; 42% current chronic pain | Physicians provided manual-based, standard medical management. During the initial sessions (45-60 minutes in phase 1 and 30-60 minutes in phase 2), the physician reviewed the patient’s medical, psychiatric, and substance use problems; recommended abstinence; and referred the patient to self-help groups. In subsequent visits (15-20 minutes), the physician assessed substance use, craving, and buprenorphine-naloxone response; recommended abstinence and self-help participation; and prescribed buprenorphine- naloxone.The comparison group received standard medical management and manual-based opioid dependence counseling (45-60 minute sessions). Opioid dependence counseling was based on drug counseling manuals with demonstrated efficacy, modified for this study of prescription opioid dependence treatment with buprenorphine. Counselors educated patients about addiction and recovery, recommended self-help groups, and emphasized lifestyle change. Using a skills-based format with interactive exercises and take-home assignments, opioid dependence counseling covered a wider range of relapse prevention issues in greater depth than did standard medication management, including coping with high-risk situations, managing emotions, and dealing with relationships. | Physicians certified to prescribe buprenorphine, trained substance abuse or mental health professionals10 study/treatment sites | Opioid use: urine toxicology and self-reportPhase 1 successfuloutcome: completing week 12 with opioid use on no more than 4 days in a month, absence of 2 consecutive opioid-positive urine test results, no additional substance use disorder treatment, and no more than 1 missing urine sample during the 12 weeks  Phase 2 successful outcome:abstaining from opioids during week 12 and during at least 2 of the previous 3 weeks | During phase 1, only 6.6% of patients had successful outcomes, with no difference between standard medical management or standard medical management plus opioid dependence counseling. During phase 2, 49% attained successful outcomes, with no difference between groups. Success rates 8 weeks after completing the buprenorphine-naloxone taper (phase 2, week 24) dropped to 8.6%, again with no difference between groups. |
| Weiss, 201513  Prescription Opioid Addiction Treatment Study (POATS) | See above | 9 month treatment; 42 month followup | 375 | USA; 56% male; 90% white; mean age 33 years old; 3.7% with alcohol dependence in past year; 5.9% with cannabis dependence in past year; 3.2% with cocaine dependence in past year; 3.5% with other stimulant dependence in past year; 4.8% with sedative-hypnotic dependence in past year; mean 5 years of opioid use; 22% had ever used heroin; 78% used opioids through route other than sublingually/ swallowed | Standard medication management included weekly visits with physician, combining medication administration with medication-focused counseling; phase 1 was 4-week medication taper; phase 2 for those who relapsed included medication for 12 weeks then 4-week taper  Opioid dependence counseling focused on relapse prevention, skill-building, and lifestyle change opioid dependence counseling twice weekly for six weeks then once weekly for 6 weeks | Office-based; primary care; Physicians for medication management and counseling  Opioid dependence counseling providers not described but appear to be physicians; research assistants conducted followup phone interviews | Followup measures: phone calls at 18, 30, and 42 months and included the Composite International Diagnostic Interview for opioid diagnosis, the ASI for substance use severity, four items from SF-36 for general health and pain, the Fagerstrom Test for Nicotine Dependence for smoking dependence severity, subset from the Pain and Opiate Analgesic Use History | Few participants had successful opioid outcomes in phase 1; almost half had successful opioid treatment in phase 2; addition of opioid dependence counseling to medication did not improve outcomes; one third of those in followup abstained and were not on agonist medication, one third were abstinent on agonist therapy and another third were using opioids (followup outcomes not described by group) |
| ***Pharmacological Therapies*** |  |  |  |  |  |  |  |  |
| Carrieri, 201414 | Induction of methadone in primary care vs. specialty care | 12 months | 221 | France; 84% male; median age 32 years (IQR: 27-38); 27% used cocaine; 72% used street opioids; 20% used psychotropic drugs; 15% drug injection users; 64% drug snorting users; 18% were daily cannabis users; 33% had hazardous alcohol consumption; 12% history of drug overdose; 17% history of suicide attempt,;2% HIV-positive, 19% HCV-positive; 49% history of drug injection | Evaluation of implementation strategy of 14-day supervised methadone induction, with starting dose of 30-40 mg, with 10 mg increases every 2-4 days, until dose stabilization. Took into account those who switched from buprenorphine to methadone at enrollment. | Physicians in 10 sites; specialty care and primary care physicians with field experience in care for opioid dependence and/or training in care for drug dependence | Abstinence from street-opioids at 12 months using a validated question administered during phone interviews, engagement in treatment computed as the proportion of patients who actually started methadone and remained in the trial until the stabilization of dosages, retention in methadone maintenance treatment only for patients who actually started methadone treatment recorded as the time between the first day of methadone induction and the last known date that the patient was still receiving treatment, and patient satisfaction on a 5-point Likert scale that was dichotomized as very satisfied vs. other. Pharmacies and physicians recorded overdoses, signs of intoxication, and lost-to-followup. A list of 50 health-related symptoms was included in a questionnaire that helped document self-reported symptoms. | Under appropriate conditions, methadone induction in primary care is feasible and acceptable to both physicians and patients. It is as effective as induction in specialized care in reducing street-opioid use and ensuring engagement and retention in treatment for opioid dependence. |
| (Carrieri 2014 pilot study)  Roux, 201215 | See above | 2 weeks induction 12 months followup for outcomes | 195 | Study conducted in France, no other information provided | Induction model included: 1) study-specific pretraining for primary care physicians; 2) a shared care model, based on the patient primary care physicians-Center for Substance Abuse Prevention Association -pharmacist network; 3) the exclusion of patients with triple codependence on opioids/benzodiazepines/alcohol, as screened by Mini-International Neuropsychiatric Interview; 4) the daily supervision at the local pharmacy during the initiation phase for patients starting methadone in primary care; 5) patient accountability for treatment intake and appropriate storage | Primary care and medical center; Clinic visits and phone interviews; Trained primary care and Center for Drug Abuse Prevention Association physicians | Abstinence from street-opioids at 12 months using a validated question, retention in treatment, occurrence of overdoses, prevalence of other HCV risk transmission practices, depressive symptoms using CES-D, suicidal risk using Beck Hopelessness Scale, impulsivity using the Barratt Impulsiveness Scale, sensation seeking using the Brief Sensation Seeking Scale, tobacco dependence using the Fagerstrom test, alcohol consumption using the AUDIT questionnaire, pain assessment using the Brief Pain Inventory, adherence to methadone prescription, patient-health care provider relationship, opioid withdrawal, quality of life using SF-12, adult ADHD Self-Report Scale 6 item version, urinary drug screening, and socio-demographic information on history of incarceration and contact with associations. | NR |
| Fiellin, 200116 | Primary care-based methadone (weekly physician sessions and monthly counseling session) vs. narcotic treatment program-based methadone (1 to 3 sessions per week dose, weekly group counseling, and monthly individual counseling) | 6 months | 46 | USA; 65% male; 78% white; mean age 42 years; 17% HIV-positive; 91% with prior detoxification attempt; 72% with history of IV drug use | Office-based group had weekly physician contact for medication dosing and 6 take-home doses plus monthly counseling session   Narcotic treatment program group had 1 to 3 treatment center visits per week for methadone dose and take-home dosing plus weekly group and monthly individual counseling   Note: patients who had a positive random urine sample or urine that did not show methadone and a repeat urine sample that was positive and did not show methadone were considered clinically unstable and care was escalated | Offices of general medicine internists who provided all office-based care (4/6 were certified in Addiction Medicine);   Treatment center was site of narcotic treatment program; Physicians, counselors, social workers, and employment services provided narcotic treatment program | Illicit drug use: self-report, urine and hair toxicology Patient and clinician satisfaction: 5-point Likert scale questionnaire  Functional status: SF-36, ASI and modified Treatment Services Review; Depression: Center for Epidemiologic Studies Depression Scale | There was no significant between-group difference on illicit drug use or patients with clinical instability; Significantly more office-based patients thought that quality of care was excellent; There were no group differences in functional status or use of health, legal, or social services; Overall, results supported feasibility and efficacy of transferring stable opioid-dependent patients to primary care for methadone maintenance |
| Fudala, 200317 | Daily buprenorphine/naloxone vs. buprenorphine vs. placebo  All participants received HIV counseling and up to 1 hour of individualized counseling per week; emergency counseling and referrals provided | 4 weeks for efficacy; 48-52 weeks for safety | 323 for efficacy; 472 for safety | Efficacy sample: USA; 65% male; mean age 38 years; 61% white, 28% black, 7.1% Hispanic, 1.2% Native American, 2.2% Asian/Pacific Islander; median 84 month (range: 3 to 468) duration of heroin abuse; 51% with prior enrollment in methadone or LAAM program Safety sample: USA; 69% male; mean age 39 years; 50% white, 30% black, 17% Hispanic, 0.8% native American, 1.9% Asian/Pacific Islander; median 120 months (range: 3 to 468) duration of heroin abuse; 50% with prior enrollment in methadone or LAAM program | Provided daily MAT or placebo administered on site with take-home dosing for weekends/holidays; during open-label phase, up to 10-day supply of medication provided; all participants received HIV counseling and up to 1 hour of individualized counseling per week; emergency counseling and referrals provided | Physician's office in a clinical research program distinct from methadone clinic (provider type not described) | Opiate use: percentage of opiate-negative urine samples  Opiate craving: self report  Overall status: per participant and per clinicianIllicit drug use other than opiates: percentage of negative urine drug screens  Subject retentionRates of adverse medical events  Electrocardiography and laboratory findings | Efficacy study terminated early due to greater efficacy of buprenorphine/naloxone and buprenorphine vs. placebo; Proportion of opiate-negative urine samples significantly less among both MAT groups vs. placebo; MAT groups reported significantly less opiate craving than placebo; Rates of adverse events similar in active-treatment and placebo groups; findings from open-label followup indicated combined treatment was safe and well tolerated |
| King, 200618 | Routine care (methadone dispensing window for weekly doses and monthly counseling for 20 minutes) vs. methadone maintenance clinic (monthly observed dose, take home supply, monthly 20 minute counseling session with medical provider) vs. primary care based-methadone (monthly observed dose, take home supply, monthly 20 minute counseling session with office physician) | 12 months | 92 | USA; 62% male; 72% white; mean age 44 years; no patient included had submitted positive breath intoximeter readings in past year; mean 14 years of methadone treatment received over lifetime | Routine care group received 1-2 doses of methadone per week at dispensing window and 5-6 take-home doses with once-monthly appointments with the clinic counselorClinic-based methadone medical maintenance received one dose of methadone observed by nurse or physician and 27 days of take-home methadone every 4 weeks and monthly appointments with clinic counselor Office-based methadone medical maintenance received one dose of methadone observed by physician and 27 days of take-home doses every 4 weeks from physician's office and had monthly counseling session with physician Note: if found to have positive urine or failed medication recall, participant was stepped-up in care | Community primary health care center and one addiction treatment center as sites of office-based methadone medical maintenance; Physician provided medication and counseling  Clinic-based methadone medical maintenance at two community-based methadone maintenance treatment programs; nurse or physician provided medication and counselor provided counseling | Illicit substance use: urine specimens  Medication monitoring: random medication recalls  Addiction-related issues in past 30 days: ASI  Patient Satisfaction: Client Satisfaction Questionnaire Quality of therapeutic relationship: Helping Alliance Questionnaire for Patients  Other measures: Post-study opinion survey  Monthly hours in treatment: patient estimates of time spent engaged in treatment-based activities  Engagement in employment, family/social, and personal activities: patient estimates | Generally low rates of drug use or failed medication recall with good study retention; No between-group differences on ASI scores; Treatment satisfaction was high in all groups and patients in all groups rated strong quality of therapeutic alliance; methadone medical maintenance patients in both office and clinic-based care initiated more new employment or social/family activities than routine care; most methadone medical maintenance patients reported a preference for office-based care compared with clinic-based |
| Lintzeris, 200419 | Methadone vs. buprenorphine administered under naturalistic conditions by 18 community-based and 1 specialist-based sites by general practitioners and community pharmacists (Buprenorphine Implementation trial [BIT]) | 12 months | 139 | Australia; 58% male; mean age 30 years; mean age of first heroin use 21 years; mean duration lifetime methadone treatment 27 months; 0-32% reported no heroin use in past month | Methadone treatment consistent with state guidelines with supervised dispensing at pharmacies and one take-away dose per week for stable patients; dose, frequency or review, counseling was tailored per patients; Buprenorphine treatment consisted of flexible dosing and at least monthly review, optional psychotherapy; daily dispensing at induction with alternate-day or 3-day dosing once stable | First intake of study conducted in specialist clinic; second intake of study conducted in community setting with primary care clinicians and pharmacists | Retention in treatment: pharmacy records  Heroin use: Self report using Opiate Treatment Index | Among methadone stabilized patients, mean retention time was similar between groups; among heroin users, there was a trend towards improved retention among those taking methadone compared with those on buprenorphine, though this was not statistically significant; There were significant reductions in heroin use in all groups over time and a trend toward lower heroin use among heroin users on buprenorphine |

ADHD = attention deficit hyperactivity disorder; ART = anti-retroviral treatment; ASI = addiction severity index; AUDIT = Alcohol Use Disorders Identification Test; BFC = behavioral family counseling; CBT = cognitive behavioral therapy; CD4 = cluster of differentiation 4 glycoprotein; CES-D = Center for Epidemiological Studies Depression; ED = emergency department; EMM = enhanced medical management; HCV = hepatitis C virus; HIV = human immunodeficiency virus; IBT = individual based treatment; IV = intravenous; IQR = interquartile range; LAMM = levo-alpha-acetylmethadol; MAT = medication assisted treatment; NR = not reported; OUD= opioid use disorder; PM = physician management; RNA = ribonucleic acid; SD = standard deviation; SF-12 = Medical Outcomes Study Short-Form 12; SF-36 = Medical Outcomes Study Short-Form 36; USA = United States of America; vs. = versus