Effectiveness and cost-effectiveness of adjunctive personalised psychosocial intervention in treatment-resistant maintenance opioid agonist therapy

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Articles

Efficacy and cost-effectiveness of an adjunctive personalised psychosocial intervention in treatment-resistant maintenance opioid agonist therapy: a pragmatic, open-label, randomised controlled trial

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Summary

Background Opioid use disorder is a chronic, debilitating, and costly disorder that has increased in prevalence in many countries, with an associated sharp rise in mortality. Maintenance opioid agonist therapy is the first-line treatment, but many patients do not stop using illicit or non-prescribed drugs concomitantly. We aimed to test the efficacy and cost-effectiveness of a personalised psychosocial intervention implemented with a toolkit of behaviour-change techniques as an adjunct to opioid agonist therapy.

Methods We did a pragmatic, open-label, randomised controlled trial at a specialist UK National Health Service community addictions clinic in London, UK. Eligible patients were aged 18 years or older, met criteria for opioid or cocaine dependence, or both, in the past 12 months, and voluntarily sought continued oral maintenance opioid agonist therapy, which they had been prescribed for at least 6 weeks. All participants were treatment resistant (ie, 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). Participants were allocated (1:1) by a web-accessed randomisation sequence (stratified by opioid agonist medication, current cocaine use, and current rug use) to receive a personalised psychosocial intervention (comprising a flexible toolkit of psychological-change methods, including contingency management to reinforce abstinence, recovery activities, and clinic attendance) in addition to treatment as usual, or treatment as usual only (control group). The primary outcome was treatment response at 18 weeks, which was defined as abstinence from illicit and non-prescribed opioids and cocaine in the past 28 days, as measured with treatment outcomes profiles and urine drug screening. Taking a societal cost perspective, we did an evaluation of cost-effectiveness with a wide range of willingness-to-pay values for a unit improvement in the probability of treatment response. We also calculated quality-adjusted life-years (QALYs). Efficacy was analysed in a modified-intention-to-treat population, including all participants who were randomly allocated but excluding those who had previously completed the intervention. This trial is registered with ISRCTN, number ISRCTN69313751. The trial is completed.

Findings Between June 7, 2013, and Dec 21, 2015, we randomly allocated 136 participants to the psychosocial intervention group and 137 to the control group. The trial database was locked on April 19, 2017. Three patients (one in the psychosocial intervention group and two in the control group) who were re-randomised in error were excluded from the analysis. 22 (16%) of 135 patients in the psychosocial intervention group had a treatment response, compared with nine (7%) of 135 in the control group (adjusted log odds 1·20 [95% CI 0·01–2·37]; p=0·048). The psychosocial intervention had a higher probability of being cost-effective than treatment as usual. There was a probability range of 47–87% for willingness-to-pay thresholds of £0–1000 for a unit improvement in the probability of treatment response. QALYs were higher in the psychosocial intervention group than in the control group (mean difference 0·048 [95% CI 0·016–0·080]; p=0·004) in adjusted analyses, with 60% and 67% probabilities of cost-effectiveness at the UK National Institute for Health and Care Excellence's willingness-to-pay thresholds of £20 000 and £30 000 per QALY, respectively. The number of adverse events was similar between groups, and no severe adverse events in either group were judged to be treatment related. One participant in the control group was hospitalised with drug-injection-related sepsis and died.

Interpretation In maintenance opioid agonist therapy, an adjunctive personalised psychosocial intervention in addition to standard therapy was efficacious and cost-effective compared with standard therapy alone at helping treatment-resistant patients abstain from using illicit and non-prescribed opioids and cocaine.

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Background

- Systematic review of 6 trials **1** of opioid agonist therapy for heroin dependence (n=837) shows flexible-dose methadone more effective than flexible-dose buprenorphine for retention but not for lower heroin use.

- Systematic review of 3 trials **2** of pharmaceutical opioid use disorder (n=360), no difference between methadone and buprenorphine for retention or suppression of non-prescribed opioid use.

1 Cochrane Database Syst Rev 2014; 3: CD002207.
2 Cochrane Database Syst Rev 2016; 5: CD011117.

Limitations of opioid agonist therapy

- Many patients discontinue treatment. 1
- Some stay in treatment but do not take their prescription as directed and use illicit opioids
- An English study of 13 542 patients enrolled for 12–26 weeks, reported that 63%) used opioids on 10 or more of the past month at clinical review. 2
- An English study 7,718 patients continuously enrolled in opioid agonist therapy for 5.5 years, 1:7 had a stable pattern of nonresponse (opioids used on 15 of the past 28 days before 6-monthly clinical reviews). 3
- Cocaine use disorder 4 and co-occurring anxiety and mood disorders can moderate engagement with, and response to, opioid agonist therapy. 5

1 Hser Addiction 2014; 109: 79–87; 2 Marsden Lancet 2009; 374: 1262–70; 3 Eastwood; Drug Alcohol Depend 2018; 188: 200–08. 4 Marsden Addiction 2012; 107: 2161–72; 5 McHugh K. Harv Rev Psychiatry 2015; 23: 99–111.

Adjunctive psychosocial interventions

- Many manual-driven therapies have been trialled.
- NICE endorses only contingency management), behavioural couple interventions, and 12-step-based groups. **1**
- Cochrane review of 13 different interventions concluded that the effectiveness of opioid agonist therapy was not enhanced by the addition of any psychosocial interventions. **3**

1 Clinical Guideline 51
2 Cochrane Database Syst Rev 2011; 10: CD004147

Case formulation-driven toolkit

- Case formulation is collaborative, hypothesis of why a disorder is maintained. 1
- Focus on cognitive, affective, and interpersonal factors.
- Change methods for 12-week intervention selected from the following interventions:
  - Cognitive behavioural therapy
  - Contingency management with 3 targets: abstinence, clinic attendance, recovery activities
  - 12-step facilitation therapy
  - Social behaviour and network therapy
  - Behavioural couples therapy

1 Marsden J Drug Alcohol Depend 2014; 139: 121–31.

Participants, Setting, Outcome

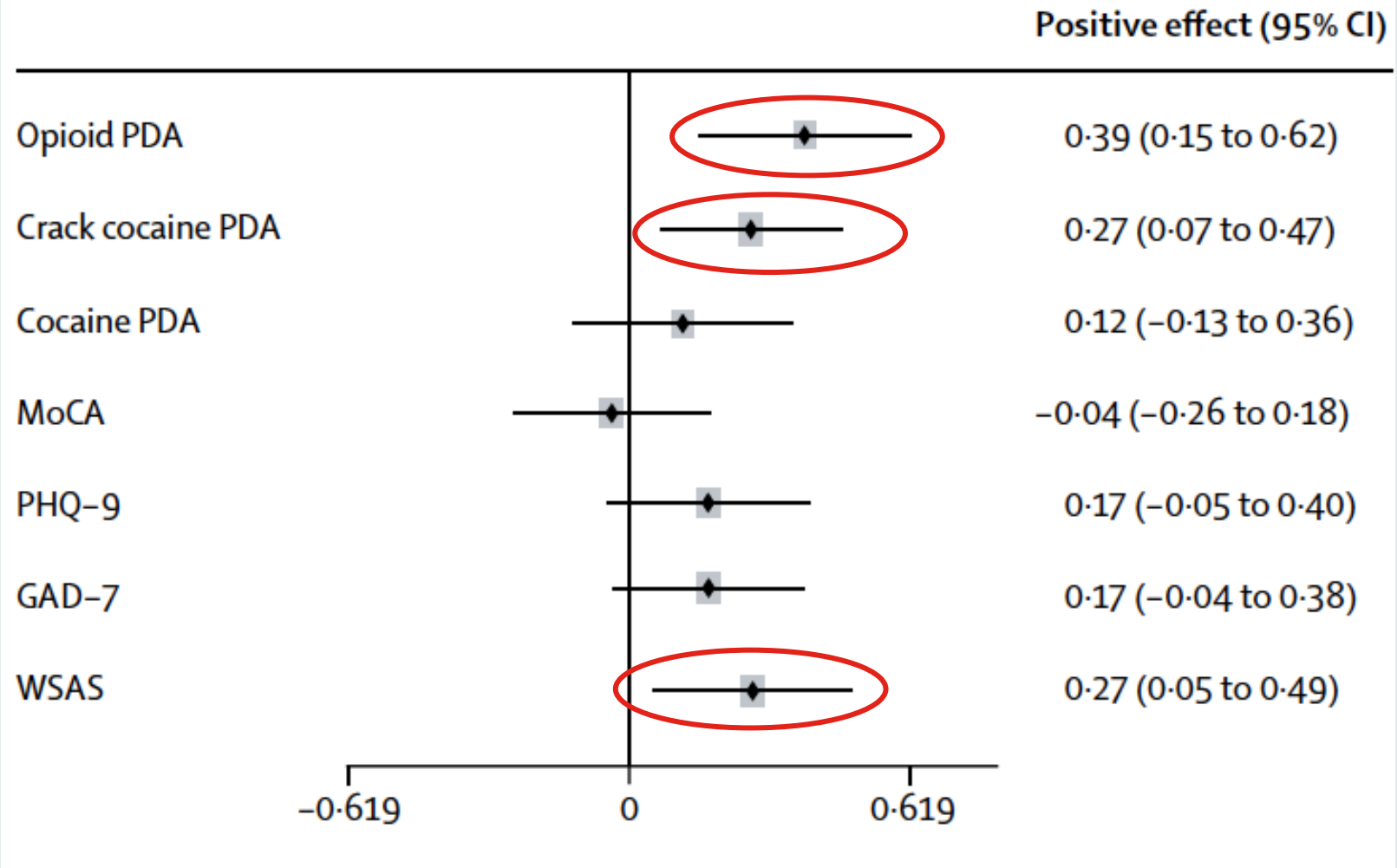
- Patients recruited were enrolled in opioid agonist therapy for at least 6 weeks in NHS community treatment service and using heroin or cocaine on 1+ days in past month (UDS verified).
- Randomisation stratified by type of opioid agonist therapy, recent cocaine use and injecting) to ongoing treatment-as-usual (TAU) and TAU plus tailored psychosocial intervention (PSI).
- Primary outcome was treatment response at 18 weeks defined as no reported use of opioids or cocaine during the 28 days before follow-up interview and one or more negative urine drug tests for heroin and cocaine (and no positive tests).

Results (1)

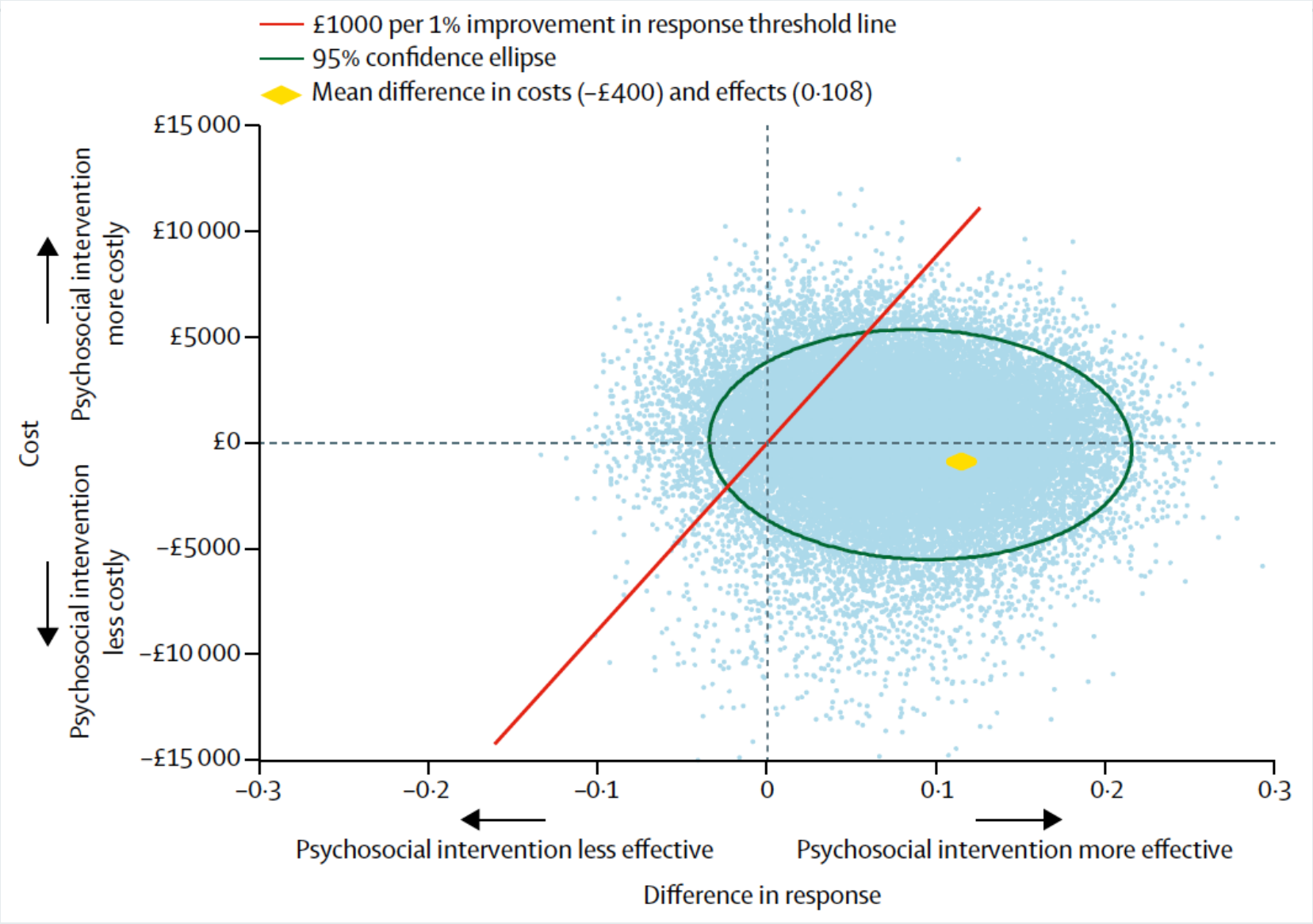
- At 18 weeks, almost all participants enrolled in opioid agonist therapy.
- No group difference in daily dose.
- PSI delivered by 5 psychology assistants and 3 senior psychologists.
- PSI participants attended 5 sessions (range: 0-20).
- 59% of PSI participants attended at least 1/3rd of sessions.

- At follow-up, 22 (16%) of 135 participants in the PSI group were treatment responders, compared with nine (7%) of 135 in the control group (adjusted log odds 1.20).

Results (2)


Positive effect (95% CI)
Opioid PDA
0·39 (0·15 to 0·62)
Crack cocaine PDA
0·27 (0·07 to 0·47)
Cocaine PDA
0·12 (−0·13 to 0·36)
MoCA
−0·04 (−0·26 to 0·18)
PHQ−9
0·17 (−0·05 to 0·40)
GAD−7
0·17 (−0·04 to 0·38)
WSAS
0·27 (0·05 to 0·49)
−0·619
0
0·619

Results (3)


£1000 per 1% improvement in response threshold line
95% confidence ellipse
Mean difference in costs (–£400) and effects (0·108)
£15 000
£10 000
£5000
£0
–£5000
–£10 000
–£15 000
Cost
Psychosocial intervention more costly
Psychosocial intervention less costly
–0·3
–0·2
–0·1
0
0·1
0·2
0·3
Psychosocial intervention less effective
Psychosocial intervention more effective
Difference in response

Conclusion

- As long noted in psychotherapy, the provision of an additional element to standard care is likely to achieve only a small average effect. 1
- NICE position based on the average treatment effect from a a mix of responders and non-responders, which potentially masks the efficacy of psychosocial interventions for responders.
- We showed that a tailored PSI for patients not responding to opioid agonist therapy was effective and cost-effective.

1 Bell; J Consult Clin Psychol 2013; 81: 722–36.