Jofre-Bonet, M; Sindelar, JL; Petrakis, IL; Nich, C; Frankforter, T; Rounsaville, BJ; Carroll, KM (2004) Cost effectiveness of disulfiram: treating cocaine use in methadone-maintained patients. Journal of substance abuse treatment, 26 (3). pp. 225-32. ISSN 0740-5472 DOI: https://doi.org/10.1016/S0740-5472(04)00004-2

DOI: 10.1016/S0740-5472(04)00004-2

Published in final edited form as:
J Subst Abuse Treat. 2004 April ; 26(3): 225–232. doi:10.1016/S0740-5472(04)00004-2.

Cost effectiveness of disulfiram: Treating cocaine use in methadone-maintained patients

Mireia Jofre-Bonet[a,*], **Jody L. Sindelar**[b], **Ismene L. Petrakis**[b], **Charla Nich**[b], **Tami Frankforter**[b], **Bruce J. Rounsaville**[b], and **Kathleen M. Carroll**[b]

[a]ICEH-London School of Hygiene and Tropical Medicine, Keppel Street, Room 9/311, London WC1E 7HT, UK

[b]Department of Epidemiology and Public Health and Department of Psychiatry, Yale University School of Medicine, New Haven, CT

Abstract

Converging evidence suggests that disulfiram is a promising treatment for cocaine dependence. We study the cost-effectiveness of providing disulfiram to methadone-maintained opioid addicts in a randomized clinical trial setting. Our economic evaluation is based on a double blind clinical trial in which 67 cocaine-dependent methadone-maintained opioid-dependent subjects were randomized to get the additional treatment of disulfiram or placebo in a 12-week trial.

Outcome measures used are the number of days of cocaine use and grams of cocaine per week. Cost measures used are the cost of providing standard methadone treatment and the incremental cost of adding disulfiram to the standard treatment. Cost measures of standard and disulfiram-enhanced treatment were collected retrospectively from the provider.

Results from this cost-effectiveness analysis imply that, even though disulfiram increases slightly the cost of methadone treatment, its increase in effectiveness may be important enough to warrant its addition for treating cocaine dependence in methadone-maintained opiate addicts.

Keywords

Cost-effectiveness; Substance abuse; Cocaine; Methadone maintenance

1. Introduction

About 58% of patients entering methadone maintenance treatment abuse cocaine (Ball & Ross, 1991). Although numerous clinical trials have failed to identify an effective pharmacologic approach for cocaine dependence (O'Brien, 1997), three recent trials have suggested the effectiveness of disulfiram in a range of settings, including methadone maintenance (MM) programs (Carroll et al., 1993, 2000; Carroll, Nich, Ball, McCance, & Rounsaville, 1998; George et al., 2000, Petrakis et al., 2000).

A number of effective pharmacotherapies for substance dependence disorders have been identified in recent years but have failed to make their way into general clinical practice. A notable example is naltrexone treatment for alcohol dependence, which, despite its being the first pharmacologic agent to receive FDA approval for this disorder in over 40 years, has had minimal impact on clinical practice. Wallack and Thomas (2001) reported that cost was

*Corresponding author. Tel.: +44 (0) 20 7958 8334; fax: +44 (0) 20 79588317. mireia.jofre-bonet@lshtm.ac.uk (M. Jofre-Bonet).

found to be the top attitude barrier to prescribing or recommending naltrexone among physicians. The high cost of naltrexone ($5–6 per day), coupled with the lack of cost-effectiveness data from early clinical trials which provided evidence of naltrexone's effectiveness (O'Malley et al., 1992; Volpicelli et al., 1992), may have contributed to its failure to be met with enthusiasm by third party payors and clinicians.

This paper describes a cost-effectiveness analysis (CEA) of the clinical trial described in Petrakis et al. (2000). Of the three existing trials supporting disulfiram's effectiveness, we selected this study because disulfiram may be most likely to be adopted in a MM program. Cocaine is a pervasive problem in MM programs and MM programs have medical staff to prescribe disulfiram. In contrast, drug-free programs are less likely to have the requisite medical staff.

Specifically, we address whether the addition of 250 mg per day of disulfiram to 'standard' methadone maintained patients was cost-effective treatment for cocaine dependence. Because the cost-effectiveness and health benefits of MM have been evaluated in detail in other reports (Barnett et al., 1999, 2000), in this report we evaluate only the additional costs of disulfiram treatment and focus only on cocaine use, the principal outcome targeted by the disulfiram.

2. Materials and methods

Here we briefly describe the clinical trial on which we based our cost-effectiveness study. Then we explain how we estimated costs retrospectively and conducted the sensitivity analysis to address potential weaknesses in our cost estimates.

2.1. Overview of design, setting, and patients

As reported in more detail in Petrakis et al. (2000), participants in the study were recruited from a community-based MM program located in New Haven, Connecticut. Subjects were required to have been stabilized on MM for a minimum of 3 months, to meet current DSM-III-R (American Psychiatric Association, 1987) criteria for cocaine dependence (assessed through scructure clinical interviews; SCID) and also to have had 3 out of 4 urine screens test positive for cocaine in the previous month. Individuals who had psychotic or bipolar disorders or medical problems that would contraindicate disulfiram treatment (see Petrakis et al., 2000 for a breakdown o f the Axis I diagnosis derived from the SCID interviews) were excluded. After a complete description of the study to the subjects, written informed consent was obtained.

Among 95 individuals screened, 13 were not eligible because of medical problems (e.g., elevated liver function tests, abnormal EKGs, or psychotic disorders that would contraindicate disulfiram treatment), and 13 subjects were not randomized because of repeated missed intake appointments, termination from the MM program, or inability to attend the program. Sixty-nine subjects were randomized, but two dropped out.

The mean age of the participants was about 33 years (SD = 5.65) for the disulfiram group and 33.97 (SD = 5.57) for the placebo group. Fifty-two percent of the sample was female, 51% Caucasian, 25% married, 20% working, and 25% had less than a high school degree. Forty-one participants (62%) used free-base cocaine, seven (11%) were intranasal users, and 18 (27%) were intravenous users. The average number of days of cocaine use in the 30 days prior to screening was 18.4 (SD = 9.8). The average number of days of alcohol use in pretreatment was 4.1 days in the 30 days before screening (SD = 7.6), and subjects reported an average of 1.9 drinks per drinking day (SD = 4.3). The disulfiram group reported somewhat higher weekly cocaine use than the placebo group, but there were no significant differences between the groups for the rest of the baseline demographic or substance use variables.

2.2. Treatments

Following baseline assessment, patients were randomly assigned to one of two 12-week treatment programs. Thirty -two patients were in the standard methadone group and 35 in the disulfiram-enhanced group. We defined our "standard MM program" around conventional clinical practices to include a blood test and medical visit at the beginning of treatment, a daily dose of methadone (the average dose for this group was 70 mg), two urine tests per month and a weekly group session. These activities were the basis for the costs attributed to "standard MM treatment" (see below).

To maintain the blind in this protocol, the standard MM group received identical treatment in all respects with the disulfiram group. Thus, in addition to all the previously described clinical procedures, subjects assigned to the standard treatment group had two urine tests per week and two medical visits per month, which included blood tests to test for liver toxicity. They also received a daily breathalyzer prior to receiving their methadone and one individual counseling session per week. These additional procedures were thought to be important for clinical monitoring of the disulfiram; they were included in the control group simply to maintain comparability for experimental purposes.

The group assigned to the disulfiram enhancement condition had a daily dose of 250 mg of disulfiram dissolved directly into the methadone by the program's pharmacist to insure compliance. To ensure blinding, an inert substance was added to the methadone of the standard treatment group so that the methadone would look similar for both groups.

2.3. Assessments

Frequency and quantity of cocaine and alcohol use were obtained weekly by a research assistant using the Time Line Follow-Back (calendar) method (Sobell, Sobell, Maisto, & Cooper, 1985). The Addiction Severity Index (McLellan et al., 1992) was administered pretreatment, and at weeks 4, 8 and 12. Patient self-reports of drug use were verified through urine toxicology screens collected twice weekly. The urines were not observed but were temperature tested. Reports of alcohol use were verified through breathalyzer readings conducted at every visit. Nine hundred sixty-one (94.5%) urine specimens matched subjects' self reports of cocaine use, two (0.2%) were negative although the patients reported cocaine use and 54 (5.3%) were positive although the patients denied recent cocaine use. Additionally, once a week, and with the help of the research assistant, all individuals retrospectively filled out daily activity calendars.

2.4. Assessment of costs

We calculated the direct program costs for both standard MM care and the addition of disulfiram. These costs include: methadone, disulfiram, breathalyzer readings, urine screens, medical care, individual counseling, group therapy, pharmacist and medical staff costs, and other related expenses. The cost of medication (methadone and disulfiram), breathalyzers, urinalysis, the average salaries, fringe rates, and overhead cost rates for counselors, pharmacists, nurses, and the medical director were obtained from the provider, a non-profit substance abuse treatment center affiliated with Yale University in New Haven, Connecticut. Extra blood tests and medical tests were included in the MM program to meet the needs of the trial. However, these services would not be used in practice outside of a clinical trial. Thus, we also calculated an alternative cost estimate that does not include research costs, as recommended in Drummond, O'Brien, Stoddart, & Torrance, (1997). We compare the cost effectiveness of the MM vs. disulfiram under the alternative cost scenarios. [1]

2.4.1. Costs of standard treatment—As explained in Table 1, we estimate the cost of MM treatment to be about $1,015 for the full 12 weeks of treatment in 1999. This estimate is a summation of the following: an average of 70 mg of daily methadone at $380/100 g; two urine tests per week at $3.75 per test; two physical examinations during the study at $104.33 each; two blood tests at $85.00 each; one weekly 30 min individual counseling session at $13.34/patient; one weekly hour group counseling session at $2.18/patient, and an imputed cost of $3.73 per week and patient for the breathalyzer. Additionally, we add charges of $11.81 per patient for the cost of the corresponding efforts of the medical director, nurses, pharmacist, and the pharmacist's assistant.

The average full time (35 h week) individual counselor salary at this clinic was $27,913 in 1999. The average salary for a full time (35 h week) group counselor was $21,135, and the average number of patients per group session is assumed to be eight. The clinic had a full time staff nurse at $28,813 per year and also paid $10,971 for 25% effort of another nurse; the pharmacist contributed approximately 180 h to the study at $40/hour; and the assistant pharmacist was paid $1,370 for 12% of his effort. The medical director was paid $4,415 for 3.5% of his effort.

We multiplied personnel expenditures by the fringe benefit rate and additionally multiplied all expenses by the indirect (or overhead) rate to account for additional expenses that we did not assess, e.g. insurance, utilities, and other. As noted in Tables 1 and 2, in 1999, the fringe rate was 24% and the indirect cost rate was 21%.

2.4.2. Costs of treatment with disulfiram enhancement—In addition to standard methadone as described above, patients randomized to the disulfiram condition received a 250 mg daily dose of disulfiram at $0.54 per tablet. Our estimate of the additional cost of the disulfiram-enhanced treatment was $54.89 per 12 weeks of treatment. The provision of disulfiram required almost no additional time of personnel. There was a negligible amount of time by the pharmacist needed to mix the disulfiram/placebo with the methadone; thus, we assume that effort is zero.

2.4.3. Sensitivity analysis—The above costs reflect the costs of MM as delivered in the clinical trial. To provide a more realistic estimate of the actual cost of MM, in Table 2 we provide an alternative set of cost estimates that eliminate those costs (breathalyzer, extra blood work, and extra medical visits) that occur only due to research needs. These costs would not be incurred in a typical MM clinical setting. The alternative cost scenario in Table 2 assumes that only those subjects taking disulfiram receive a second blood test, breathalyzer readings, and a second medical visit at the end of the 4th or 6th week. This Scenario 2, which we call "Real World Cost Scenario," compares the cost of standard methadone, delivered without the extra costs of the research protocol, with the costs of disulfiram as it was carried out in the trial. This is also how it might be carried out in standard clinical practice. Under these assumptions, the standard methadone treatment cost

[1]We examine only the direct costs of treatment. It could be hypothesized that are decreased or increased costs associated with disulfiram (e.g. health care costs or crime). However, due to the retrospective and highly focused nature of this evaluation, it was not possible to obtain estimates of possible cost offsets. Another cost that we cannot reasonably incorporate is that of an adverse event. There was a single adverse event in this study in which a subject assigned to disulfiram had one (unwitnessed) seizure that did not require hospitalization and was not clearly protocol-related, as the subject was using cocaine prior to the event. However, obtaining a valid estimate of the monetary value of this event would require many arbitrary retrospective assumptions and imputations. Because we could not definitively attribute the event to the disulfiram; and because we cannot reasonably determine associated costs, we decided not to include an estimate of these costs in our cost-effectiveness calculations.

was projected to be $732.07 per 12 weeks of treatment and the disulfiram enhanced treatment cost was estimated at $1,070.23 per 12 weeks.

As a reference, note that the weekly cost estimates we obtain for the standard MM treatment lie comfortably in the range of weekly costs reported by Roebuck, French, and McLellan (2003): Table 2 shows that the "real world" MM weekly cost estimate was $61.01. In Table 1, we obtain that the cost of MM during the trial was $84.10 per week. Using Drug Abuse Treatment Cost Analysis Program-based cost data from 11 programs, Roebuck et al. find that the 2001-normalized economic weekly costs for MM treatments range from $42 to $166, with a mean of $91, S.D. of $33, and a median of $86.

2.5. Measures of effectiveness

As described above, for this cost-effectiveness analysis, we focused on cocaine use outcomes only, with days of cocaine used during the past 30 days and mean grams of cocaine consumed in the previous week, as the primary outcome variables. For each outcome variable, we obtained an effectiveness measure that was the change in the outcome variable from baseline to followup, by treatment group, as reported in Table 3. This change is calculated by subtracting the followup outcome measure from the baseline measure for each group. As explained in Petrakis et al. (2000), there was a significant disulfiram × time effect for both frequency ($Z = 1.97$, $p = .04$) and quantity ($Z = 2.23$; $p = .02$) of cocaine use, with subjects assigned to disulfiram reporting less cocaine use over time compared with the methadone only group.

2.6. Cost-effectiveness analysis

The appropriate way to calculate the cost-effectiveness of disulfiram added to standard MM is to use the 'incremental' cost effectiveness approach—see Drummond et al. (1995) and Gold et al. (1996). We used this approach because disulfiram was added to standard MM; clients did not get disulfiram alone.

To calculate the incremental cost-effectiveness ratios (ICER), we estimated the incremental changes in costs and outcomes in: (1) moving from 'no care' to standard MM care; and (2) going from standard MM care to disulfiram-enhanced care. Thus, we wanted to compare a base treatment alone with the alternative of adding an enhancement to the treatment.

This clinical trial did not have a 'no care' arm, due to ethical issues; thus, the 'no care' component is represented by the levels at baseline. As usual, the 'no care' arm was assumed to have no program costs and no change in the number of days or grams of cocaine used.

3. Results

The incremental costs and effects calculated from the earlier tables are displayed in Table 4 for the readers' convenience.

The estimated improvement in going from 'no care' to adding standard MM care is 10.06 for reduced days of cocaine use out of the previous month (16.74 − 6.68 = 10.06) and 1.05 for reduced grams of cocaine used during the previous week (1.46 − 0.41 = 1.05).

The gains in going from 'no care' to MM enhanced with disulfiram treatment are 14.06 days of cocaine use out of the last 30 (from subtracting 4.96 from 19.65), and 2.57 g in terms of last week's cocaine use (from subtracting 0.59 from 3.16).

The incremental gains of adding disulfiram to standard MM are calculated by subtracting the gains from standard MM from the gains from MM plus disulfiram. In terms of days of cocaine use out the last 30, the gain is 4.63 (14.69 − 10.06 = 4.63) and in terms of grams of cocaine used during the previous week, the gain is 1.52 (2.57 − 1.05 = 1.52).

The gains are used to calculate the four Incremental Cost-Effectiveness Ratios displayed in Table 5. These ratios are obtained as the incremental costs over the incremental gains and they measure the cost per unit of effect produced. Accordingly, ICERs can be interpreted as how much one day (or one gram) reduction in the use of cocaine in the last 30 days (in a week for grams) costs.

We calculate ICERs for days of cocaine use and for grams of cocaine use. For each of these measures of effectiveness, we provide the two alternative estimates of costs presented in Tables 1 and 2: The first estimate was calculated using costs as they occurred in the trial, and the second one was calculated as treatment might be delivered in 'real world' (non-trial) use, that is, without the extra trial-related blood and medical tests.

Additionally, in Table 5 we provide another set of estimates that assume that the gains to treatment have occurred equally over the entire 12 week treatment period. Consequently, these alternative ICERs are calculated using the cocaine use out of the last 30 days measure of effectiveness multiplied by 3—to account for the fact that those in treatment could have experienced improvements during the 3 months of treatment and not only during the last month. And, similarly, we also obtain ICERs for the measure of effectiveness in terms of grams of cocaine used last week by multiplying by 12 to account for the potential gains over a 12-week period. This estimation of the cumulative gains provides an overestimate of the likely benefits during treatment, but is displayed for sensitivity analysis. It is important to realize that it is not the magnitude of the ICER that matters but rather the comparison of the ICER for standard MM compared to the ICER for disulfiram.

In order to determine which treatment is more cost-effective in reducing the use of cocaine, we compare the ICER of standard MM to that of adding disulfiram. As can be seen from the data in Tables 1–3, disulfiram enhanced treatment had both a greater effectiveness (achieves greater reductions in cocaine days and grams) and was more expensive. Calculating the ICER formalizes the relationship between the two.

As can be seen in Table 5, in all sets of study condition comparisons, the ICER for standard MM is greater than that for treatment enhanced with disulfiram. The ICER for standard MM is about $101 for standard MM and about $12 for disulfiram when effectiveness is measured by days of drug use and using the study conditions for costs. We provide a set of adjusted ICERs for which we have used the estimated 3-month improvements instead of using just the last month. Implicitly, we assume that the time path is the same for standard MM and for MM with disulfiram added.

Note that this is an upper bound of improvement during the 12 weeks of treatment. However, as we do not measure gains past the 12 weeks of treatment, this may not be the upper bound of the effect of treatment if one includes the post treatment benefit. If these estimates are recalculated allowing benefits to accrue over the entire12-week period, the corresponding ratios are about $34 and $4 for MM and disulfiram respectively. The latter would suggest that it would cost about $4 more per reduced day of cocaine use if disulfiram were added to standard MM. Similar results are found for cost and effectiveness figures when grams of cocaine are used as the dependent measure. In this case standard MM has a larger ICER than that of the adding disulfiram. The ICERs are $967 for MM alone and $36 for disulfiram and these are adjusted for effectiveness over the 12-week period to be about $81 and $3.

In Table 5 we also provide a set of ICERs calculated using treatment as it might be provided in the real world. Thus the extra tests associated with disulfiram would not be included in the costs for MM. Excluding these costs heightens the cost difference between MM alone and the addition of disulfiram. Thus, the ICER for MM declines, while that of disulfiram increases. In the cases of alternative cost estimates the ICERs for days of cocaine use are almost identical to each other at about $73 each ($24 for the adjusted effectiveness) across the two treatment arms. For grams of cocaine, the ICER for MM alone remains greater than for disulfiram at $697 and $222 respectively ($58 and $19 for the adjusted effectiveness measures).

4. Discussion

We conclude that the addition of disulfiram is likely to be more cost-effective in reducing cocaine use than MM alone; and that the addition of disulfiram is likely to be worth the extra expense in terms of reducing cocaine use during the trial. We conclude this because the ICER is larger for standard MM than for the addition of disulfiram in all cases but one, and in the exception, they are almost identical. Thus, the addition of disulfiram is likely to be cost-effective with respect to standard MM. The reason is that the enhanced treatment produces a unit reduction in days (or grams) of cocaine use at a generally cheaper cost than that of standard MM alone. Thus if society is willing to pay the higher amount per unit of drug reduction using MM alone, the lower per unit cost of reducing cocaine with disulfiram should also be acceptable as well.[2]

Others have found the addition of disulfiram to be effective and feasible. We find it often to be cost effective relative to standard MM. The increment in the cost of disulfiram enhancement, even with the included extra blood work and medical tests, is generally offset by its associated increased effectiveness in reducing cocaine use. It is also important to note that the administering disulfiram in this context is quite compatible with the available resources, culture, and experience of methadone maintenance programs. That is, unlike other potential enhancements to treatment effectiveness that might require the addition of a specialized employee (e.g. therapist) or elaborate training of staff, the administration of disulfiram is well within the available skill set and fits comfortably within the standard operating procedures of most clinics. Combined, these are important findings as they mean that standard clinical practice in MM settings could specifically treat cocaine using disulfiram and it would be relatively cost effective as measured from the perspective of cost per unit of cocaine reduction. The value may be even higher than we estimated as we did not consider the broader impacts of cocaine use on society, e.g. crime and worsened health. Thus there are important real world benefits to society of reducing cocaine use.

This CEA has strengths and limits. One of the strengths is that the effectiveness measures come from a controlled clinical trial, and hence the suggestion of causality. However, the use of the clinical trial comes with concomitant limitations. One is the small sample size, which might restrict the generalizability of these findings. Further, as discussed in Petrakis et al. (2000), it is not clear whether these results would be generalizable to treatment in other settings. The initial effectiveness study and this CEA examine only adding disulfiram to MM. We also did not compare the cost effectiveness of disulfiram to other possible methods of addressing cocaine use (e.g. counseling only) as this is outside the scope of this paper. Another limitation is that costs were not collected simultaneously with the effectiveness

[2]As noted in Sindelar, Jofre-Bonet, French, & McLellan (2004), the fact that enhanced care has a lower ICE-Ratio than standard MM care for all cocaine measures of effectiveness (with the exception of one case where they are practically equivalent) is fortunate in terms of interpreting our CE ratios. The reason is that the substance abuse treatment field does not have a threshold or benchmark value for the cost-effectiveness of drug treatment. If enhanced care had an increased effectiveness, but this came at a higher cost per unit than standard care, then one would need to know if society was willing to pay the increased cost per unit of effect.

measures. Instead, we relied on a retrospective reporting of costs and prices. Also, given that the study was only 12 weeks long, the findings cannot necessarily be extrapolated beyond this period.

We utilize cocaine use as the only outcome of the trial. In a CEA, only one outcome at a time can be used (Sindelar, Jofre-Bonet, French, & McLellan, 2004). However, there would be other potential benefits, including the impact of the treatments on other illicit drugs used (especially heroin and alcohol), medical care used outside MM, and crime related expenses among other factors. Inclusion of all of these and other factors would provide a more comprehensive evaluation. However, one would need to measure all the benefits in monetary terms and aggregate them for use in a cost-benefit analysis. This is the preferred method but is beyond the scope of this study due to data limitations. Another limitation is that we assume no change from baseline to followup for those not in treatment.

Despite the potential weaknesses, this is the only CEA of disulfiram and it adds to the small but growing literature of cost effectiveness studies drawn from well-controlled randomized trials of substance abuse treatment. Inclusion of cost-effectiveness analyses in randomized clinical trials such as these may thus help bridge the gap between research and practice. While the broader use of disulfiram for the treatment for cocaine dependence will require multiple supportive trials in a range of settings and populations, these findings suggest that the added costs of disulfiram may be justified in a MM program.

Acknowledgments

The authors acknowledge the invaluable help of the APT foundation—in particular of David Relyea—and the generous support of grants P50 DA09241, U10DA1308, NIAAA K02-AA00164 and NIDA R01 DA14471 to Yale University. Also, we would like to thank the comments and suggestions made by Todd Olmstead, three referees, and the editor as they helped improve substantially the first version of this paper.

References

American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 3. Washington, DC: Author; 1987. rev

Avants SK, Margolin A, Sindelar JL, Rounsaville BJ, Schottenfeld R, Stine S, Cooney NL, Rosenheck RA, Li SH, Kosten TR. Day treatment versus enhanced standard methadone services for opioid-dependent patients: a comparison of clinical efficacy and cost. American Journal of Psychiatry. 1999; 156:27–33. [PubMed: 9892294]

Ball, JC.; Ross, A. The effectiveness of methadone maintenance treatment. New York: Springer-Verlag; 1991.

Barnett PG. The cost-effectiveness of methadone maintenance as a health care intervention. Addiction. 1999; 94:479–488. [PubMed: 10605844]

Barnett PG, Hui SS. The cost-effectiveness of methadone maintenance. Mt Sinai Journal of Medicine. 2000; 67:365–374.

Carroll KM, Nich C, Ball SA, McCance E, Rounsaville BJ. Treatment of cocaine and alcohol dependence with psychotherapy and disulfiram. Addiction. 1998; 93:713–728. [PubMed: 9692270]

Carroll KM, Nich C, Ball SA, McCance-Katz EF, Frankforter T, Rounsaville BJ. One year follow-up of disulfiram and psychotherapy for cocaine-alcohol abusers: Sustained effects of treatment. Addiction. 2000; 95:1335–1349. [PubMed: 11048353]

Carroll KM, Ziedonis D, O'Malley SS, McCance-Katz E, Gordon L, Rounsaville BJ. Pharmacologic interventions for abusers of alcohol and cocaine: A pilot study of disulfiram versus naltrex-one. American Journal on Addictions. 1993; 2:77–79.

Chaisson RE, Bacchetti P, Osmond D, Brodie B, Sande MA, Moss AR. Cocaine use and HIV infection in intravenous drug users in San Francisco. JAMA. 1989; 261:561–565. [PubMed: 2909798]

Cushman P. Cocaine use in a population of drug abusers on methadone. Hospital and Community Psychiatry. 1990; 39:1205–1207. [PubMed: 3224958]

Drummond, MF.; O'Brien, B.; Stoddart, GL.; Torrance, GW. Methods for the economic evaluation of health care programmes. 2. New York: Oxford Medical Publications, Oxford University Press Inc; 1997.

George TP, Chawarski MC, Pakes J, Carroll KM, Kosten TR, Schottenfeld RS. Disulfiram versus placebo for cocaine dependence in buprenorphine-maintained subjects: A preliminary trial. Biological Psychiatry. 2000; 47:1080–1086. [PubMed: 10862808]

Gold, MR.; Siegel, JE.; Russell, LB.; Weinstein, MC. Cost-effectiveness in Health and Medicine. New York: Oxford University Press; 1996.

Hunt D, Spunt B, Lipton D, Goldsmith D, Strug D. The costly bonus: Cocaine related crime among methadone treatment clients. Advances in Alcohol and Substance Abuse. 1986; 6:107–122. [PubMed: 3604786]

Kolar AF, Brown BS, Weddington WW, Goldsmith D, Strug D. A treatment crisis: Cocaine use by clients in methadone maintenance programs. Journal of Substance Abuse Treatment. 1990; 7:101–107. [PubMed: 2388310]

Kosten TR, Rounsaville BJ, Kleber HD. A 2.5 year follow-up of cocaine use among treated opioid addicts. Archives of General Psychiatry. 1987; 44:281–284. [PubMed: 3827521]

Kosten TR, Rounsaville BJ, Kleber HD. Antecedents and consequences of cocaine abuse among opioid addicts: A 2.5 year follow-up. Journal of Nervous and Mental Disease. 1988; 176:176–181. [PubMed: 3343591]

Margolin A, Avants SK, Rounsaville B, Kosten TR, Schottenfeld RS. Motivational factors in cocaine pharmacotherapy trials with methadone-maintained patients: Problems and paradoxes. Journal of Psychoactive Drugs. 1997; 29:205–212. [PubMed: 9250948]

McLellan AT, Kushner H, Metzger D, Peters R, Smith I, Grissom G, Pettinati H, Argeriou M. The Fifth Edition of the Addiction Severity Index. Journal of Substance Abuse Treatment. 1992; 9:199–213. [PubMed: 1334156]

Meandzija B, O'Connor P, Fitzgerald B, Rounsaville BJ, Kosten TR. HIV infection and cocaine use in methadone maintained and untreated intravenous drug users. Drug and Alcohol Dependence. 1994; 36:109–113. [PubMed: 7851277]

O'Brien CP. A range of research-based pharmacotherapies for addiction. Science. 1997; 278:66–70. [PubMed: 9311929]

O'Malley SS, Jaffe AJ, Chang G, Schottenfeld RS, Meyer RE, Rounsaville B. Naltrexone and coping skills therapy for alcohol dependence. A controlled study. Archives of General Psychiatry. 1992; 49:881–887. [PubMed: 1444726]

Petrakis IL, Carroll KM, Nich C, Gordon LT, McCance-Katz EF, Frankforter T, Rounsaville BJ. Disulfiram treatment for cocaine dependence in methadone maintained opioid addicts. Addiction. 2000; 95:219–228. [PubMed: 10723850]

Roebuck MC, French MT, McLellan T. DATStats: Results from 85 studies using the Drug Abuse Treatment Cost Analysis Program (DATCAP). Journal of Substance Abuse Treatment. 2003; 25:51–57. [PubMed: 14512108]

Sindelar J, Jofre-Bonet M, French MT, McLellan TA. Cost-effectiveness analysis of treatments for abuse of illicit drugs: Paradoxes of multivariate outcomes. Journal of Drug and Alcohol Dependence. 2004; 73:41–50.

Sobell, LC.; Sobell, MB.; Maisto, SA.; Cooper, AM. Time-line follow-back assessment methods. In: Lettieri, DJ.; Nelson, JE.; Sayer, MA., editors. NIAAA Treatment Handbook, Series 2: Alcoholism treatment assessment research instruments. DHHS Publication No. ADM 85 – 1380. Rockville, MD: U.S. Government Printing Office; 1985. p. 530-534.

Volpicelli JR, Alterman AI, Hayashida M, O'Brien CP. Naltrexone in the treatment of alcohol dependence. Archives of General Psychiatry. 1992; 49:876–880. [PubMed: 1345133]

Wallack, S.; Thomas, C. Barriers to the diffusion of naltrexone in clinical practice. presented at NIAAA offices; Rockville, Maryland. May 2001; 2001.

Table 1

Research scenario cost calculation (1999 costs)

Standard methadone maintenance treatment cost:	Cost/unit	# units	Per patient/week	Cost per 12 weeks tx
Methadone @ $380/100 gm	$0.004	70 mg/daily	$1.86	$22.34
Urine test	$3.75	2/week	$7.50	$90.00
Medical exams	$104.33	2/12 weeks	$17.39	$208.67
Blood tests	$85.00	2/12 weeks	$14.17	$170.00
Cost per session of individual counselling[a]	$13.34	1/week	$13.34	$160.06
Group counsel cost per session[b]	$2.18	1/week	$2.18	$26.14
Breathalyzer ($250)[c]			$3.73	$44.78
Total medical tests and drugs			$60.17	$721.98
Total medical tests and drugs/patient including 21% overhead			$72.80	$873.60
Medical director[d]			$0.70	$8.38
Pharmacist[e]			$2.03	$24.39
Nurse[f]			$9.08	$108.97
Total cost/patient including 21% overhead and 24% fringe benefits on personnel			$84.61	$1,015.34

Methadone maintenance with disulfiram treatment cost	Cost/unit	# units	Per patient/week	Cost per 12 weeks tx
Disulfiram $54/100 250 mg tablets	$0.54	250 mg/daily	$3.78	$45.36
Additional weekly cost Disulfiram/patient × 21% overhead			$4.57	$54.89
Total cost/patient including 21% overhead and 24% fringe benefits			$89.19	$1,070.23

[a]The average individual counselors' salary is $27,913. Thus, cost per minute is ($27,913.×1.24×1.21.1)/(52×35×60min) = 0.44$/min.

[b]The average Rehab counselors' salary is $21,135.88. Thus, cost per minute is ($21,135.88×1.24×1.211)/(52×35×60min)/8=0.04$/min.

[c]To obtain the cost per breathalyzer test, the total price is divided by 67 subjects that participated in the study, which is an upper bound of the cost.

[d]Medical director: ($97,533×1.24×1.211)/patient-week.

[e]Pharmacist & Assistant: ($8,346.77×1.24×1.211) + ($1,370×1.24×1.211)/patient-week.

[f]Nurse ($10,971.37×1.24×1.211 + $28,813×1.24×1.211)/patient-week.

Table 2

Real world scenario cost calculation (1999 costs)

Standard methadone maintenance treatment cost:	Cost/unit	# units	Per patient/week	Cost per 12 weeks tx
Methadone @ $380/100 gm	$0.004	70 mg/daily	$1.86	$22.34
Urine test	$3.75	2/week	$7.50	$90.00
Medical exams	$104.33	1/12 weeks	$8.69	$104.33
Blood tests	$85.00	1/12 weeks	$7.08	$85.00
Cost per session of individual treatment[a]	$13.34	1/week	$13.34	$160.06
Cost per group counselling session[b]	$2.18	1/week	$2.18	$26.14
Total medical tests and drugs			$40.66	$487.87
Total medical tests and drugs/patient including 21% overhead			$49.19	$590.33
Medical director[d]			$0.70	$8.38
Pharmacist[e]			$2.03	$24.39
Nurse[f]			$9.08	$108.97
Total cost/patient including 21% overhead and 24% fringe benefits			$61.01	$732.07

Methadone maintenance with disulfiram treatment cost	Cost/unit	# units	Per patient/week	Cost per 12 weeks tx
Disulfiram $54/100–250 mg tablets	$0.54	250 mg/daily	$3.78	$45.36
Medical exams	$104.33	2/12 weeks	$4.35	$104.33
Blood tests	$85.00	2/12 weeks	$3.54	$85.00
Breathalyzer ($250)[c]			$3.73	$44.78
Total medical tests and drugs			$15.40	$279.47
Incremental cost of adding disulfiram (including 21% overhead)			$18.63	$338.16
Total cost/patient including 21% overhead and 24% fringe benefits			$89.19	$1,070.23

[a]The average individual counselors' salary is $27,913. Thus, cost per minute is ($27,913.×1.24×1.21.1)/(52×35×60min) = 0.44$/min.

[b]The average Rehab counselors' salary is $21,135.88. Thus, cost per minute is ($21,135.88×1.24×1.211)/(52×35×60min)/8=0.04$/min.

[c]To obtain the cost per breathalyzer test, the total price is divided by 67 subjects that participated in the study, which is an upper bound of the cost.

[d]Medical director: ($97,533×1.24×1.211)/patient-week.

[e]Pharmacist and Assistant: ($8,346.77×1.24×1.211) + ($1,370×1.24×1.211)/patient-week.

[f]Nurse ($10,971.37×1.24×1.211+$28,813×1.24×1.211)/patient-week.

Table 3

Cocaine use at baseline and at the end of treatment

	Initial sample (67 observations)			
	Standard methadone (32)		Disulfiram (35)	
	Mean	±Standard deviation	Mean	±Standard deviation
Days of cocaine use, past 30 days				
Pre-treatment	16.74	±9.78	19.65	±9.86
End of treatment	6.68	±7.03	4.96	±7.50
Mean grams cocaine used weekly, past 30 days				
Pre-treatment	1.46	±1.92	3.16	±5.07
End of treatment	0.41	±0.51	0.59	±1.28

Source: Petrakis et al., (2000).

Table 4

Cost and effects of standard methadone maintenance treatment vs disulfiram enhanced methadone maintenance

Costs	Cost scenario 1 study condition	Cost scenario 2 real world
Cost of standard methadone maintenance alone	$1,015.34	$732.07
Incremental cost of adding disulfiram	$54.89	$338.16
Improvements in Days of Cocaine Use in the last 30 days		Adjusted for 12 weeks *
Effect of standard methadone maintenance alone	10.06	30.18
Incremental effect of adding disulfiram	4.63	13.89
Improvements in Days of Grams of Cocaine Used during last week		Adjusted for 12 weeks **
Effect of standard methadone maintenance alone	1.05	12.6
Incremental effect of adding disulfiram	1.52	18.24

Source: Petrakis et al. (2001) and our own.

* Adjusted effectiveness multiplies by 3 the effectiveness in terms of days of cocaine used during the last month, to obtain the effectiveness attributed to 3 months of treatment. This assumes that the reduction is stable over treatment and it is therefore possibly an upper bound of the effectiveness.

** Adjusted effectiveness multiplies by 12 the effectiveness in terms of grams of cocaine used during the last week, to obtain the effectiveness attributable to 12 weeks of treatment. This assumes that the reduction is stable over treatment and it is therefore possibly an upper bound of the effectiveness.

NIH-PA Author Manuscript
NIH-PA Author Manuscript

Table 5

Incremental cost effectiveness Ratios

	CE Ratio	ICER: cost per day of cocaine reduced	Adjusted ICER*	ICER: cost per gram of cocaine reduced	Adjusted ICER**
Study Conditions:					
Std methadone maint. treatment	$\frac{\text{Costs}}{\text{Effect}}$	$\frac{\$1,015.34}{10.06}=\$101$	$34	$\frac{\$1,015.34}{1.05}=\$967$	$81
Disulfiram enhanced methadone maint. treatment	$\frac{\text{Additional cost}}{\text{Additional effectiveness}}$	$\frac{\$54.89}{4.63}=\$12$	$4	$\frac{\$54.89}{1.52}=\$36$	$3
Real World Conditions:					
Std methadone maint. treatment	$\frac{\text{Costs}}{\text{Effects}}$	$\frac{\$732.07}{10.06}=\$73$	$24	$\frac{\$732.07}{1.05}=\$697$	$58
Disulfiram enhanced methadone maint. treatment	$\frac{\text{Additional cost}}{\text{Additional effectiveness}}$	$\frac{\$338.16}{4.63}=\$73$	$24	$\frac{\$338.16}{1.52}=\$222$	$19

* Adjusted ICER uses the Adjusted Effectiveness for 12 weeks in the denominator. The Adjusted Effectiveness mutiplies by 3 the effectiveness in terms of days of cocaine used during the last 30 days, in order to obtain the effectiveness attributable to 3 months of treatment. This assumes that the reduction is stable over treatment and it is therefore possibly a lower bound of the ICER.

** Adjusted ICER uses the Adjusted Effectiveness for 12 weeks in the denominator. The Adjusted Effectiveness multiplies by 12 the effectiveness obtained during the last week, to obtain the effectiveness attributable to 12 weeks of treatment. This assumes that the reduction is stable over treatment and it is therefore possibly a lower bound of the ICER.