

# Litteratursøk – Behandling av kokainavhengighet

Rapport fra Kunnskapssenteret nr 18 –2009

Litteratursøk med sortering



 kunnskapssenteret

**Bakgrunn:** Nasjonalt kunnskapssenter for helsetjenesten fikk i januar 2009 i oppdrag fra Helse Sør-Øst å oppsummere tilgjengelig forskning om effektiv rusbehandling. Etter muntlige avklaringer i juni ble bestillingen spisset til å gjelde et litteratursøk med sortering. **Metode:** Vi søkte i databasene OVID MEDLINE, OVID PsycInfo, Cochrane Library of Systematic Reviews og DARE. Søket inneholdt termer for kokain og behandling. I MEDLINE og PsycInfo ble søket avgrenset med søkefilter for systematiske oversikter. **Resultat:** Søket ga 223 treff totalt, etter duplikatsjekk. 165 referanser ble ekskludert og 58 referanser ble vurdert som mulig relevante. Dette er referanser til oversiktsartikler av ulik kvalitet. Vi har ikke lest artiklene i full tekst eller vurdert den metodiske kvaliteten.

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kunnskapssenteret

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Nasjonalt kunnskapssenter for helsetjenesten fremskaffer og formidler kunnskap om effekt av metoder, virkemidler og tiltak og om kvalitet innen alle deler av helsetjenesten. Målet er å bidra til gode beslutninger slik at brukerne får best mulig helsetjenester. Senteret er formelt et forvaltningsorgan under Helsedirektoratet, uten myndighetsfunksjoner. Kunnskapssenteret kan ikke instrueres i faglige spørsmål.

Kunnskapssenteret vil takke bibliotekar Hege Sletsjøe i Helsedirektoratet for å ha bidratt med sin ekspertise i dette prosjektet. Kunnskapssenteret tar det fulle ansvaret for synspunktene som er uttrykt i rapporten.

Nasjonalt kunnskapssenter for helsetjenesten  
Oslo, 23.07.2009

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# Forord

Nasjonalt kunnskapssenter for helsetjenesten fikk i januar 2009 i oppdrag fra Helse Sør-Øst å oppsummere tilgjengelig forskning om effektiv rusbehandling. Etter muntlige avklaringer i juni ble bestillingen spisset til å gjelde et litteratursøk med sortering. Hensikten var å fremskaffe referanser til eksisterende systematiske oversikter om behandling av *kokainavhengighet*. Vi oversendte resultatet fra litteratursøket til bestiller i juli 2009.

Når forskningsfunn benyttes som beslutningsgrunnlag, bør det tas utgangspunkt i tilgjengelig forskning med best mulig kvalitet. Studiedesign, utførelse og analyser påvirker vår tillit til studienes resultat. I dette arbeidet har vi ikke lest artiklene i fulltekst eller vurdert den metodiske kvaliteten av dem. I vedlegget til Kunnskapssenterets håndbok "Slik oppsummerer vi forskning" finnes det sjekklister som kan brukes til å vurdere kvaliteten av ulike typer studier. Sjekklister kan være gode hjelpemidler i det videre arbeidet med å ta stilling til forskningens kvalitet, herunder gyldighet og troverdighet. Håndboken med sjekklister er tilgjengelig på nettsiden til Kunnskapssenteret [www.kunnskapssenteret.no/Verktoy/2139.cms](http://www.kunnskapssenteret.no/Verktoy/2139.cms)

Denne rapporten er ment å hjelpe beslutningstakere i spesialisthelsetjenesten til å fatte velinformerte beslutninger. I møtene med den enkelte pasient må forskningsbasert dokumentasjon ses i sammenheng med andre relevante forhold, pasientenes behov og egne kliniske erfaringer.

Gro Jamtvedt  
*Avdelingsdirektør*

Geir Smedslund  
*Fung. forskningsleder*

Therese K. Dalsbø  
*Seniorrådgiver*

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# Metode

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## LITTERATURSØK

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Vi søkte etter systematiske oversikter (definert som en oversikt der forfatterne har brukt en systematisk og tydelig fremgangsmåte for å finne, vurdere og oppsummere all relevant, pålitelig og tilgjengelig forskning om et effektspørsmål) som dekket ulike tiltak i behandling av kokainavhengighet. Vi søkte i databasene OVID MEDLINE, OVID PsycInfo, Cochrane Library of Systematic Reviews og DARE. Søket inneholdt termer for kokain og behandling. I MEDLINE og PsycInfo ble søket avgrenset med søkefilter for systematiske oversikter. Detaljert søkestrategi er gjengitt i vedlegg 1. I tillegg til søket i databasene søkte vi Kunnskapssenterets publikasjonsliste for relevante publikasjoner med søkeordet kokain.

<http://www.kunnskapssenteret.no/Publikasjoner?reportsandnotes=1&count=1000>

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## REFERANSEUTVALG

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Etter en gjennomgang av titler og sammendrag, laget vi en liste over mulig relevante referanser. Fullstendig liste er tilgjengelig i referanselisten. Kriteriene for å anses som mulig relevant for systematiske oversikter var en eksplisitt bruk av ord som eksempelvis:

- Overview
- Review
- Critically view
- Critically appraisal
- Litterature search
- Meta-analysis

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## SORTERING AV REFERANSENE

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Etter at referansene var identifisert som mulige systematiske oversikter, grupperte vi de utvalgte oversiktene i fire kategorier med utgangspunkt i behandlingstiltak:

- Medikamentell behandling
- Psykososial behandling
- Kombinasjon av medikamentell og psykososial behandling
- Akupunktur

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# Resultat

Bibliotekar Hege Sletsjøe i Helsedirektoratet utførte litteratursøket den 11. juni 2009. Søket ga 223 treff totalt, etter duplikatsjekk. 165 referanser ble ekskludert og 58 referanser ble vurdert som mulig relevante. Dette er referanser til oversiktsartikler av ulik kvalitet. Vi har ikke lest artiklene i full tekst eller vurdert den metodiske kvaliteten. Vi fant ingen relevante rapporter fra Kunnskapssenteret. Ut fra tittel og sammendrag sorterte vi de 58 referansene i forhold til ulike tiltak som vist i tabell 1.

**Tabell 1: Antall oversiktsartikler sortert etter behandlingstype**

Tiltak	Antall referanser
<b>Medikamentell behandling</b>	39
<b>Psykososial behandling</b>	23
<b>Kombinasjon av medikamentell og psykososial behandling</b>	10
<b>Akupunktur</b>	6

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## **MEDIKAMENTELL BEHANDLING AV KOKAINAVHENGIGHET (39 OVERSIKTER)**

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- (1) Amato L, Minozzi S, Pani PP, Davoli M. Antipsychotic medications for cocaine dependence. *Cochrane Database Syst Rev* 2007;(3):CD006306.

Abstract: BACKGROUND: Cocaine dependence is a public health problem characterized by recidivism and a host of medical and psychosocial complications. Cocaine dependence remains a disorder for which no pharmacological treatment of proven efficacy exists, although considerable advances in the neurobiology of this addiction could guide future medication development OBJECTIVES: To evaluate the efficacy and the acceptability of antipsychotic medications for cocaine dependence SEARCH STRATEGY: We searched the following sources: MEDLINE (1966 to October 2006), EMBASE (1980 to October 2006), CINAHL (1982 to October 2006), Cochrane Drug

and Alcohol Group Specialised Register (October 2006). We also searched the reference lists of trials, the main electronic sources of ongoing trials (National Research Register, meta-Register of Controlled Trials; Clinical Trials.gov) and conference proceedings likely to contain trials relevant to the review. All searches included also non-English language literature. **SELECTION CRITERIA:** All randomised controlled trials and controlled clinical trials with focus on the use of any antipsychotic medication for cocaine dependence **DATA COLLECTION AND ANALYSIS:** Two authors independently evaluated the papers, extracted data, rated methodological quality **MAIN RESULTS:** Seven small studies were included (293 participants): the antipsychotic drugs studied were risperidone, olanzapine and haloperidol. No significant differences were found for any of the efficacy measures comparing any antipsychotic with placebo. Risperidone was found to be superior to placebo in diminishing the number of dropouts, four studies, 178 participants, Relative Risk (RR) 0.77 (95% CI 0.77 to 0.98). Most of the included studies did not report useful results on important outcomes such as side effects, use of cocaine during treatment and craving. The results on olanzapine and haloperidol come from studies too small to give conclusive results. **AUTHORS' CONCLUSIONS:** Although caution is needed when assessing results from a limited number of small clinical trials there is no current evidence, at the present, supporting the clinical use of antipsychotic medications in the treatment of cocaine dependence. Furthermore, most of the included studies did not report useful results on important outcomes such as side effects, use of cocaine during the treatment and craving. Aiming to answer the urgent demand of clinicians, patients, families, and the community as a whole for an adequate treatment for cocaine dependence, larger randomised investigations should be designed investigating relevant outcomes and reporting data to allow comparison of results between studies. Moreover some efforts should be done also to investigate the efficacy of other type medications, like anticonvulsant, currently used in clinical practice. [References: 74]

- (2) Back SE, Waldrop AE, Brady KT, Hien D. Evidence-based time-limited treatment of co-occurring substance-use disorders and civilian-related posttraumatic stress disorder. [References]. *Brief Treatment and Crisis Intervention* 2006; 6(4):283-294.  
 Abstract: Substance use disorders (SUDs) and posttraumatic stress disorder (PTSD) frequently co-occur, and this comorbidity results in a more severe clinical presentation and treatment outcome. Consensus is lacking regarding best practices; however, a number of integrated psychosocial treatments (e.g., Seeking Safety, Substance-Dependence PTSD Therapy, Concurrent Treatment of PTSD and Cocaine Dependence) have shown empirically supported promise in reducing symptoms of both disorders. Very little research has been conducted to date on pharmacological treatments for this dual diagnosis or on assessments. This article reviews the developing literature in this area and discusses future directions for research. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)
- (3) Ballon JS, Feifel D. A Systematic Review of Modafinil: Potential Clinical Uses and Mechanisms of Action. [References]. *J Clin Psychiatry* 2006; 67(4):554-566.  
 Abstract: Background: Modafinil is a novel wake-promoting agent that has U.S. Food



and Drug Administration approval for narcolepsy and shift work sleep disorder and as adjunctive treatment of obstructive sleep apnea/hypopnea syndrome. Modafinil has a novel mechanism and is theorized to work in a localized manner, utilizing hypocretin, histamine, epinephrine, gamma -aminobutyric acid, and glutamate. It is a well-tolerated medication with low propensity for abuse and is frequently used for off-label indications. The objective of this study was to systematically review the available evidence supporting the clinical use of modafinil. Data Sources: The search term modafinil OR Provigil was searched on PubMed. Selected articles were mined for further potential sources of data. Abstracts from major scientific conferences were reviewed. Lastly, the manufacturer of modafinil in the United States was asked to provide all publications, abstracts, and unpublished data regarding studies of modafinil. Data Synthesis: There have been 33 doubleblind, placebo-controlled trials of modafinil. Additionally, numerous smaller studies have been performed, and case reports of modafinil's use abound in the literature. Conclusions: Modafinil is a promising drug with a large potential for many uses in psychiatry and general medicine. Treating daytime sleepiness is complex, and determining the precise nature of the sleep disorder is vital. Modafinil may be an effective agent in many sleep conditions. To date, the strongest evidence among off-label uses exists for the use of modafinil in attention-deficit disorder, postanesthetic sedation, and cocaine dependence and withdrawal and as an adjunct to antidepressants for depression. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (4) Berglund M, Thelander S, Jonsson E. Treating alcohol and drug abuse: An evidence based review. [References]. An evidence based review, 2003.
- Abstract: (from the foreword) For much of its history, the field of alcohol and drug abuse treatment has been steeped in lore and tradition. Empirical research has not been seen as a necessary basis for clinical practice in this area. During the past decade, however, interest in evidence-based practice in medicine generally and the increasing "medicalization" of substance abuse treatment have led to a greater emphasis on the scientific method to generate practice guidelines for the diagnosis and treatment of addictive disorders. Most notably, the randomized clinical trial has become the agreed-upon standard in substance abuse treatment research. In large measure, however, evidence-based treatments for substance use disorders have lagged behind the treatment of other disorders, including psychiatric disorders such as schizophrenia and mood disorders. The current volume, which is comprehensive and detailed, should help to narrow this gap. The volume, consisting of 10 chapters, covers a full range of topics in alcohol and drug abuse treatment. It begins with a review of interventions for hazardous drinking. The pharmacological treatment of alcohol withdrawal is covered next. Separate chapters on the psychosocial and pharmacological treatment of alcoholism follow. A chapter on the long-term course of alcohol and drug dependence provides the transition to four chapters on the treatment of drug dependence. As is true for alcohol dependence, there is a separate chapter on psychosocial treatments for drug dependence. Three chapters on the pharmacological treatment of drug dependence (i.e., treatment of opioid withdrawal, treatment of

opioid dependence and treatment of cocaine dependence) follow. A final chapter reviews the literature on substance abuse during pregnancy and the neonatal period. Three appendices provide a list of the contributors and scientific reviewers, the criteria used to rate the quality of the articles reviewed and guidelines employed to estimate effect size. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (5) Brebner K, Childress AR, Roberts DCS. A potential role for GABA-sub(B ) agonists in the treatment of psychostimulant addiction. *Alcohol and Alcoholism* 2002; 37(5):478-484.  
Abstract: Briefly reviews the evidence that gamma -aminobutyric acid (GABA-sub(B)) agonists may be useful in the treatment of cocaine addiction. A number of schedules of reinforcement have been used to model various aspects of cocaine reinforcement and addiction. The results show that systemic pretreatment with baclofen can reduce cocaine intake at doses that do not affect responding for other positive reinforcers. Direct intracerebral injections of baclofen also produce a specific reduction in cocaine self-administration. Recent clinical evidence and case reports indicate some therapeutic value for baclofen in controlling cocaine intake and craving. Perhaps the most intriguing data come from human imaging studies, wherein cocaine addicts report increased cocaine craving and activation of orbital-frontal cortex, anterior cingulate and amygdala when shown videotapes of drug paraphernalia and other addicts taking cocaine. The craving is reduced and the limbic activation is eliminated in cocaine-dependent patients who had been taking baclofen for 7-10 days. Systematic clinical studies of GABA-sub(B ) agonists are needed to determine the extent to which these drugs might serve as tools to promote abstinence in cocaine users seeking treatment for their addiction. (PsycINFO Database Record (c) 2008 APA, all rights reserved)
- (6) Buckley PF. Substance abuse in schizophrenia: A review. *J Clin Psychiatry* 1998; 59(Suppl 3):26-30.  
Abstract: Approximately half of the patients who suffer from schizophrenia are also substance abusers at some time during their illness. The motivational drive toward abusive consumption is compounded in individuals with schizophrenia who turn toward substances with reinforcing properties to alleviate aspects of psychosis. This review examines the prevalence, etiology, and clinical effects of substance abuse (e.g., alcohol, nicotine, cocaine) among individuals with schizophrenia. Clearly, substance abuse persists despite and in spite of treatment with typical antipsychotics. The efficacy of newer generation antipsychotics in the reduction of substance abuse among the schizophrenic population has yet to be established, but clozapine has been shown to reduce alcohol, smoking, and cocaine use. Hence, clozapine is a therapeutic option for dually diagnosed patients because of its superior efficacy relative to conventional neuroleptics and its capacity to control substance abuse. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)
- (7) Carroll KM. Integrating psychotherapy and pharmacotherapy to improve drug abuse outcomes. *Addict Behav* 1997; 22(2):233-245.

Abstract: Reviews the roles of pharmacotherapy and psychotherapy in the treatment of drug abuse and summarizes recent examples of the benefits of combining treatments for drug abuse. The differences in treatments are discussed in terms of their mode of action, time to effect, target symptoms, durability, and applicability across drugs of abuse. While each has specific indications and strengths, no psychotherapy or pharmacotherapy is universally effective, and both forms of treatment have some limitations, particularly when used alone. Several recent examples of the benefits of combined treatments for drug abusers suggest that, for many substance use disorders, outcomes can be broadened, enhanced, and extended by combining the most effective forms of psychotherapy and pharmacotherapy. Examples applicable to methadone maintenance, naltrexone/agonist treatment, and cocaine dependence are explored. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (8) Castells X, Casas M, Vidal X, Bosch R, Roncero C, Ramos-Quiroga JA et al. Efficacy of central nervous system stimulant treatment for cocaine dependence: a systematic review and meta-analysis of randomized controlled clinical trials (Provisional abstract). *Addiction* 2007; 102:1871-1887.

- (9) Cousins MS, Roberts DCS, de Wit H. GABA-sub(B ) receptor agonists for the treatment of drug addiction: A review of recent findings. [References]. *Drug Alcohol Depend* 2002; 65(3):209-220.

Abstract: Reviews preclinical and clinical literature concerning the effects of gamma-aminobutyric acid (GABA) type B receptor agonists, particularly baclofen, in promoting abstinence and reduction of the use of cocaine, heroin, alcohol, and nicotine. GABA-sub(B ) receptor agonists such as baclofen appear to reduce the reinforcing effects of abused drugs in animal models under multiple experimental procedures. However, baclofen failed to suppress a self-administration of high unit doses of cocaine in rats, suggesting that this drug may be more effective for users with limited access to cocaine, rather than high-dose users on binges. Several preliminary studies and case reports in humans suggest that baclofen may be useful in the treatment of cocaine, nicotine, and ethanol dependence. Important questions remaining to be addressed include the effects of GABA-sub(B ) receptor agonists on overall drug taking. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (10) Crosby RD, Halikas JA, Carlson G. Pharmacotherapeutic interventions for cocaine abuse: Present practices and future directions. *Journal of Addictive Diseases* 1991; 10(4):13-30.

Abstract: Reviews the use of agents in physical and psychological withdrawal symptoms of cocaine addicts. Many medications have been used in the treatment of cocaine withdrawal and dependence, using as a rationale known pharmacologic effects of cocaine on neurotransmitters. Animal observations related to dopamine depletion, receptor supersensitivity, cocaine-induced kindling, and serotonin depletion have all generated pharmacotherapeutic interventions for cocaine abuse. Pharmacotherapeutic strategies in dealing with the methadone-maintained cocaine abuser

suggest that patients maintained on buprenorphine or naltrexone may have a lower rate of cocaine use. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (11) Haile CN, Kosten TR, Kosten TA. Genetics of dopamine and its contribution to cocaine addiction. [References]. *Behavior Genetics* 2007; 37(1):119-145.

Abstract: Cocaine addiction is a major health and social problem for which there are presently no effective pharmacotherapies. Many of the most promising medications target dopamine based on the large literature that supports its role in addiction. Recent studies show that genetic factors are also important. Rodent models and gene knock-out technology have helped elucidate the involvement of specific genes in the function of the dopamine reward system and intracellular cascades that lead to neuronal changes in this system. Human epidemiological, linkage, and association studies have identified allelic variants (polymorphisms) that give rise to altered metabolism of dopamine and its functional consequences. Individuals with these polymorphisms respond differently to psychostimulants and possibly to pharmacotherapies. Here we review the literature on genetic variations that affect dopamine neurotransmission, responses to psychostimulants and potential treatments for cocaine addiction. Behavioral responses to psychostimulants in animals with different or modified genetics in dopamine signaling are discussed. We also review polymorphisms in humans that affect dopaminergic neurotransmission and alter the subjective effects of psychostimulants. Pharmacotherapies may have increased efficacy when targeted to individuals possessing specific genetic polymorphisms in dopamine's metabolic and intracellular messenger systems. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (12) Higgins ST, Wong CJ. Treating cocaine abuse: What does research tell us? Behavior, pharmacology, and clinical applications, 1998.

Abstract: (from the chapter) The purpose of this chapter is to review what has been learned scientifically about how to effectively treat cocaine abuse. The chapter focuses on individuals who are seeking or enrolled in treatment for cocaine abuse (i.e., primary cocaine abusers). The following topics are addressed: in-hospital vs out-of-hospital patient care; early attrition; treatment duration, intensity, and format; and treatment context (behavioral treatments, pharmacological treatments, multiple drug use and abuse). (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (13) Johansson BA. Pharmacotherapy for cocaine dependence. [References]. An evidence based review, 2003.

Abstract: (from the chapter) In the central nervous system, cocaine mainly affects the activity of dopamine and noradrenalin. The inhibition of reuptake greatly increases signal transmission. Three pharmacological principles have been studied to deal with cocaine dependence: antidepressants, dopamine agonists, and antiepileptics. The concept of antidepressive treatment has been to restore dysregulated reward mechanisms and to treat existing depression. The reward effect of cocaine is probably due to the blocking of dopamine reuptake. The increased concentration of dopamine is also thought to cause cocaine-induced euphoria and the addictive effect

of the drug. Cocaine withdrawal inhibits function in the target area for dopamine. The neurotransmitter level decreases, resulting in anxiety, anhedonia, craving, and depression. Dopamine agonist treatment is mainly intended to address these symptoms. Dopamine agonists are otherwise used in treating, e.g., Parkinson's syndrome. Craving can be understood as a kindling phenomenon. In animal models, a successful anti-kindling effect with carbamazepine has been achieved and serves as the theoretical basis of studies in humans. The aim of this systematic literature review is to attempt to answer the following question: Does pharmacological treatment have an effect on cocaine dependence and on cocaine abstinence? The primary material used in the meta-analyses contains some weaknesses. For example, the authors did not always use the same principles to classify a urine test as positive for narcotics. Some studies report the average number of positive analyses during the episode of care, while others report the number of analyses during a specified period, e.g., the last week of treatment. Some data have not been reported in the text, but have secondary origins based on figures in the articles. Antidepressive treatment is not superior to placebo in reducing cocaine abuse or to retain patients in treatment. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (14) Karila L, Gorelick D, Weinstein A, Noble F, Benyamina A, Coscas S et al. New treatments for cocaine dependence: A focused review. [References]. *Int J Neuropsychopharmacol* 2008; 11(3):425-438.
- Abstract: Cocaine, already a significant drug problem in North and South America, has become a more prominent part of the European drug scene. Cocaine dependence has major somatic, psychological, psychiatric, socio-economic, and legal implications. No specific effective pharmacological treatment exists for cocaine dependence. Recent advances in neurobiology have identified various neuronal mechanisms implicated in cocaine addiction and suggested several promising pharmacological approaches. Data were obtained from Medline, EMBASE, and PsycINFO searches of English-language articles published between 1985 and June 2007 using the key words: cocaine, addiction, cocaine dependence, clinical trials, pharmacotherapy(ies) singly and in combination. Large well-controlled studies with appropriate statistical methods were preferred. Pharmacological agents such as GABA agents (topiramate, tiagabine, baclofen and vigabatrin) and agonist replacement agents (modafinil, disulfiram, methylphenidate) seem to be the most promising in treatment of cocaine dependence. The results from trials of first- and second-generation neuroleptics are largely negative. Aripiprazole, a partial dopaminergic agonist that may modulate the serotonergic system, shows some promise. Preliminary results of human studies with anti-cocaine vaccine, N-acetylcysteine, and ondansetron, are promising, as are several compounds in preclinical development. While no medication has received regulatory approval for the treatment of cocaine dependence, several medications marketed for other indications have shown efficacy in clinical trials. An anti-cocaine vaccine and several compounds in preclinical development have also shown promise. Findings from early clinical trials must be confirmed in larger, less selective patient

populations. (PsycINFO Database Record (c) 2009 APA, all rights reserved) (journal abstract)

- (15) Kenna GA, Nielsen DM, Mello P, Schiesl A, Swift RM. Pharmacotherapy of dual substance abuse and dependence. [References]. *CNS Drugs* 2007; 21(3):213-237.  
Abstract: The US FDA has approved a limited number of treatments for alcohol, nicotine and opioid dependence; however, no treatments for other abused drugs such as marijuana, cocaine or methamphetamine are approved. This review focuses on research into drug pharmacotherapies, particularly single-drug therapies, for substance abuse and dependence contributing to the most important dual substance use disorders (SUDs). Given the implications of poly-substance abuse, it is essential that clinicians and researchers be aware of potential pharmacotherapies for the treatment of dual SUDs. A substantial number of patients abuse more than one drug concurrently, complicating the treatment of SUD and leaving clinicians with few FDA-approved drug options for their patients. In this era of evidence-based medicine, such patients are typically treated with therapeutically proven medications, but in ways that are outside the scope of a drug's original indication by the FDA. Such 'off-label' prescribing has become an important therapeutic strategy for practitioners seeking treatments for other diseases in subpopulations such as paediatrics and gerontology or for medical conditions such as oncology or mental illness. Similarly, the information that most clinicians use to make their decisions for treating patients abusing multiple drugs stems from trials treating a single SUD, anecdotal experiences from their own practice or that of their colleagues, or single-case studies reported in the literature. The existing evidence suggests there are few treatments for SUDs that confer significant reductions in substance use across a broad patient population. Moreover, even fewer clinical efficacy trials have been conducted that provide evidence of therapeutic benefit for these drugs. Recognising the difficulty in making the proper drug choice for facilitating maximum treatment success, this review highlights the single drugs or drug combinations that show some potential for treating dual SUDs. This review finds strongest support for the use of disulfiram for treatment of alcohol and cocaine dependence (with or without concomitant methadone maintenance), baclofen for alcohol and cocaine dependence (but not opioid-dependent cocaine users), tiagabine for cocaine dependence in methadone-maintained patients, and topiramate for alcohol, nicotine and cocaine dependence. While ondansetron and olanzapine show some efficacy in treating alcohol and cocaine dependence, more research is needed to better delineate the subpopulation in which these drugs may provide their maximum effect. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)
- (16) Lima Reisser Anelise ARL, Silva dLM, Soares Bernardo Garcia de Oliveira, Farrell M. Carbamazepine for cocaine dependence. *Cochrane Database of Systematic Reviews: Reviews*. *Cochrane Database of Systematic Reviews* 2009 Issue 1. Chichester (UK): John Wiley & Sons, Ltd, 2009.  
Abstract: BACKGROUND: Cocaine dependence has become a public health problem, developing a significant number of medical, psychological and social problems. Al-

though there is no consensus regarding how to treat cocaine dependence, effective pharmacotherapy has a potentially major role to play as part of a broader treatment milieu. The anti-convulsant carbamazepine, a tricyclic medication that is widely used to treat a variety of neurological and psychiatric disorders, has been used for treatment of cocaine dependence, although its effectiveness has not been established.

**OBJECTIVES:** To determine whether carbamazepine is effective for the treatment of cocaine dependence. **SEARCH STRATEGY:** We searched: Cochrane Controlled Trials Register (Cochrane Library issue 1, 1999), MEDLINE (1966 - October 1997), EMBASE (1980 - October 1997), PsycLIT (1974 - July 1997), Biological Abstracts and LILACS (1982 - 1997); scan of reference list of relevant articles; personal communication; conference abstracts; unpublished trials from pharmaceutical industry; book chapters on treatment of cocaine dependence. The specialised register of trials of Cochrane Group on Drugs and Alcohol until February 2003. **SELECTION CRITERIA:** All randomised controlled trials focused on the use of carbamazepine versus placebo on the treatment of cocaine dependence. Trials including patients with additional diagnosis such as opiate dependence were also eligible. **DATA COLLECTION AND ANALYSIS:** The reviewers extracted the data independently, Odds Ratios, weighted mean difference and number needed to treat were estimated. Qualitative assessments of the methodology of eligible studies were carried out using validated checklists. The reviewers assumed that people who died or dropped out had no improvement and tested the sensitivity of the final results to this assumption. Where possible analysis was carried out according to the "intention to treat" principles.

**MAIN RESULTS:** 5 studies were included (455 participants). No differences regarding positive urine sample for cocaine metabolites. Scores on Spielberg State Anxiety Inventory slightly favoured carbamazepine, but not statistical significance. Dropouts were high in both groups, less dropout occurred in the carbamazepine group (RR 0.87 95%CI 0.71-1.06). When no retention in treatment was due to side effects no differences were found. The number of participants presenting at least one side effect, was higher in the carbamazepine group (RR 4.33 95% CI 1.45-12.91). **AUTHORS' CONCLUSIONS:** There is no current evidence supporting the clinical use of Carbamazepine in the treatment of cocaine dependence. Larger randomised investigation must be considered taking into account that these time-consuming efforts should be reserved for medications showing more relevant and promising evidence.

**CARBAMAZEPINE DOES NOT APPEAR TO BE EFFECTIVE IN REDUCING COCAINE DEPENDENCE, WITH HIGH DROPOUT RATES AND ADVERSE EFFECTS:** Cocaine use has become a substantial health problem in the United States and some South American countries. Cocaine dependence involves a number of medical, psychological and social problems, including the spread of infectious diseases and violence. carbamazepine, a drug used to treat some neurological and psychiatric problems, is sometimes used for cocaine dependence. However, the review of trials found that carbamazepine has not been shown to help reduce cocaine dependence. The dropout rate from treatment was high, adverse effects were common, and there was no significant drop in cocaine use

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- (17) Lima MS, Reisser AA, Soares BG, Farrell M. Antidepressants for cocaine dependence. *Cochrane Database Syst Rev* 2001;(4):CD002950.
- Abstract: **BACKGROUND:** Cocaine dependence is a common and serious condition, which has become nowadays a substantial public health problem. The past decade has witnessed a sustained search for an effective pharmacotherapeutic agent for the treatment of cocaine dependence. While administration of cocaine acutely increases intercellular dopamine, serotonin, and norepinephrine levels by blocking their pre-synaptic reuptake, chronic cocaine abuse leads to down-regulation of monoamine systems. Post-cocaine use depression and cocaine craving may be linked to this down-regulation. Antidepressant pharmacotherapy, by augmenting monoamine levels, may alleviate cocaine abstinence symptomatology, as well as relieving dysphoria and associated craving by general antidepressant action. **OBJECTIVES:** To conduct a systematic review of all RCTs on the use of antidepressants for treating cocaine dependence. **SEARCH STRATEGY:** We searched the Cochrane Controlled Trials Register (Cochrane Library, issue 4, 2000), MEDLINE (from 1966 - 2000), EMBASE (from 1980 - 2000), LILACS (from 1982 - 2000), PsycLIT (from 1974 - 2000), Biological Abstracts (1982 to 2000). Other searches:reference searching; personal communication; conference abstracts; unpublished trials from pharmaceutical industry; book chapters on treatment of cocaine dependence. **SELECTION CRITERIA:** The inclusion criteria for all randomised controlled trials were that they should focus on the use of antidepressants on the treatment of cocaine dependence. Trials including patients with additional diagnosis such as opiate dependence were also eligible. **DATA COLLECTION AND ANALYSIS:** The reviewers extracted the data independently and Relative Risks, weighted mean difference and number needed to treat were estimated. The reviewers assumed that people who died or dropped out had no improvement and tested the sensitivity of the final results to this assumption. **MAIN RESULTS:** 18 studies were included in the review, with 1177 people randomised. Positive urine sample for cocaine metabolites was the main efficacy outcome, with no significant results obtained regardless the type of antidepressant. Compared to other drugs, desipramine performed better but showing just a non significant trend with heterogeneity present as revealed by the chi-square test (8.6, df=3; p=0.04). One single trial showed imipramine performed better than placebo in terms of clinical response according to patient's self-report. A similar rate of patients remaining in treatment was found for both patients taking desipramine or placebo. Results from one single trial suggest fluoxetine patients on SSRIs are less likely to dropout. Similar results were obtained for trials where patients had additional diagnosis of opioid dependence and/or were in methadone maintenance treatment. **REVIEWER'S CONCLUSIONS:** There is no current evidence supporting the clinical use of antidepressants in the treatment of cocaine dependence. Given the high rate of dropouts in this population, clinicians may consider adding psychotherapeutic supportive measures aiming to keep patients in treatment. [References: 44]
- (18) Minozzi S, Amato L, Davoli M, Farrell M, Lima Reisser AARL, Pani PP et al. Anticonvulsants for cocaine dependence. *Cochrane Database Syst Rev* 2008;(2):CD006754.



**Abstract: BACKGROUND:** Cocaine dependence is a major public health problem that is characterized by recidivism and a host of medical and psychosocial complications. Although effective pharmacotherapy is available for alcohol and heroin dependence none exists currently for cocaine dependence despite two decades of clinical trials primarily involving antidepressant, anti convulsivant and dopaminergic medications. There has been extensive consideration of optimal pharmacological approaches to the treatment of cocaine dependence with consideration of both dopamine antagonists and agonists. Anticonvulsants have been candidates for the treatment of addiction based on the hypothesis that seizure kindling-like mechanisms contribute to addiction. **OBJECTIVES:** To evaluate the efficacy and the acceptability of anticonvulsants for cocaine dependence **SEARCH STRATEGY:** We searched the Cochrane Drugs and Alcohol Groups specialised register (issue 4, 2007), MEDLINE (1966 - march 2007), EMBASE (1988 - march 2007), CINAHL (1982- to march 2007) **SELECTION CRITERIA:** All randomised controlled trials and controlled clinical trials which focus on the use of anticonvulsants medication for cocaine dependence **DATA COLLECTION AND ANALYSIS:** Two authors independently evaluated the papers, extracted data, rated methodological quality **MAIN RESULTS:** Fifteen studies (1066 participants) met the inclusion criteria for this review: the anticonvulsants drugs studied were carbamazepine, gabapentin, lamotrigine, phenytoin, tiagabine, topiramate, valproate. No significant differences were found for any of the efficacy measures comparing any anticonvulsants with placebo. Placebo was found to be superior to gabapentin in diminishing the number of dropouts, two studies, 81 participants, Relative Risk (RR) 3.56 (95% CI 1.07 to 11.82) and superior to phenytoin for side effects, two studies, 56 participants RR 2.12 (95% CI 1.08 to 4.17). All the other single comparisons are not statistically significant. **AUTHORS' CONCLUSIONS:** Although caution is needed when assessing results from a limited number of small clinical trials at present there is no current evidence supporting the clinical use of anticonvulsants medications in the treatment of cocaine dependence. Aiming to answer the urgent demand of clinicians, patients, families, and the community as a whole for an adequate treatment for cocaine dependence, we need to improve the primary research in the field of addictions in order to make the best possible use out of a single study and to investigate the efficacy of other pharmacological agent. [References: 92]

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**Abstract:** Examines the validity of a cue-reactivity paradigm for evaluating medications to treat cocaine dependence and critically reviews cocaine pharmacotherapy studies that use this method. A Medline computerized search was performed to identify randomized, controlled medication studies for cocaine dependence that employed a cue-reactivity paradigm. Relevant bibliographies of these articles were also reviewed. 11 placebo-controlled studies were identified in the English language literature. From a methodological viewpoint, most studies have shown that exposure to

cocaine-related stimuli increases subjective and physiological reactivity in cocaine-dependent patients, but methods used to present the cues and to measure cue reactivity have not been consistent across studies. Similarly, the observed increase in subjective and physiological reactivity to cocaine cues has varied with and across studies. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (20) O'Brien CP, McKay JR. Psychopharmacological treatments of substance use disorders. Oxford University Press, 1998.

Abstract: (from the chapter) This chapter on the psychopharmacological treatment of substance use disorders and addiction consists of 4 distinct reviews focusing on the major drugs or drug categories: nicotine, alcohol, stimulants (cocaine), and opioids (heroin). (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (21) Olbrich R, Olbrich R. Using disulfiram (AntabuseReg.) in substance-abuse treatment. [German]. [References]. Sucht: Zeitschrift für Wissenschaft und Praxis 2007; 53(2):72-81.

Abstract: Aim: To review studies from 1996 through 2005 on the effectiveness of disulfiram in the treatment of alcohol and other kinds of substance abuse. Method: A systematic literature search using two databases. Results: With the selection criteria, ten studies were identified that used random assignment to groups and intent-to-treat analyses. Compared to a placebo, treatment with disulfiram led to a significant increase in number of days that patients were abstinent from alcohol. Similar results were observed with regard to cocaine use in cocaine-dependent patients. Conclusions: The effectiveness of disulfiram in alcohol-abuse treatment was confirmed in studies of high methodological standards. In addition, disulfiram has a new application in the treatment of cocaine dependence, but for the time being empirical support for it is limited. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (22) Rawson RA, McCann MJ, Hasson AJ, Ling W. Cocaine abuse among methadone maintenance patients: Are there effective treatment strategies? J Psychoactive Drugs 1994; 26(2):129-136.

Abstract: Reviews empirical evidence on the effectiveness of several categories of techniques for treating cocaine abuse among patients in methadone maintenance treatment. These include pharmacotherapies, behavioral methods (contingency management and relapse prevention), and methadone dose adjustment. Other treatment interventions that may be efficacious for this population, including day treatment and sober-living facilities, are described. Suggestions are made for the successful implementation of cocaine focus groups. Methadone clinic management procedures that may aid in the reduction of cocaine abuse by methadone patients are discussed. Although many of these efforts are in early stages of evaluation, there are some reasons for optimism in the development of treatment for these patients. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (23) Rawson RA, Obert JL, McCann MJ, Castro FG. Cocaine abuse treatment: A review of current strategies. *Journal of Substance Abuse* 1991; 3(4):457-491.  
Abstract: Many of the strategies that are being developed to treat cocaine abusers have been adapted from drug and alcoholism treatment systems. These include the use of established programs that are minimally modified for cocaine abusers, such as the 28-day inpatient hospital, therapeutic community, and 12-step programs. Other approaches have created specific techniques to meet the clinical needs of cocaine abusers, such as behavioral, pharmacologic, and nontraditional interventions. Other attempts have been made to create integrated outpatient approaches. However, few data exist to definitively address the effectiveness of any of the treatment modalities. This article reviews treatment efforts that have been conducted, overviews research data, and offers recommendations regarding currently available treatment options. (PsycINFO Database Record (c) 2008 APA, all rights reserved)
- (24) Roberts DCS, Brebner K. GABA modulation of cocaine self-administration. [References]. New York Academy of Sciences, 2000.  
Abstract: (from the chapter) Recent experiments suggest that GABA compounds produce a clinically relevant modulation of cocaine reinforcement. This review summarizes the results of a number of studies that examined the effect of the GABA-sub(B) agonist baclofen on cocaine self-administration using a variety of schedules of reinforcement. The results demonstrate that baclofen causes a dramatic reduction in cocaine self-administration which does not appear to be accounted for by a general disruption of behavior. However, the effect is dependent on the unit injection dose of cocaine and on the response requirements of the schedule. These results predict that in a clinical setting any potential therapeutic effect of baclofen will interact with the cost and availability of cocaine. (PsycINFO Database Record (c) 2008 APA, all rights reserved)
- (25) Rohsenow DJ, Monti PM. Relapse among cocaine abusers: Theoretical, methodological, and treatment considerations. [References]. Yale University Press, 2001.  
Abstract: (from the chapter) Focuses on treatment for cocaine abuse, reviewing approaches that have resulted in significant improvements in outcomes. Behavioral approaches for preventing relapse among cocaine abusers have shown considerable growth in recent years. At the same time, the medications development portfolio at NIDA continues to thrive in the search for medications that may decrease the probability of relapse during treatment and early recovery, and thereby buy time for skills training and lifestyle changes to produce lasting effects on outcome. The most promising of the behavioral approaches are those that are solidly rooted in social learning theory models of behavior. Two of the most effective types of approaches are contingency management approaches and cognitive-behavioral coping skills training approaches, each with several studies showing effectiveness. (PsycINFO Database Record (c) 2008 APA, all rights reserved)
- (26) Roozen HG, Boulogne JJ, van Tulder MW, van den Brink W, De Jong CAJ, Kerkhof AJFM. A systematic review of the effectiveness of the community reinforcement ap-

proach in alcohol, cocaine and opioid addiction. [References]. *Drug Alcohol Depend* 2004; 74(1):1-13.

Abstract: The community reinforcement approach (CRA) has been applied in the treatment of disorders resulting from alcohol, cocaine and opioid use. The objectives were to review the effectiveness of (1) CRA compared with usual care, and (2) CRA versus CRA plus contingency management. Studies were selected through a literature search of RCTs focusing on substance abuse. The search yielded 11 studies of mainly high methodological quality. The results of CRA, when compared to usual care: there is strong evidence that CRA is more effective with regard to number of drinking days, and conflicting evidence with regard to continuous abstinence in the alcohol treatment. There is moderate evidence that CRA with disulfiram is more effective in terms of number of drinking days, and limited evidence that there is no difference in effect in terms of continuous abstinence. Furthermore, there is strong evidence that CRA with 'incentives' is more effective with regard to cocaine abstinence. There is limited evidence that CRA with 'incentives' is more effective in an opioid detoxification program. There is limited evidence that CRA is more effective in a methadone maintenance program. Finally, there is strong evidence that CRA with abstinence-contingent 'incentives' is more effective than CRA (non-contingent incentives) treatment aimed at cocaine abstinence. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

(27) Rounsaville BJ. Treatment of Cocaine Dependence and Depression. [References]. *Biological Psychiatry* 2004; 56(10):803-809.

Abstract: In common with all other classes of substance use disorders, cocaine dependence has been shown to be strongly associated with depression by community and clinical surveys. Diagnosing depression in cocaine abusers can be challenging because it is difficult to distinguish transient symptoms caused by cocaine from enduring depression syndromes. Nonetheless, both "substance-induced" and "independent" depression syndromes require clinical attention, especially when symptoms have been persistent and severe before entering treatment. Use of antidepressant medications for combined cocaine dependence and depression is supported by a preponderance of evidence from 4 randomized clinical trials (RCTs) that prospectively targeted both depression and cocaine dependence and 7 RCTs in which a post hoc analyses demonstrated efficacy in the subgroup of cocaine abusers with comorbid depression. Notably, most negative studies have evaluated SSRIs while positive studies have used agents such as desipramine or bupropion. A substantial clinical trials literature supports the efficacy of behavioral treatments for general populations of cocaine abusers and of patients with depression but few studies have addressed patients with both disorders. Treatment development and research are needed on models of care that truly integrate strategies for addressing both cocaine use and depression. Recent advances have paved the way for a new generation of research. These include validation of efficacious cocaine treatments, improved diagnostic methods, organization of the Clinical Trials Network and development of guidelines for managing methodological challenges posed by high rates of current

medication use and polysubstance abuse in treatment entering cocaine abusers.  
(PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

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(29) Silva dLM, Farrell M, Lima Reisser Anelise ARL, Soares B. Antidepressants for cocaine dependence. *Cochrane Database of Systematic Reviews: Reviews*. Cochrane Database of Systematic Reviews 2003 Issue 2. Chichester (UK): John Wiley & Sons, Ltd, 2003.

**Abstract:** **BACKGROUND:** The past decade has witnessed a sustained search for an effective pharmacotherapeutic agent for the treatment of cocaine dependence. While administration of cocaine acutely increases intercellular dopamine, serotonin, and norepinephrine levels by blocking their presynaptic reuptake, chronic cocaine abuse leads to down-regulation of monoamine systems. Post-cocaine use depression and cocaine craving may be linked to this down-regulation. Antidepressant pharmacotherapy, by augmenting monoamine levels, may alleviate cocaine abstinence symptomatology, as well as relieving dysphoria and associated craving by general antidepressant action. **OBJECTIVES:** To evaluate the efficacy and the acceptability of antidepressants for cocaine dependence **SEARCH STRATEGY:** We searched Cochrane Drug and Alcohol Group Specialised Register (July 2007), MEDLINE (1966 to July 2007), CINAHL (1982 to July 2007), SCOPUS (July 2007); reference searching; personal communication; conference abstracts; unpublished trials, ongoing trials, relevant web-sites. **SELECTION CRITERIA:** All randomised controlled trials and controlled clinical trials which focus on the use of any antidepressants for cocaine dependence **DATA COLLECTION AND ANALYSIS:** The authors independently evaluated the papers, extracted data, rated methodological quality. Doubts were solved through discussion between all the authors. **MAIN RESULTS:** 18 studies were included in the review (1177 participants). Positive urine sample for cocaine metabolites was the main efficacy outcome, with no significant results obtained regardless of the type of antidepressant. Compared to other drugs, desipramine performed better but showing just a non significant trend with heterogeneity present as revealed by the chi-square test (8.6, df=3; p=0.04). One single trial showed imipramine performed better than placebo in terms of clinical response according to patient's self-report. A similar rate of patients remaining in treatment was found for both patients taking desipramine or placebo. Results from one single trial suggest fluoxetine patients on SSRIs are less likely to dropout. Similar results were obtained for trials where patients had additional diagnosis of opioid dependence and/or were in methadone maintenance treatment. **AUTHORS' CONCLUSIONS:** There is no current evidence supporting the clinical use of antidepressants in the treatment of cocaine dependence. Given the high rate of dropouts in this population, clinicians may consider adding psychotherapeutic supportive measures aiming to keep patients in treatment. **ANTIDEPRESSANTS HAVE NOT BEEN PROVEN TO REDUCE COCAINE DEPENDENCE, ALTHOUGH THIS MAY BECAUSE PEOPLE COMMONLY**

**STOP USING THE ANTIDEPRESSANTS TOO SOON:** As dependence on cocaine became more common and caused major personal and social problems, several methods have been tried to help reduce dependence. Antidepressants are often tried to help people manage the depression and cravings that occur when people stop using cocaine. The review found that trials have not shown that antidepressants can help reduce cocaine dependence, although this may partly be because many people quit using the antidepressants. It may be that more people might benefit if they were helped to keep using antidepressants, including those who are also dependent on heroin or on methadone programs

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Abstract: (from the chapter) This chapter reviews interventions used to treat cocaine use in methadone patients. The chapter has 4 main sections. The 1st section reviews research on the effects of methadone itself on cocaine use. The high rates of cocaine use in methadone patients has prompted concern that methadone itself may increase cocaine use, either directly or indirectly. To look thoroughly for evidence of potential undesirable effects of methadone on cocaine use, this section reviews a number of descriptive studies relevant to this issue, in addition to controlled studies. The next 3 sections review controlled trials of the 3 major types of interventions that have been employed in drug abuse treatment: pharmacological, psychosocial, or behavioral, and other less conventional types of treatment. (PsycINFO Database Record (c) 2008 APA, all rights reserved)
- (31) Soares BG, Lima MS, Reisser AA, Farrell M. Dopamine agonists for cocaine dependence. Cochrane Database Syst Rev 2001;(4):CD003352.  
Abstract: **BACKGROUND:** Cocaine is a major drug of abuse. Cocaine dependence is a common and serious condition, which has become nowadays a substantial public health problem. There is a wide and well documented range of consequences associated to chronic use of this drug, such as medical, psychological and social problems, including the spread of infectious diseases (e.g. AIDS, hepatitis and tuberculosis), crime, violence and neonatal drug exposure. Therapeutic management of the cocaine addicts includes an initial period of abstinence from the drug. During this phase the subjects may experience, besides the intense craving for cocaine, symptoms such as depression, fatigue, irritability, anorexia, and sleep disturbances. It was demonstrated that the acute use of cocaine may enhance dopamine transmission and chronically it decreases dopamine concentrations in the brain. Pharmacological treatment that affects dopamine could theoretically reduce these symptoms and contribute to a more successful therapeutic approach. **OBJECTIVES:** To evaluate the efficacy and acceptability of dopamine agonists for treating cocaine dependence. **SEARCH STRATEGY:** We searched: The Cochrane Controlled Trials Register (Cochrane Library, issue 4, 2000), MEDLINE (from 1966 - 2000), EMBASE (from 1980 - 2000), LILACS (from 1982 - 2000), PsycLIT (from 1974 - 2000), Biological Abstracts (1982 to 2000). Reference searching; personal communication; conference abstracts; unpublished trials from pharmaceutical industry; book chapters on treat-

ment of cocaine dependence. **SELECTION CRITERIA:** The inclusion criteria for all randomised controlled trials were that they should focus on the use of dopamine agonists on the treatment of cocaine dependence. Trials including patients with additional diagnosis such as opiate dependence were also eligible. **DATA COLLECTION AND ANALYSIS:** The reviewers extracted the data independently and Relative Risks, weighted mean difference and number needed to treat were estimated. The reviewers assumed that people who died or dropped out had no improvement and tested the sensitivity of the final results to this assumption. **MAIN RESULTS:** Twelve studies were included, with 587 participants randomised. Amantadine and Bromocriptine were compared to placebo in most of trials. In two studies amantadine was directly compared to bromocriptine, while amantadine was compared to desipramine, an antidepressant in three. The main efficacy outcome presented was positive urine sample for cocaine metabolites, with no significant differences between interventions. When retention in treatment was assessed as an acceptability measure, it was found a similar rate of patients remaining in treatment in both placebo and active drugs. There were no significant differences in trials where participants had primary cocaine dependence or had additional diagnosis of opioid dependence and/or were in methadone maintenance treatment. **REVIEWER'S CONCLUSIONS:** Current evidence does not support the clinical use of dopamine agonists in the treatment of cocaine dependence. Given the high rate of dropouts in this population, clinicians may consider adding psychotherapeutic supportive measures aiming to keep patients in treatment. [References: 43]

- (32) Soares BGO, Lima MS, Reisser AAP, Farrell M. Dopamine agonists for cocaine dependence. *Cochrane Database Syst Rev* 2003;(2):CD003352.

**Abstract:** **BACKGROUND:** Cocaine dependence is a common and serious condition, which has become nowadays a substantial public health problem. There is a wide and well documented range of consequences associated to chronic use of this drug, such as medical, psychological and social problems, including the spread of infectious diseases (e.g. AIDS, hepatitis and tuberculosis), crime, violence and neonatal drug exposure. Therapeutic management of the cocaine addicts includes an initial period of abstinence from the drug. During this phase the subjects may experience, besides the intense craving for cocaine, symptoms such as depression, fatigue, irritability, anorexia, and sleep disturbances. It was demonstrated that the acute use of cocaine may enhance dopamine transmission and chronically it decreases dopamine concentrations in the brain. Pharmacological treatment that affects dopamine could theoretically reduce these symptoms and contribute to a more successful therapeutic approach. **OBJECTIVES:** To evaluate the efficacy and acceptability of dopamine agonists for treating cocaine dependence. **SEARCH STRATEGY:** Electronic searches of Cochrane Library, EMBASE, MEDLINE, PsycLIT, Biological Abstracts and LILACS; reference searching; personal communication; conference abstracts; unpublished trials from pharmaceutical industry; book chapters on treatment of cocaine dependence, was performed for the primary version of this review in 2001. Another search of the electronic databases was done in December of 2002 for this update.

The specialised register of trials of the Cochrane Group on Drugs and Alcohol was searched until February 2003. **SELECTION CRITERIA:** The inclusion criteria for all randomised controlled trials were that they should focus on the use of dopamine agonists on the treatment of cocaine dependence. **DATA COLLECTION AND ANALYSIS:** The reviewers extracted the data independently and Relative Risks, weighted mean difference and number needed to treat were estimated. The reviewers assumed that people who died or dropped out had no improvement and tested the sensitivity of the final results to this assumption. **MAIN RESULTS:** Seventeen studies were included, with 1224 participants randomised. Amantadine, bromocriptine, and pergolide were the drugs evaluated. The main outcomes evaluated were positive urine sample for cocaine metabolites, for efficacy, and retention in treatment, as an acceptability measure. There were no significant differences between interventions, and in trials where participants had primary cocaine dependence or had additional diagnosis of opioid dependence and/or were in methadone maintenance treatment. **REVIEWER'S CONCLUSIONS:** Current evidence does not support the clinical use of dopamine agonists in the treatment of cocaine dependence. Given the high rate of dropouts in this population, clinicians may consider adding other supportive measures aiming to keep patients in treatment. [References: 55]

- (33) Soares B, Lima Reisser Anelise ARL, Farrell M, Silva dLM. Dopamine agonists for cocaine dependence. *Cochrane Database of Systematic Reviews: Reviews*. Cochrane Database of Systematic Reviews 2003 Issue 2. Chichester (UK): John Wiley & Sons, Ltd, 2003.

**Abstract:** **BACKGROUND:** Cocaine dependence is a common and serious condition, which has become a substantial public health problem. There is a wide and well documented range of consequences associated to chronic use of cocaine, such as medical, psychological and social problems.. Therapeutic management of the cocaine addicts includes an initial period of abstinence from the drug. During this phase the subjects may experience, besides the intense craving for cocaine, symptoms such as depression, fatigue, irritability, anorexia, and sleep disturbances. It was demonstrated that the acute use of cocaine may enhance dopamine transmission and chronically it decreases dopamine concentrations in the brain. Pharmacological treatment that affects dopamine could theoretically reduce these symptoms and contribute to a more successful therapeutic approach. **OBJECTIVES:** To evaluate the efficacy and acceptability of dopamine agonists for treating cocaine dependence. **SEARCH STRATEGY:** Electronic searches of Cochrane Library, EMBASE, MEDLINE, PsycLIT, Biological Abstracts and LILACS; reference searching; personal communication; conference abstracts; unpublished trials from pharmaceutical industry; book chapters on treatment of cocaine dependence, was performed for the primary version of this review in 2001. Another search of the electronic databases was done in December of 2002 for this update. The specialised register of trials of the Cochrane Group on Drugs and Alcohol was searched until February 2003. **SELECTION CRITERIA:** The inclusion criteria for all randomised controlled trials were that they should focus on the use of dopamine agonists on the treatment of cocaine



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Abstract: Behavioral and pharmacological therapies have been used alone and in combination for the treatment of substance abuse; however, to date, no single treatment approach for psychostimulant abuse has demonstrated widespread efficacy. This paper describes the various functions that are served by both behavioral therapies and pharmacotherapies and their respective mechanisms of action. It is argued that combined treatments can be expected to produce additive effects because the two approaches operate through different and potentially complementary mechanisms. Illustrations of these underlying principles and experimental support for the use of combined treatments are drawn from smoking cessation research, which has broadly applied combined behavioral and pharmacological therapies for treating abuse of nicotine, a mild stimulant. In addition, the results of recent studies that have evaluated the efficacy of behavioral techniques and/or potential pharmacotherapies for treating cocaine abuse are reviewed. Finally, methodological strategies are recommended for future evaluations of combined therapy approaches to conclusively evaluate separate and combined efficacy of treatments for psychostimulant abuse. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (35) Suh JJ, Pettinati HM, Kampman KM, O'Brien CP. The status of disulfiram: A half of a century later. [References]. *J Clin Psychopharmacol* 2006; 26(3):290-302.  
Abstract: For more than 55 years, disulfiram has been approved by the Food and Drug Administration for the treatment of alcohol dependence. It is a unique medication that relies on "psychological threat" to avoid disulfiram-ethanol reactions. This paper reviews the history of disulfiram treatment, the current status of disulfiram treatment, the ensuing developments in disulfiram use in treating various addictions, and future directions. Clinical trials using disulfiram for the treatment of alcohol, cocaine, or co-occurring alcohol + cocaine dependence were included in this review. Disulfiram efficacy studies focusing on supervised, implant, and combination pharmacotherapies were also examined. In clinical trials, disulfiram has demonstrated inconsistent results in helping patients to abstain from alcohol, and patients poorly adhere to a disulfiram-treatment regimen. This has raised questions about disulfiram's practicality in the treatment of alcohol dependence. Recently, however, disulfiram has gained attention as a complementary agent to newer pharmacological medications, such as an opiate antagonist that specifically reduces alcohol craving. One hypothesis is that disulfiram would assist patients in gaining psychological control over drinking when given in conjunction with an opiate antagonist that would act directly on reducing alcohol craving. Preliminary evidence also suggests that disulfiram treatment could be a viable treatment for cocaine dependence because it was shown to reduce cocaine use among nonalcoholic, cocaine-dependent patients. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)
- (36) Torrens M, Fonseca F, Mateu G, Farre M. Efficacy of antidepressants in substance use disorders with and without comorbid depression A systematic review and meta-analysis. [References]. *Drug Alcohol Depend* 2005; 78(1):1-22.  
Abstract: Antidepressants are commonly used in substance abusers due to the potential effect on some underlying mechanisms involved in drug use disorders and to treat comorbid depression. A systematic review of the literature of the efficacy of antidepressant drugs in subjects with drug abuse disorders, including alcohol, cocaine, nicotine and opioid, with and without comorbid depression was performed. Only randomised, double-blind, controlled trials have been evaluated. A meta-analysis was done with the included studies that used common evaluation procedures in alcohol, cocaine and opioid dependence. Based on the present review some recommendations may be proposed. The prescription of antidepressants for drug abuse seems only clear for nicotine dependence with or without previous comorbid depression (bupropion and nortryptiline). In alcohol dependence without comorbid depression, the use of any antidepressant seems not justified, while in cocaine dependence has to be clarified. The use of antidepressants in alcohol, cocaine or opioid dependence with comorbid depression needs more studies in well-defined samples, adequate doses and duration of treatment to be really conclusive. Interestingly, SSRIs do not seem to offer significant advantages compared with tricyclic drugs in substance abuse disorders. Differences both related to individual characteristics and

specific antidepressant drugs need to be clarified in future studies. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (37) Tutton CS, Crayton JW. Current pharmacotherapies for cocaine abuse: A review. *Journal of Addictive Diseases* 1993; 12(2):109-127.

Abstract: Summarizes the results of clinical trials on various pharmacotherapies for cocaine abuse (CAB) described in the literature. A wide variety of drugs have been used for CAB. They include drugs for the treatment of coexisting psychiatric disorders, cocaine antagonists, dopamimetic agents, L-DOPA/carbidopa, the amino acids tyrosine and tryptophan, antidepressants, anticonvulsants, and antabuse-like drugs. Emphasis is placed throughout this review on how extensively each drug has been tested, how successful each drug has proven to be in treating CAB, and on which drugs require further investigation. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (38) Vocci FJ, Elkashef A. Pharmacotherapy and other treatments for cocaine abuse and dependence. *Current Opinion in Psychiatry* 2005; 18(3):265-270.

Abstract: Purpose of review: This review examines progress being made in the treatment of cocaine abuse and dependence, with a particular focus on pharmacotherapies. Medications with apparently very different mechanisms of action have been reported to reduce cocaine use in controlled clinical trials in outpatient settings. This review will summarize the latest findings in this area. Recent findings: Of all the medications tested to date, disulfiram has demonstrated the most consistent effect to reduce cocaine use. Several medications have been reported to reduce cocaine use in double-blind, placebo-controlled clinical trials, namely baclofen, modafinil, tiagabine, and topiramate. All pharmacotherapy trials in cocaine-dependent patients include a behavioral therapy that is common to all participants. Consequently, these pharmacotherapy trials can be considered to evaluate whether the medication is adding to the effect of the behavioral therapy. Summary: Confirmatory clinical studies are necessary to replicate the initial efficacy findings for baclofen, modafinil, tiagabine, and topiramate. More research is needed in both cocaine and cocaine-alcohol dependent populations. Once confirmatory studies have been carried out, testing of rational medication combinations with different behavioral therapies is an obvious next step to increase the ability to manage cocaine dependence. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (39) Weddington WW. Cocaine: Diagnosis and treatment. *Psychiatric Clinics of North America* 1993; 16(1):87-95.

Abstract: Reviews recent research on diagnosing cocaine addiction and on effective treatment interventions. Diagnosis takes into account such factors as route of administration, toxicity, effects of detoxification, and psychiatric comorbidity. Standard treatment for addiction is based on the 12-step AA recovery model, has a goal of total abstinence from all addictive substances, and uses a format that consists of educational and group sessions. Experimental treatments include cogni-

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## **PSYKOSOSIAL BEHANDLING AV KOKAINAVHENGIGHET (23 OVERSIKTER)**

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- (1) Carroll KM. A Paradigm Shift in Treating Drug Dependence: Skinner 1, Ideology o. [References]. 1945.  
Abstract: Originally published in *Contemporary Psychology: APA Review of Books*, 2000, Vol 45(6), 684-687. The reviewer states that this book (see record 1999-02363-000) is essentially a comprehensive overview of the current state of contingency management research with substance abusers. The volume is extremely well organized, with five major sections (Basics of Contingency Management, Treatment of Cocaine Abusers, Treatment of Special Populations, Treatment of Opioid Abusers, and Research Development and Dissemination), each made up of several chapters describing various applications of CM with a range of substance abusing populations. As such, it will be primarily of interest to clinical researchers in substance abuse; however, there is much here to provoke and inspire more general readers as well (PsycINFO Database Record (c) 2008 APA, all rights reserved)
  
- (2) Carroll KM. Integrating psychotherapy and pharmacotherapy to improve drug abuse outcomes. *Addict Behav* 1997; 22(2):233-245.  
Abstract: Reviews the roles of pharmacotherapy and psychotherapy in the treatment of drug abuse and summarizes recent examples of the benefits of combining treatments for drug abuse. The differences in treatments are discussed in terms of their mode of action, time to effect, target symptoms, durability, and applicability across drugs of abuse. While each has specific indications and strengths, no psychotherapy or pharmacotherapy is universally effective, and both forms of treatment have some limitations, particularly when used alone. Several recent examples of the benefits of combined treatments for drug abusers suggest that, for many substance use disorders, outcomes can be broadened, enhanced, and extended by combining the most effective forms of psychotherapy and pharmacotherapy. Examples applicable to methadone maintenance, naltrexone/agonist treatment, and cocaine dependence are explored. (PsycINFO Database Record (c) 2008 APA, all rights reserved)
  
- (3) Carroll KM. Relapse prevention as a psychosocial treatment: A review of controlled clinical trials. *Experimental and Clinical Psychopharmacology* 1996; 4(1):46-54.  
Abstract: More than 24 randomized controlled trials have evaluated the effectiveness of cognitive-behavioral relapse prevention treatment on substance use outcomes among adult smokers, alcohol, cocaine, marijuana, and other types of substance abusers. Review of this body of literature suggests that, across substances of abuse but most strongly for smoking cessation, there is evidence for the effectiveness of re-

lapse prevention compared with no-treatment controls. However, evidence regarding its superiority relative to discussion control conditions or other active treatments has been less consistent. Outcomes in which relapse prevention may hold particular promise include reducing severity of relapses when they occur, enhanced durability of effects, and patient treatment matching, particularly for patients at higher levels of impairment along dimensions such as psychopathology or dependence severity. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (4) Crits-Christoph P, Siqueland L. Psychosocial treatment for drug abuse: selected review and recommendations for national health care. *Archives of General Psychiatry* 1996; 53(8):749-756.

Abstract: Reviews selected research articles relevant to the psychosocial treatment of substance abuse (excluding alcohol abuse), including controlled efficacy studies of opiate, cocaine, and marijuana abuse and dependence. Based on these articles, recommendations are made about the type and amount of psychosocial services that might serve as a starting point for a national health care insurance program. Suggestions for future research are also included. While the authors grant that successful treatment of substance abuse will likely involve a variety of components, including medical care, medications, and practical assistance, this review focuses on the narrow perspective of psychosocial interventions, such as cognitive, behavioral, psychodynamic, and family therapies. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (5) Dutra L, Stathopoulou G, Basden SL, Leyro TM, Powers MB, Otto MW. A meta-analytic review of psychosocial interventions for substance use disorders. [References]. *Am J Psychiatry* 2008; 165(2):179-187.

Abstract: Objective: Despite significant advances in psychosocial treatments for substance use disorders, the relative success of these approaches has not been well documented. In this meta-analysis, the authors provide effect sizes for various types of psychosocial treatments, as well as abstinence and treatment-retention rates for cannabis, cocaine, opiate, and polysubstance abuse and dependence treatment trials. Method: With a comprehensive series of literature searches, the authors identified a total of 34 well-controlled treatment conditions-five for cannabis, nine for cocaine, seven for opiate, and 13 for polysubstance users-representing the treatment of 2,340 patients. Psychosocial treatments evaluated included contingency management, relapse prevention, general cognitive behavior therapy, and treatments combining cognitive behavior therapy and contingency management. Results: Overall, controlled trial data suggest that psychosocial treatments provide benefits reflecting a moderate effect size according to Cohen's standards. These interventions were most efficacious for cannabis use and least efficacious for polysubstance use. The strongest effect was found for contingency management interventions. Approximately one-third of participants across all psychosocial treatments dropped out before treatment completion compared to 44.6% for the control conditions. Conclusions: Effect sizes for psychosocial treatments for illicit drugs ranged from the low-moderate to high-moderate range, depending on the substance disorder and treatment under study.

Given the long-term social, emotional, and cognitive impairments associated with substance use disorders, these effect sizes are noteworthy and comparable to those for other efficacious treatments in psychiatry. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (6) Higgins ST, Abbott PJ. CRA and treatment of cocaine and opioid dependence. Cambridge University Press, 2001.  
Abstract: (from the chapter) Reviewed positive results from a series of well-controlled clinical trials supporting the efficacy of Community Reinforcement Approach (CRA) treatments for cocaine and opioid dependence. The fact that much of the research on the use of CRA in the treatment of cocaine and opioid dependence has involved voucher-based incentives merits comment. The evidence is clear that vouchers are an effective element. Conceptually, the vouchers intervention is congruent with the operant conceptual framework of CRA and thus reasonably can be considered as simply an additional element of the CRA treatment package. However the vouchers considered, CRA has made contributions to the treatment of cocaine and opioid dependence apart from them. A theoretical note worth underscoring is that the research reviewed in this chapter illustrates the fundamental importance of the principle of reinforcement to understanding and effectively treating cocaine, opioid and other drug dependence. (PsycINFO Database Record (c) 2008 APA, all rights reserved)
- (7) Higgins ST, Wong CJ. Treating cocaine abuse: What does research tell us? Behavior, pharmacology, and clinical applications, 1998.  
Abstract: (from the chapter) The purpose of this chapter is to review what has been learned scientifically about how to effectively treat cocaine abuse. The chapter focuses on individuals who are seeking or enrolled in treatment for cocaine abuse (i.e., primary cocaine abusers). The following topics are addressed: in-hospital vs out-of-hospital patient care; early attrition; treatment duration, intensity, and format; and treatment context (behavioral treatments, pharmacological treatments, multiple drug use and abuse). (PsycINFO Database Record (c) 2008 APA, all rights reserved)
- (8) Higgins ST, Alessi SM, Dantona RL. Voucher-based incentives: A substance abuse treatment innovation. [References]. *Addict Behav* 2002; 27(6):887-910.  
Abstract: Provides an overview of research on the voucher-based incentives approach to substance abuse treatment. This approach was originally developed as a novel method for improving retention and increasing cocaine abstinence among cocaine-dependent outpatients. The efficacy of vouchers for those purposes is now well established, and plans are underway to move the intervention into effectiveness testing in community clinics. The use of vouchers also has been extended to the treatment of alcohol, marijuana, nicotine, and opioid dependence. Particularly noteworthy is that vouchers hold promise as an efficacious intervention with special populations of substance abusers, including pregnant and recently postpartum women, adolescents, and those with serious mental illness. It is concluded that voucher-based incentives hold promise as an innovative treatment intervention that has effi-

cacy across a wide range of substance abuse problems and populations. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (9) Knapp WP, Soares BGO, Farrel M, Lima MS. Psychosocial interventions for cocaine and psychostimulant amphetamines related disorders. *Cochrane Database Syst Rev* 2007;(3):CD003023.  
Abstract: **BACKGROUND:** The consumption of psychostimulants for non-medical reasons probably occurs because of their euphoriant and psychomotor-stimulating properties. Chronic consumption of these agents results in development of stereotyped behaviour, paranoia, and possibly aggressive behaviour. Psychosocial treatments for psychostimulant use disorder are supposed to improve compliance, and to promote abstinence. Evidence from randomised controlled trials in this subject needs to be summarised. **OBJECTIVES:** To conduct a systematic review of all RCTs on psychosocial interventions for treating psychostimulant use disorder. **SEARCH STRATEGY:** Electronic searches of Cochrane Library, EMBASE, MEDLINE, and LILACS (to may 2006); reference searching; personal communication; conference abstracts; unpublished trials from pharmaceutical industry; book chapters on treatment of psychostimulants abuse/ dependence. **SELECTION CRITERIA:** All randomised-controlled trials focusing on psychosocial interventions for treating psychostimulants abuse/ dependence. **DATA COLLECTION AND ANALYSIS:** Three authors extracted the data independently and Relative Risks, weighted mean difference and number needed to treat were estimated, when possible. The reviewers assumed that people who died or dropped out had no improvement (intention to treat analysis) and tested the sensitivity of the final results to this assumption. **MAIN RESULTS:** Twenty-seven randomised controlled studies (3663 participants) fulfilled inclusion criteria and had data that could be used for at least one of the main comparisons. There was a wide heterogeneity in the interventions evaluated: this did not allow to provide a summary estimate of effect and results cannot be summarised in a clear cut way. The comparisons between different type of Behavioural Interventions showed results in favour of treatments with some form of Contingency management in respect to both reducing drop outs and lowering cocaine use.. **AUTHORS' CONCLUSIONS:** Overall this review reports little significant behavioural changes with reductions in rates of drug consumption following an intervention. Moreover, with the evidence currently available, there are no data supporting a single treatment approach that is able to comprise the multidimensional facets of addiction patterns and to significantly yield better outcomes to resolve the chronic, relapsing nature of addiction, with all its correlates and consequences. [References: 68]
- (10) Prendergast M, Podus D, Finney J, Greenwell L, Roll J. Contingency management for treatment of substance use disorders: A meta-analysis. [References]. *Addiction* 2006; 101(11):1546-1560.  
Abstract: **Aims:** To examine the effectiveness of contingency management (CM) techniques in treating substance use disorders (i.e. illicit drugs, alcohol, tobacco). **Design:** Meta-analysis was used to determine the average effect size and potential moderators in 47 comparisons of the effectiveness of CM from studies based on a

treatment-control group design and published between 1970 and 2002. Findings: The mean effect size (ES) of CM was positive, with a magnitude of  $d = 0.42$  using a fixed effects model. The magnitude of the ES declined over time, following treatment. CM was more effective in treating opiate use ( $d = 0.65$ ) and cocaine use ( $d = 0.66$ ), compared with tobacco ( $d = 0.31$ ) or multiple drugs ( $d = 0.42$ ). Larger effect sizes were associated with higher researcher involvement, earlier studies and shorter treatment duration. Conclusions: Study findings suggest that CM is among the more effective approaches to promoting abstinence during the treatment of substance use disorders. CM improves the ability of clients to remain abstinent, thereby allowing them to take fuller advantage of other clinical treatment components. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (11) Rawson RA, McCann MJ, Hasson AJ, Ling W. Cocaine abuse among methadone maintenance patients: Are there effective treatment strategies? *J Psychoactive Drugs* 1994; 26(2):129-136.

Abstract: Reviews empirical evidence on the effectiveness of several categories of techniques for treating cocaine abuse among patients in methadone maintenance treatment. These include pharmacotherapies, behavioral methods (contingency management and relapse prevention), and methadone dose adjustment. Other treatment interventions that may be efficacious for this population, including day treatment and sober-living facilities, are described. Suggestions are made for the successful implementation of cocaine focus groups. Methadone clinic management procedures that may aid in the reduction of cocaine abuse by methadone patients are discussed. Although many of these efforts are in early stages of evaluation, there are some reasons for optimism in the development of treatment for these patients. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (12) Rawson RA, Obert JL, McCann MJ, Castro FG. Cocaine abuse treatment: A review of current strategies. *Journal of Substance Abuse* 1991; 3(4):457-491.

Abstract: Many of the strategies that are being developed to treat cocaine abusers have been adapted from drug and alcoholism treatment systems. These include the use of established programs that are minimally modified for cocaine abusers, such as the 28-day inpatient hospital, therapeutic community, and 12-step programs. Other approaches have created specific techniques to meet the clinical needs of cocaine abusers, such as behavioral, pharmacologic, and nontraditional interventions. Other attempts have been made to create integrated outpatient approaches. However, few data exist to definitively address the effectiveness of any of the treatment modalities. This article reviews treatment efforts that have been conducted, overviews research data, and offers recommendations regarding currently available treatment options. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (13) Rohsenow DJ, Monti PM. Relapse among cocaine abusers: Theoretical, methodological, and treatment considerations. [References]. Yale University Press, 2001.

Abstract: (from the chapter) Focuses on treatment for cocaine abuse, reviewing approaches that have resulted in significant improvements in outcomes. Behavioral



approaches for preventing relapse among cocaine abusers have shown considerable growth in recent years. At the same time, the medications development portfolio at NIDA continues to thrive in the search for medications that may decrease the probability of relapse during treatment and early recovery, and thereby buy time for skills training and lifestyle changes to produce lasting effects on outcome. The most promising of the behavioral approaches are those that are solidly rooted in social learning theory models of behavior. Two of the most effective types of approaches are contingency management approaches and cognitive-behavioral coping skills training approaches, each with several studies showing effectiveness. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (14) Roozen HG, Boulogne JJ, van Tulder MW, van den Brink W, De Jong CAJ, Kerkhof AJFM. A systematic review of the effectiveness of the community reinforcement approach in alcohol, cocaine and opioid addiction. [References]. *Drug Alcohol Depend* 2004; 74(1):1-13.

Abstract: The community reinforcement approach (CRA) has been applied in the treatment of disorders resulting from alcohol, cocaine and opioid use. The objectives were to review the effectiveness of (1) CRA compared with usual care, and (2) CRA versus CRA plus contingency management. Studies were selected through a literature search of RCTs focusing on substance abuse. The search yielded 11 studies of mainly high methodological quality. The results of CRA, when compared to usual care: there is strong evidence that CRA is more effective with regard to number of drinking days, and conflicting evidence with regard to continuous abstinence in the alcohol treatment. There is moderate evidence that CRA with disulfiram is more effective in terms of number of drinking days, and limited evidence that there is no difference in effect in terms of continuous abstinence. Furthermore, there is strong evidence that CRA with 'incentives' is more effective with regard to cocaine abstinence. There is limited evidence that CRA with 'incentives' is more effective in an opioid detoxification program. There is limited evidence that CRA is more effective in a methadone maintenance program. Finally, there is strong evidence that CRA with abstinence-contingent 'incentives' is more effective than CRA (non-contingent incentives) treatment aimed at cocaine abstinence. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (15) Roth A, Fonagy P. *What works for whom: A critical review of psychotherapy research*, 2nd ed. [References]. A critical review of psychotherapy research, 2nd ed, 1 A.D.  
Abstract: (from the introduction) This book attempts to identify and review evidence that can help answer the challenging question "What works for whom?"--in other words, which psychotherapeutic interventions are of demonstrated benefit to which patient groups? There is, of course, no single entity called "psychotherapy," and in order to help the reader distinguish between therapies, we begin this book with a description of the theory and practice of the major schools of psychological therapy. In Chapter 2, we outline the methodologies used by psychotherapy researchers and the way in which these limit the application of research findings to clinical practice. In the final introductory chapter, Chapter 3, we try to place research in the context of

health care delivery systems and present a model relating research findings to clinical practice. In many ways, the model is a guide to interpretation of all that follows. The body of the book contains research evidence relating to the treatment of each of a wide range of psychological problems. Our strategy has been to examine available reviews of treatments, together with individual studies, where these are relevant. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (16) Schumacher JE, Milby JB, Wallace D, Meehan DC, Kertesz S, Vuchinich R et al. Meta-analysis of day treatment and contingency-management dismantling research: Birmingham Homeless Cocaine Studies (1990-2006). [References]. *J Consult Clin Psychol* 2007; 75(5):823-828.

Abstract: Four successive randomized clinical trials studying contingency management (CM), involving various treatment arms of drug-abstinent housing and work therapy and day treatment (DT) with a behavioral component, were compared on common drug abstinence outcomes at 2 treatment completion points (2 and 6 months). The clinical trials were conducted from 1990 to 2006 in Birmingham, Alabama, with a total of 644 homeless persons with primary crack cocaine addiction. The meta-analysis utilized the weighted least squares approach to integrate data encompassing 9 different treatment arms to assess the effects of CM and DT (neither, DT only, CM only, and CM = DT) on a common estimate of prevalence of drug abstinence. Taken together, the results show much stronger benefits from CM = DT and from CM only than for DT alone. Throughout all of the Birmingham Homeless Cocaine Studies, the CM = DT consistently produced higher abstinence prevalence than did no CM. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (17) Silverman K, Bigelow GE, Stitzer ML. Treatment of cocaine abuse in methadone maintenance patients. Behavior, pharmacology, and clinical applications, 1998.

Abstract: (from the chapter) This chapter reviews interventions used to treat cocaine use in methadone patients. The chapter has 4 main sections. The 1st section reviews research on the effects of methadone itself on cocaine use. The high rates of cocaine use in methadone patients has prompted concern that methadone itself may increase cocaine use, either directly or indirectly. To look thoroughly for evidence of potential undesirable effects of methadone on cocaine use, this section reviews a number of descriptive studies relevant to this issue, in addition to controlled studies. The next 3 sections review controlled trials of the 3 major types of interventions that have been employed in drug abuse treatment: pharmacological, psychosocial, or behavioral, and other less conventional types of treatment. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (18) Stitzer ML, Walsh SL. Psychostimulant abuse: The case for combined behavioral and pharmacological treatments. *Pharmacology, Biochemistry and Behavior* 1 A.D.; 57(3):Jul-470.

Abstract: Behavioral and pharmacological therapies have been used alone and in combination for the treatment of substance abuse; however, to date, no single treat-

ment approach for psychostimulant abuse has demonstrated widespread efficacy. This paper describes the various functions that are served by both behavioral therapies and pharmacotherapies and their respective mechanisms of action. It is argued that combined treatments can be expected to produce additive effects because the two approaches operate through different and potentially complementary mechanisms. Illustrations of these underlying principles and experimental support for the use of combined treatments are drawn from smoking cessation research, which has broadly applied combined behavioral and pharmacological therapies for treating abuse of nicotine, a mild stimulant. In addition, the results of recent studies that have evaluated the efficacy of behavioral techniques and/or potential pharmacotherapies for treating cocaine abuse are reviewed. Finally, methodological strategies are recommended for future evaluations of combined therapy approaches to conclusively evaluate separate and combined efficacy of treatments for psychostimulant abuse. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (19) Terplan M, Lui S. Psychosocial interventions for pregnant women in outpatient illicit drug treatment programs compared to other interventions. *Cochrane Database of Systematic Reviews: Reviews*. Cochrane Database of Systematic Reviews 2007 Issue 4. Chichester (UK): John Wiley & Sons, Ltd, 2007.
- Abstract: **BACKGROUND:** Illicit drug use in pregnancy is a complex social and public health problem. It is important to develop and evaluate effective treatments. There is evidence for the effectiveness of psychosocial in this population; however, to our knowledge, no systematic review on the subject has been undertaken. **OBJECTIVES:** To evaluate the effectiveness of psychosocial interventions in pregnant women enrolled in illicit drug treatment programs on birth and neonatal outcomes, on attendance and retention in treatment, as well as on maternal and neonatal drug abstinence. In short, do psychosocial interventions translate into less illicit drug use, greater abstinence, better birth outcomes, or greater clinic attendance.? **SEARCH STRATEGY:** We searched the Cochrane Drugs and Alcohol Group's trial register (May 2006), the Cochrane Central Register of Trials (Central- The Cochrane Library, Issue 3, 2005); MEDLINE (1.1996-8.2006); EMBASE (1.1996-8.2006); CINAHL (1.1982-8.2006), and reference lists of articles. **SELECTION CRITERIA:** Randomised studies comparing any psychosocial intervention versus pharmacological interventions or placebo or non-intervention or another psychosocial intervention for treating illicit drug use in pregnancy. **DATA COLLECTION AND ANALYSIS:** Two reviewers independently assessed trial quality and extracted data. **MAIN RESULTS:** Nine trials involving 546 pregnant women were included. Five studies considered contingency management (CM), and four studies considered manual based interventions such as motivational interviewing (MI). The main finding was that contingency management led to better study retention. There was only minimal effect of CM on illicit drug abstinence. In contrast, motivational interviewing led towards poorer study retention, although this did not approach statistical significance. For both, no difference in birth or neonatal outcomes was found, but this was an outcome rarely

captured in the studies. **AUTHORS' CONCLUSIONS:** The present evidence suggests that CM strategies are effective in improving retention of pregnant women in illicit drug treatment programs as well as in transiently reducing illicit drug use. There is insufficient evidence to support the use of MI. Overall the available evidence has low numbers and, therefore, it is impossible to accurately assess the effect of psychosocial interventions on obstetrical and neonatal outcomes. It is important to develop a better evidence base to evaluate psychosocial modalities of treatment in this important population. **PSYCHOSOCIAL INTERVENTIONS FOR PREGNANT WOMEN IN OUTPATIENT ILLICIT DRUG TREATMENT PROGRAMS COMPARED TO OTHER INTERVENTIONS:** The effectiveness of psychosocial interventions in pregnant women enrolled in illicit drug treatment programs. Women who use illicit drugs while pregnant are more likely to give birth early and have low weight infants that are at risk of neonatal abstinence syndrome and requiring intensive care. A pregnant woman reduces the risk of these complications by undergoing prenatal drug treatment. Maternal concern for the infant can also motivate her. The length of time on treatment is important. Psychosocial interventions may help to overcome the many barriers to staying in a treatment program and reduce the use of illicit drugs. Contingency management uses positive, supportive reinforcement with, for example, monetary vouchers or giving work and a salary only when abstaining from drug use or attending treatment to change behaviour. Manual based interventions include motivational interviewing with a directive, counselling style. This systematic review found that contingency management is effective in improving retention of pregnant women in illicit drug treatment programs but with minimal effects on their abstaining from illicit drugs. Motivational interviewing over three to six sessions may, if anything, lead to poorer retention in treatment. These findings are based on nine controlled trials over 14 days to 24 weeks, five studies used contingency management (346 women) and four studies (266 women) that considered motivational interviewing. All but one took place in the United States. Many of the young women were African American, single, never married or divorced, and unemployed. They were receiving methadone maintenance, using cocaine, or opiate dependent and marijuana and alcohol use was also involved in six studies. In two trials, almost all women were nicotine dependent. No difference in birth outcomes or length of hospital detoxification for the newborns was found, from two studies. None of the included studies stated how the women were referred to treatment. Manual based interventions are less likely to be effective among coerced individuals. It is also unlikely to be used on their own in clinical practice

- (20) Trujols J, Luquero E, Sinol N, Banuls E, Tejero A, Batlle F et al. Cognitive-behavioral therapy for the treatment of cocaine dependence. [References]. *Actas Esp Psiquiatr* 2007; 35(3):190-198.

**Abstract:** The past two decades have been characterized by marked progress in the development of effective cognitive-behavioral therapies for cocaine dependence, for which no generally effective pharmacotherapies have been identified. The increasing literature on the efficacy of several types of cognitive-behavioral therapies (commu-

nity reinforcement approach plus vouchers, cue exposure treatment, relapse prevention therapy and motivational interviewing) for cocaine use disorders is reviewed, followed by discussion of a number of issues that arise when integrating these cognitive-behavioral interventions into clinical practice. Overall, this review describes a vigorous area of research that has much to contribute to the treatment of cocaine use disorders. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (21) Van Horn DHA, Frank AF. Psychotherapy for cocaine addiction. [References]. *Psychology of Addictive Behaviors* 1998; 12(1):47-61.

Abstract: Cocaine abuse continues to be a major public health problem. Drug abuse researchers and practitioners have developed theoretically diverse cocaine-specific psychological treatments, including behavioral and cognitive-behavioral therapies, psychodynamic therapies, and integrative outpatient programs. In 1991, a major literature review identified several promising approaches, but there was little empirical evidence for their efficacy (R. A. Rawson, J. L. Obert, M. J. McCann, F. G. Castro, & W. Ling, 1991). Since then, outpatient psychotherapies for cocaine addiction have increasingly been empirically evaluated. This article summarizes prominent current approaches, with emphasis on empirical studies that have appeared since the Rawson et al. (1991) review, and evaluates progress in the field. Studies of treatment retention and the effect of comorbid psychopathology on treatment response are reviewed, and directions for future research are proposed. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (22) Vocci FJ, Elkashef A. Pharmacotherapy and other treatments for cocaine abuse and dependence. *Current Opinion in Psychiatry* 2005; 18(3):265-270.

Abstract: Purpose of review: This review examines progress being made in the treatment of cocaine abuse and dependence, with a particular focus on pharmacotherapies. Medications with apparently very different mechanisms of action have been reported to reduce cocaine use in controlled clinical trials in outpatient settings. This review will summarize the latest findings in this area. Recent findings: Of all the medications tested to date, disulfiram has demonstrated the most consistent effect to reduce cocaine use. Several medications have been reported to reduce cocaine use in double-blind, placebo-controlled clinical trials, namely baclofen, modafinil, tiagabine, and topiramate. All pharmacotherapy trials in cocaine-dependent patients include a behavioral therapy that is common to all participants. Consequently, these pharmacotherapy trials can be considered to evaluate whether the medication is adding to the effect of the behavioral therapy. Summary: Confirmatory clinical studies are necessary to replicate the initial efficacy findings for baclofen, modafinil, tiagabine, and topiramate. More research is needed in both cocaine and cocaine-alcohol dependent populations. Once confirmatory studies have been carried out, testing of rational medication combinations with different behavioral therapies is an obvious next step to increase the ability to manage cocaine dependence. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

(23) Weddington WW. Cocaine: Diagnosis and treatment. *Psychiatric Clinics of North America* 1993; 16(1):87-95.

Abstract: Reviews recent research on diagnosing cocaine addiction and on effective treatment interventions. Diagnosis takes into account such factors as route of administration, toxicity, effects of detoxification, and psychiatric comorbidity. Standard treatment for addiction is based on the 12-step AA recovery model, has a goal of total abstinence from all addictive substances, and uses a format that consists of educational and group sessions. Experimental treatments include cognitive/behavioral approaches, psychotherapy, and psychopharmacotherapy. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

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## KOMBINASJON AV MEDIKAMENTELL OG PSYKOSOSIAL BEHANDLING AV KOKAINAVHENGIGHET (10 OVERSIKTER)

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- (1) Carroll KM. Integrating psychotherapy and pharmacotherapy to improve drug abuse outcomes. *Addict Behav* 1997; 22(2):233-245.  
Abstract: Reviews the roles of pharmacotherapy and psychotherapy in the treatment of drug abuse and summarizes recent examples of the benefits of combining treatments for drug abuse. The differences in treatments are discussed in terms of their mode of action, time to effect, target symptoms, durability, and applicability across drugs of abuse. While each has specific indications and strengths, no psychotherapy or pharmacotherapy is universally effective, and both forms of treatment have some limitations, particularly when used alone. Several recent examples of the benefits of combined treatments for drug abusers suggest that, for many substance use disorders, outcomes can be broadened, enhanced, and extended by combining the most effective forms of psychotherapy and pharmacotherapy. Examples applicable to methadone maintenance, naltrexone/agonist treatment, and cocaine dependence are explored. (PsycINFO Database Record (c) 2008 APA, all rights reserved)
  
- (2) Higgins ST, Wong CJ. Treating cocaine abuse: What does research tell us? *Behavior, pharmacology, and clinical applications*, 1998.  
Abstract: (from the chapter) The purpose of this chapter is to review what has been learned scientifically about how to effectively treat cocaine abuse. The chapter focuses on individuals who are seeking or enrolled in treatment for cocaine abuse (i.e., primary cocaine abusers). The following topics are addressed: in-hospital vs out-of-hospital patient care; early attrition; treatment duration, intensity, and format; and treatment context (behavioral treatments, pharmacological treatments, multiple drug use and abuse). (PsycINFO Database Record (c) 2008 APA, all rights reserved)
  
- (3) Rawson RA, McCann MJ, Hasson AJ, Ling W. Cocaine abuse among methadone maintenance patients: Are there effective treatment strategies? *J Psychoactive Drugs* 1994; 26(2):129-136.  
Abstract: Reviews empirical evidence on the effectiveness of several categories of techniques for treating cocaine abuse among patients in methadone maintenance treatment. These include pharmacotherapies, behavioral methods (contingency management and relapse prevention), and methadone dose adjustment. Other treatment interventions that may be efficacious for this population, including day treatment and sober-living facilities, are described. Suggestions are made for the successful implementation of cocaine focus groups. Methadone clinic management procedures that may aid in the reduction of cocaine abuse by methadone patients are discussed. Although many of these efforts are in early stages of evaluation, there are some reasons for optimism in the development of treatment for these patients. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

- (4) Rawson RA, Obert JL, McCann MJ, Castro FG. Cocaine abuse treatment: A review of current strategies. *Journal of Substance Abuse* 1991; 3(4):457-491.  
Abstract: Many of the strategies that are being developed to treat cocaine abusers have been adapted from drug and alcoholism treatment systems. These include the use of established programs that are minimally modified for cocaine abusers, such as the 28-day inpatient hospital, therapeutic community, and 12-step programs. Other approaches have created specific techniques to meet the clinical needs of cocaine abusers, such as behavioral, pharmacologic, and nontraditional interventions. Other attempts have been made to create integrated outpatient approaches. However, few data exist to definitively address the effectiveness of any of the treatment modalities. This article reviews treatment efforts that have been conducted, overviews research data, and offers recommendations regarding currently available treatment options. (PsycINFO Database Record (c) 2008 APA, all rights reserved)
- (5) Rohsenow DJ, Monti PM. Relapse among cocaine abusers: Theoretical, methodological, and treatment considerations. [References]. Yale University Press, 2001.  
Abstract: (from the chapter) Focuses on treatment for cocaine abuse, reviewing approaches that have resulted in significant improvements in outcomes. Behavioral approaches for preventing relapse among cocaine abusers have shown considerable growth in recent years. At the same time, the medications development portfolio at NIDA continues to thrive in the search for medications that may decrease the probability of relapse during treatment and early recovery, and thereby buy time for skills training and lifestyle changes to produce lasting effects on outcome. The most promising of the behavioral approaches are those that are solidly rooted in social learning theory models of behavior. Two of the most effective types of approaches are contingency management approaches and cognitive-behavioral coping skills training approaches, each with several studies showing effectiveness. (PsycINFO Database Record (c) 2008 APA, all rights reserved)
- (6) Roozen HG, Boulogne JJ, van Tulder MW, van den Brink W, De Jong CAJ, Kerkhof AJFM. A systematic review of the effectiveness of the community reinforcement approach in alcohol, cocaine and opioid addiction. [References]. *Drug Alcohol Depend* 2004; 74(1):1-13.  
Abstract: The community reinforcement approach (CRA) has been applied in the treatment of disorders resulting from alcohol, cocaine and opioid use. The objectives were to review the effectiveness of (1) CRA compared with usual care, and (2) CRA versus CRA plus contingency management. Studies were selected through a literature search of RCTs focusing on substance abuse. The search yielded 11 studies of mainly high methodological quality. The results of CRA, when compared to usual care: there is strong evidence that CRA is more effective with regard to number of drinking days, and conflicting evidence with regard to continuous abstinence in the alcohol treatment. There is moderate evidence that CRA with disulfiram is more effective in terms of number of drinking days, and limited evidence that there is no difference in effect in terms of continuous abstinence. Furthermore, there is strong evidence that CRA with 'incentives' is more effective with regard to cocaine abstinence.



There is limited evidence that CRA with 'incentives' is more effective in an opioid detoxification program. There is limited evidence that CRA is more effective in a methadone maintenance program. Finally, there is strong evidence that CRA with abstinence-contingent 'incentives' is more effective than CRA (non-contingent incentives) treatment aimed at cocaine abstinence. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (7) Silverman K, Bigelow GE, Stitzer ML. Treatment of cocaine abuse in methadone maintenance patients. *Behavior, pharmacology, and clinical applications*, 1998.  
Abstract: (from the chapter) This chapter reviews interventions used to treat cocaine use in methadone patients. The chapter has 4 main sections. The 1st section reviews research on the effects of methadone itself on cocaine use. The high rates of cocaine use in methadone patients has prompted concern that methadone itself may increase cocaine use, either directly or indirectly. To look thoroughly for evidence of potential undesirable effects of methadone on cocaine use, this section reviews a number of descriptive studies relevant to this issue, in addition to controlled studies. The next 3 sections review controlled trials of the 3 major types of interventions that have been employed in drug abuse treatment: pharmacological, psychosocial, or behavioral, and other less conventional types of treatment. (PsycINFO Database Record (c) 2008 APA, all rights reserved)
- (8) Stitzer ML, Walsh SL. Psychostimulant abuse: The case for combined behavioral and pharmacological treatments. *Pharmacology, Biochemistry and Behavior* 1 A.D.; 57(3):Jul-470.  
Abstract: Behavioral and pharmacological therapies have been used alone and in combination for the treatment of substance abuse; however, to date, no single treatment approach for psychostimulant abuse has demonstrated widespread efficacy. This paper describes the various functions that are served by both behavioral therapies and pharmacotherapies and their respective mechanisms of action. It is argued that combined treatments can be expected to produce additive effects because the two approaches operate through different and potentially complementary mechanisms. Illustrations of these underlying principles and experimental support for the use of combined treatments are drawn from smoking cessation research, which has broadly applied combined behavioral and pharmacological therapies for treating abuse of nicotine, a mild stimulant. In addition, the results of recent studies that have evaluated the efficacy of behavioral techniques and/or potential pharmacotherapies for treating cocaine abuse are reviewed. Finally, methodological strategies are recommended for future evaluations of combined therapy approaches to conclusively evaluate separate and combined efficacy of treatments for psychostimulant abuse. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)
- (9) Vocci FJ, Elkashef A. Pharmacotherapy and other treatments for cocaine abuse and dependence. *Current Opinion in Psychiatry* 2005; 18(3):265-270.  
Abstract: Purpose of review: This review examines progress being made in the

treatment of cocaine abuse and dependence, with a particular focus on pharmacotherapies. Medications with apparently very different mechanisms of action have been reported to reduce cocaine use in controlled clinical trials in outpatient settings. This review will summarize the latest findings in this area. Recent findings: Of all the medications tested to date, disulfiram has demonstrated the most consistent effect to reduce cocaine use. Several medications have been reported to reduce cocaine use in double-blind, placebo-controlled clinical trials, namely baclofen, modafinil, tiagabine, and topiramate. All pharmacotherapy trials in cocaine-dependent patients include a behavioral therapy that is common to all participants. Consequently, these pharmacotherapy trials can be considered to evaluate whether the medication is adding to the effect of the behavioral therapy. Summary: Confirmatory clinical studies are necessary to replicate the initial efficacy findings for baclofen, modafinil, tiagabine, and topiramate. More research is needed in both cocaine and cocaine-alcohol dependent populations. Once confirmatory studies have been carried out, testing of rational medication combinations with different behavioral therapies is an obvious next step to increase the ability to manage cocaine dependence. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (10) Weddington WW. Cocaine: Diagnosis and treatment. *Psychiatric Clinics of North America* 1993; 16(1):87-95.

Abstract: Reviews recent research on diagnosing cocaine addiction and on effective treatment interventions. Diagnosis takes into account such factors as route of administration, toxicity, effects of detoxification, and psychiatric comorbidity. Standard treatment for addiction is based on the 12-step AA recovery model, has a goal of total abstinence from all addictive substances, and uses a format that consists of educational and group sessions. Experimental treatments include cognitive/behavioral approaches, psychotherapy, and psychopharmacotherapy. (PsycINFO Database Record (c) 2008 APA, all rights reserved)

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## AKUPUNKTUR FOR KOKAINAVHENGIGHET (6 OVERSIKTER)

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- (1) D'Alberto A. Auricular acupuncture in the treatment of cocaine/crack abuse: a review of the efficacy, the use of the National Acupuncture Detoxification Association protocol, and the selection of sham points (DARE structured abstract). *J Altern Complement Med* 2004; 10:985-1000.
  
- (2) Gates S, Smith LA, Foxcroft DR. Auricular acupuncture for cocaine dependence. *Cochrane Database Syst Rev* 2006;(1):CD005192.  
Abstract: BACKGROUND: Auricular acupuncture (insertion of acupuncture into a number, usually five, of specific points in the ear) is a widely-used treatment for cocaine dependence. OBJECTIVES: To determine whether auricular acupuncture is an effective treatment for cocaine dependence, and to investigate whether its effectiveness is influenced by the treatment regimen. SEARCH STRATEGY: We searched the Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 3, 2004); MEDLINE (January 1966 to October 2004) , EMBASE (January 1988 to October 2004); PsycInfo (1985 to October 2004); CINAHL (1982 to October 2004); SIGLE (1980 to October 2004) and reference lists of articles. SELECTION CRITERIA: Randomised controlled trials comparing a therapeutic regimen of auricular acupuncture with sham acupuncture or no treatment for reduction of cocaine use in cocaine dependents. DATA COLLECTION AND ANALYSIS: Two authors independently extracted data from published reports and assessed study quality using the Drug and Alcohol CRG checklist. All authors were contacted for additional information; two provided data. Separate meta-analyses were conducted for studies comparing auricular acupuncture with sham acupuncture, and with no treatment. For the main cocaine use outcomes, analyses were conducted by intention to treat, assuming that missing data were treatment failures. Available case analyses, using only individuals who provided data, were also conducted. MAIN RESULTS: Seven studies with a total of 1,433 participants were included. All were of generally low methodological quality. No differences between acupuncture and sham acupuncture were found for attition RR 1.05 (95% CI 0.89 to 1.23) or acupuncture and no acupuncture: RR 1.06 (95% CI 0.90 to 1.26) neither for any measure of cocaine or other drug use. However, the number of participants included in meta-analyses was low, and power was limited. Moderate benefit or harm is not ruled out by these results. Methodological limitations of the included studies may have also made the results open to bias. AUTHORS' CONCLUSIONS: There is currently no evidence that auricular acupuncture is effective for the treatment of cocaine dependence. The evidence is not of high quality and is inconclusive. Further randomised trials of auricular acupuncture may be justified. [References: 42]
  
- (3) Kim YH, Schiff E, Waalen J, Hovell M. Efficacy of acupuncture for treating cocaine addiction: A review paper. [References]. *Journal of Addictive Diseases* 2005; 24(4):115-132.

Abstract: Acupuncture is being used in more than three hundred treatment facilities for treating substance abuse including cocaine addiction. Previous review papers could not evaluate the role of acupuncture for treating cocaine addiction because of lack of clinical trials at the time. Since then, several important studies were conducted in the field. This paper reviews existing clinical trials using acupuncture to treat cocaine addiction. The existing evidence fails to document the benefit of acupuncture in treating cocaine addiction as the sole treatment. Further efforts to document the efficacy of the NADA protocol to treat cocaine addiction as the sole treatment should be re-evaluated. There is a limited amount of evidence showing possible benefits of acupuncture when used as an adjunctive therapy to complement existing substance abuse treatment program. Future efforts should concentrate on systematic studies investigating the role of acupuncture as an adjunctive treatment for cocaine addiction. In addition, more formative research exploring the efficacy of different types and protocols of acupuncture treatments for cocaine addiction should be thoroughly investigated. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (4) Kunz S, Schulz M, Syrbe G, Driessen M. Acupuncture of the ear as therapeutic approach in the treatment of alcohol and substance abuse--A systematic review. [German]. [References]. *Sucht: Zeitschrift für Wissenschaft und Praxis* 2004; 50(3):196-203.

Abstract: Aims: Acupuncture as a treatment of substance-related disorders has reached increasing acceptance. A systematic review of the available studies is provided to determine, if this trend is supported by the scientific evidence from RCT's. Methodology: A systematic literature search and critical appraisal of the studies was done. Results: Fourteen randomised controlled studies (RCT) of ear acupuncture in the treatment of withdrawal from opiate-, cocaine- or alcohol-dependent patients were identified. A meta-analysis of the studies based on effect size could not be performed because of varying objectives, methods, sample characteristics and different dropout rates. Conclusion: The available scientific evidence does not support the efficacy of acupuncture in the treatment of withdrawal in opiate-, cocaine- and alcohol-dependent patients. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (journal abstract)

- (5) Mills EJ, Wu P, Gagnier J, Ebbert JO. Efficacy of acupuncture for cocaine dependence: a systematic review and meta-analysis (DARE structured abstract). *Harm Reduction Journal* 2005; 2:4.

- (6) Moner SE. Acupuncture and addiction treatment. *Journal of Addictive Diseases* 1996; 15(3):79-100.

Abstract: Reviews the literature on clinical trials using acupuncture in drug treatment. Clinical trials selected were those conducted for efficacy of acupuncture treatment with opiate, alcohol, cocaine and nicotine dependence. Mechanisms of action of acupuncture and drug treatment are discussed. Acupuncture's role in substance abuse treatment is just beginning, but the efficacy of

acupuncture in drug treatment is encouraging. (PsycINFO Database Record (c)  
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- (3) Ballon JS, Feifel D. A Systematic Review of Modafinil: Potential Clinical Uses and Mechanisms of Action. [References]. *J Clin Psychiatry* 2006; 67(4):554-566.
- (4) Berglund M, Thelander S, Jonsson E. Treating alcohol and drug abuse: An evidence based review. [References]. *An evidence based review*, 2003.
- (5) Brebner K, Childress AR, Roberts DCS. A potential role for GABA-sub(B) agonists in the treatment of psychostimulant addiction. *Alcohol and Alcoholism* 2002; 37(5):478-484.
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- (9) Carroll KM. Integrating psychotherapy and pharmacotherapy to improve drug abuse outcomes. *Addict Behav* 1997; 22(2):233-245.
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- (11) Cousins MS, Roberts DCS, de Wit H. GABA-sub(B ) receptor agonists for the treatment of drug addiction: A review of recent findings. [References]. *Drug Alcohol Depend* 2002; 65(3):209-220.
- (12) Crits-Christoph P, Siqueland L. Psychosocial treatment for drug abuse: selected review and recommendations for national health care. *Archives of General Psychiatry* 1996; 53(8):749-756.
- (13) Crosby RD, Halikas JA, Carlson G. Pharmacotherapeutic interventions for cocaine abuse: Present practices and future directions. *Journal of Addictive Diseases* 1991; 10(4):13-30.
- (14) D'Alberto A. Auricular acupuncture in the treatment of cocaine/crack abuse: a review of the efficacy, the use of the National Acupuncture Detoxification Association protocol, and the selection of sham points (DARE structured abstract). *J Altern Complement Med* 2004; 10:985-1000.
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# Vedlegg

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## SØKESTRATEGI

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### Cochrane 11.06.2009

Uke 24

Cochrane reviews 10 treff

Cochrane other reviews (DARE) 4 treff

#1	MeSH descriptor Cocaine explode all trees	Kokain misbruk
#2	MeSH descriptor Substance-Related Disorders explode all trees	
#3	#1 AND #2	
#4	MeSH descriptor Cocaine-Related Disorders explode all trees	
#5	cocaine near/3 (use* or depend* or addict* or abuse* or misuse*):ti,ab	
#6	(#4 OR #5)	
#7	(#3 OR #6)	
#8	MeSH descriptor Drug Therapy explode all trees	Behandling
#9	MeSH descriptor Treatment Outcome explode all trees	
#10	(treatment* or therap* or rehabilitat*):ti,ab	
#11	(#8 OR #9 OR #10)	
#12	(#7 AND #11)	Ga 10 treff i Cochrane reviews og 4 i DARE

### Medline 1950 to June Week 1 2009

11.06.09

Uke 24

Antall treff 57 m/søkefilter reviews (specificity)

1	exp Cocaine/	Kokain mis-
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2	exp Substance-Related Disorders/	bruk
3	1 and 2	
4	exp Cocaine-Related Disorders/	
5	(cocaine adj3 (abuse* or misuse* or addiction* or dependen* or use*)).tw.	
6	4 or 5	
7	6 or 3	
8	drug therapy/ or drug rehabilitation/ or treatment outcome/	
9	(treatment or therapy).fs.	
10	or/8-10	
11	11 and 7	
12	limit 12 to "reviews (specificity)"	57 treff

Search filter for review (specificity): search strategy.tw.

### PsycInfo 1806 to June Week 1 2009

11.06.2009

Uke 24

Antall treff 175

1	exp cocaine/	Kokain misbruk
2	exp drug abuse/	
3	exp drug addiction/	
4	1 and (1 or 2)	
5	(cocaine adj3 (abuse* or misuse* or addiction* or dependen* or use*)).tw.	
6	4 or 5	
7	drug therapy/ or drug rehabilitation/ or treatment outcome/	Behandling
8	(treatment* or therap* or rehabilitation*).tw.	
9	8 or 7	
10	6 and 9	
11	meta analysis/	Avgrensing filter systematiske oversik- ter
12	(metaanaly\$ or (meta adj analy\$)).tw.	
13	((systematic or comprehensive or literature or quantitative or critical or integrative or evidence\$) adj2 (review\$1 or overview\$1)).tw.	
14	literature study.tw.	
15	(critical adj (appraisal or analysis)).tw.	
16	"literature review"/	
17	Meta Analysis.md.	
18	literature review.md.	

19	cochrane or medline or embase or cinahl og cinhal or psychlit or psyclit or science citation index or bids or cancerlit).ab.	
20	reference list\$.ab.	
21	bibliograph\$.ab.	
22	(handsearch\$ or hand search\$).ab.	
23	relevant journals.ab.	
24	manual search\$.ab.	
25	data extraction.ab.	
26	selection criteria.ab.	
27	or/11-26	
28	comment reply.dt.	
29	editorial.dt.	
30	letter.dt.	
31	nonclinical case study.md.	
32	clinical case study.md.	
33	animal.po.	
34	human.po.	
35	33 not (33 and 34)	
36	or/28-32,35	
37	27 not 36	
38	37 and 10	175 treff