Table 2. Description of studies that evaluated the effectiveness of community maintenance with buprenorphine.

Study	Study design	Sample	Intervention	Provider	Outcome measures	Notes
Ahmadi (2002), Iran[20]	Prospective, single-blinded, randomised controlled trial.	105 opiate-dependent subjects, mean age 32 years (16-64).	17 weeks of sublingual buprenorphine daily: 1 mg, 2 mg or 4 mg. All subjects were offered a weekly 1-hour individual counselling session.	Outpatient clinic.	Retention in treatment.	Moderate risk of selection bias; doses of buprenorphine may have fallen at the lower end of their therapeutic effectiveness.
Ahmadi (2002), Iran[21]	Prospective, single-blinded, randomised controlled trial.	330 opiate-dependent subjects, mean age 37 years (19-72).	18 weeks of sublingual buprenorphine daily: 1 mg, 2 mg or 4 mg. All subjects were offered a weekly 1-hour individual counselling session.	Outpatient clinic.	Retention in treatment.	Moderate risk of selection bias; doses of buprenorphine may have fallen at the lower end of their therapeutic effectiveness.
Amass *et al* (1994), US[22]	Prospective, double-blinded, cross-over, randomised controlled trial.	13 opiate-dependent subjects with a long history of opiate use, mean age 39 years (28-45).	21 days of daily buprenorphine administration (4 mg/70 kg) or alternate day buprenorphine administration (twice the daily maintenance dose every other day with placebo on the interposed day). Weekly individual counselling.	Outpatient clinic. Care provided by nurse.	Reduction in illicit opiate use and withdrawal severity.	Small sample size; brief intervention phase.

Amass *et al* (1998), US[23]	Prospective, double-blinded, cross-over, randomised controlled trial.	18 opiate-dependent subjects with a long history of opiate use, mean age 37 years (28-45).	14 days of blind daily dosing, open daily dosing, blind alternate-day dosing (double maintenance doses every 48 hours, placebo on interposing days), or open alternate-day dosing (double maintenance doses on Monday, Wednesday, and Friday, and maintenance dose on Sunday). Subjects were exposed twice to each dosing schedule. Subjects then chose either daily or alternate-day schedules each week for one month. Doses were titrated to the individual subject (2 to 8 mg/70 kg).	Outpatient clinic.	Abstinence and withdrawal severity.	Small sample size; brief intervention phase.
Bickel *et al* (1999), US[24]	Prospective, double-blinded, placebo-controlled, cross-over, randomised controlled trial.	16 opiate-dependent subjects with a long history of opiate use, mean age 37 years (21-44).	21 days of daily buprenorphine administration (4 mg / 70 kg); double the daily maintenance dose every 48 hours; triple the daily maintenance dose every 72 hours. All subjects received weekly individual counselling.	Outpatient clinic. Care provided by counsellor.	Abstinence and withdrawal severity.	Small sample size; brief intervention phase.
de los Cobos *et al* (2000), Spain[25]	Prospective, double-blinded, randomised controlled trial.	Sixty highly-dependent opiate users, mean age 28 years (21-45).	12 weeks of sublingual buprenorphine daily (8 mg) or thrice-weekly (16 mg on Mondays and Wednesdays, 24 mg on Fridays). All subjects were urged to attend a weekly group-therapy session and an	Outpatient clinic. Care provided by nurse.	Reduction in illicit opiate use, withdrawal severity, length of stay,	Small sample size; fixed dose of buprenorphine which may have fallen at the lower end

			individual counselling session every two weeks.		retention in treatment, and quality of life.	of its therapeutic effectiveness.
Eissenberg *et al* (1997), US[26]	Prospective, double-blinded, randomised controlled trial.	8 opiate-dependent subjects, mean age 35 years (24-36), 38% white; 62% afro-american.	11 weeks of maintenance control condition (placebo i.m. injection and 8 mg s.l. buprenorphine on days 0-3), double dose plus omission condition (placebo i.m. injection on days 0-3 and 16 mg s.l. buprenorphine on day 0, s.l. placebo on days 1 and 2 and 8 mg s.l. buprenorphine on day 3), single dose plus omission condition (placebo i.m. injection on days 0-3 and 8 mg s.l. buprenorphine on day 0, s.l. placebo on days 1 and 2 and 8 mg s.l. buprenorphine on day 3), and the naloxone control condition (placebo i.m. injections, 8 mg s.l. buprenorphine on day 0-2, 10 mg / 70 kg naloxone and 8 mg s.l. buprenorphine one hour later on day 3).	Outpatient clinic. Care provided by nurse and counsellor.	Withdrawal severity.	High risk of selection bias; small sample size; brief intervention phase; sample of subjects who abstained from illicit drug use during first two weeks of treatment.
Greenwald *et al* (1999), US[27]	Prospective, double-blinded, cross-over, randomised controlled trial.	14 heroin-dependent subjects with a long history of opiate use,	3 months of hydromorphone 0, 4, 8, or 16 mg / 70 kg i.m. in subjects maintained on buprenorphine at doses of 2, 4, or 8 mg, each for 2 weeks.	Outpatient clinic.	Abstinence and withdrawal severity.	High risk of performance bias; high risk of attrition bias; small

		mean age 39 years (20-48), 50% afro-american.				sample size.
Gross *et al* (2001), US[29]	Prospective, double-blinded, cross-over, randomised controlled trial.	14 opiate-dependent subjects with a long history of opiate use, mean age 38 years (28-51), 100% white.	8 weeks of quintuple doses (5 x daily maintenance dose) every 120 hours or sextuple doses (6 x daily maintenance dose) every 120 hours. Daily sublingual maintenance doses were 4 mg / 70 kg or 8 mg / 70 kg.	Outpatient clinic.	Withdrawal severity.	Small sample size.
Johnson *et al* (1995), US[30]	Prospective, double-blinded, cross-over, randomised controlled trial.	150 opiate-dependent subjects.	2 weeks of sublingual buprenorphine daily (2 mg or 8 mg) or placebo. All subjects attended group therapy sessions a minimum of once per week.	Outpatient clinic. Care provided by counsellor.	Abstinence.	High risk of selection bias; moderate risk of attrition bias; brief intervention phase.
Petry *et al* (1999), US[33]	Prospective, double-blinded, cross-over, randomised controlled trial.	14 opiate-dependent subjects with a long history of opiate use.	4 dosing regimens of buprenorphine for 5 repetitions of each: daily maintenance dose every 24 hours, double the daily maintenance dose every 48 hours, triple the daily maintenance dose every 72 hours, and quadruple the daily maintenance dose every 96 hours. Sublingual buprenorphine daily maintenance doses of either 4 mg / 70 kg or 8 mg/70 kg. All	Outpatient clinic.	Abstinence, withdrawal severity, and retention in treatment.	Small sample size; brief intervention phase.

			subjects received weekly counselling.			
Petry *et al* (2000), US[34]	Prospective, cross-over, randomised controlled trial.	14 opiate-dependent subjects with a long history of opiate use, mean age 39 years (21-48).	4 dosing regimens of buprenorphine for 5 repetitions of each: daily maintenance dose every 24 hours, double the daily maintenance dose every 48 hours, triple the daily maintenance dose every 72 hours, and quadruple the daily maintenance dose every 96 hours. Sublingual buprenorphine daily maintenance doses of either 4 mg / 70 kg or 8 mg / 70 kg. All subjects received weekly counselling.	Outpatient clinic.	Abstinence, withdrawal severity, and retention in treatment.	Small sample size; brief intervention phase.
Petry *et al* (2000), US[34]	Prospective, cross-over, randomised controlled trial.	14 opiate-dependent subjects with a long history of opiate use, mean age 39 years (21-48).	1 of 6 choice conditions using buprenorphine: 1) daily maintenance dose or double the maintenance dose every other day; 2) daily maintenance dose or triple the maintenance dose every third day; 3) daily maintenance dose or quadruple the maintenance dose every fourth day; 4) double the maintenance dose every other day or triple the maintenance dose every third day; 5) double the maintenance dose every	Outpatient clinic.	Abstinence and retention in treatment.	High risk of attrition bias; small sample size; brief intervention phase.

			other day or quadruple the maintenance dose every fourth day; 6) triple the maintenance dose every third day or quadruple the maintenance dose every fourth day. Each condition was kept in effect for 12 days. All subjects were presented with each of the six conditions.			
Petry *et al* (2001), US[35]	Prospective, double-blinded, cross-over, randomised controlled trial.	25 opiate-dependent subjects with a long history of opiate use, mean age 35 years (22-51).	3 dosing regimens of buprenorphine for 5 repetitions of each: daily maintenance dose every 24 hours, triple the daily maintenance dose every 72 hours, or quintuple the daily maintenance dose every 120 hours. Sublingual buprenorphine daily maintenance doses of either 4 mg / 70 kg or 8 mg / 70 kg. All subjects received weekly counselling.	Outpatient clinic.	Abstinence, withdrawal severity, and retention in treatment.	Brief intervention phase.
Resnick *et al* (1992), US[36]	Prospective, double-blinded, randomised controlled trial.	85 heroin users, mean age 35 years (21-50), 48% white; 15% afro-american; 37% hispanic.	Maintenance for 4 to 12 weeks on the lowest dose of buprenorphine that blocked heroin craving (8 mg max). All subjects received psychosocial counselling. Following maintenance, abstinent subjects received either dose reductions for five	Outpatient clinic. Care provided by nurse and social worker.	Abstinence, withdrawal severity, and retention in treatment.	High risk of attrition bias.

			weeks of 10% twice weekly to zero dose, then placebo for two weeks; or the same dose for seven weeks.			
Schottenfeld *et al* (2000), US[37]	Prospective, double-blinded, randomised controlled trial.	92 opiate-dependent subjects, mean age 37 years, 75% white.	12 weeks of buprenorphine administered daily (16 mg / 70 kg) or thrice-weekly (34 mg / 70 kg on Fridays and Sundays, and 44 mg / 70 kg on Tuesdays). All subjects received weekly group counselling.	Outpatient clinic. Care provided by nurse.	Abstinence, reduction in illicit opiate use, and retention in treatment.	Low risk of bias; limited statistical power; high and fixed dose of buprenorphine.

Notes: 'low' risk of bias reflects plausible bias unlikely to seriously alter the results; 'moderate' risk of bias reflects plausible bias that raises some doubt about the results; 'high' risk of bias reflects plausible bias that seriously weakens confidence in the results.