

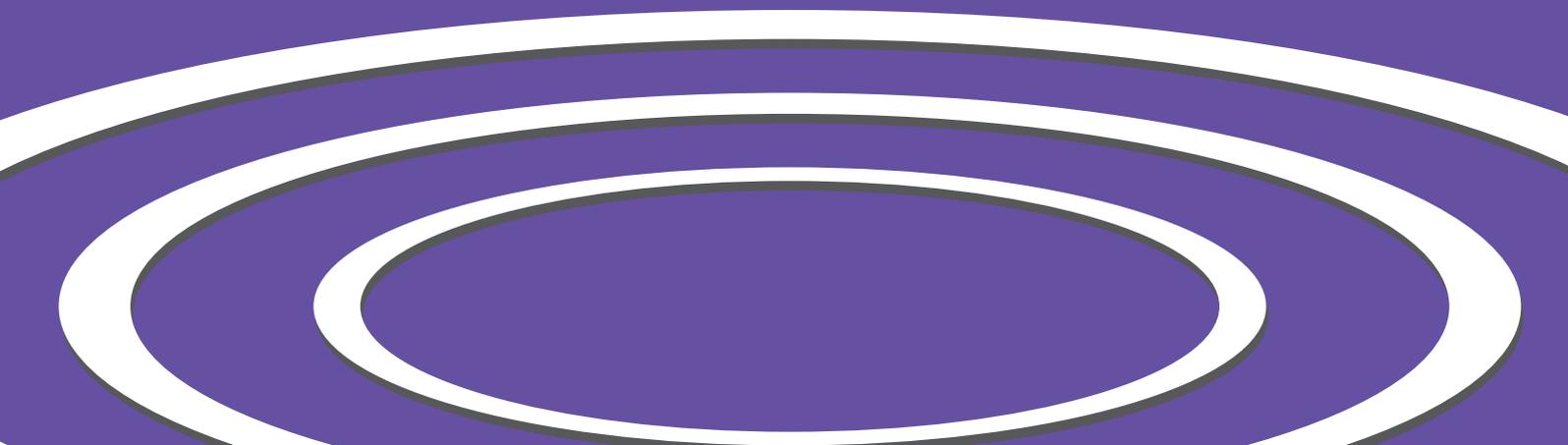


## Executive Summary

# Dexamphetamine Substitution as a Treatment of Amphetamine Dependence: a Two-Centre Randomised Controlled Trial Final Report submitted to the Department of Health

December 2004

Report prepared by:  
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Anthony Tetlow, Chris Roberts, Karin Arnold, Jennifer Crean,  
Sophie Lomax, Bill Deakin



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## **Executive Summary**

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### **Report prepared by:**

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### **Disclaimer**

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## Aims and Objectives

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### Aim

- *To investigate the impact of dexamphetamine prescribing for the treatment of amphetamine dependence*

### Objectives

- *To assess the practicalities of a research methodology for studying dexamphetamine prescribing in UK clinical settings.*
- *To assess the effectiveness of dexamphetamine substitution on recognised best available treatment of amphetamine dependence.*
- *To describe the nature and extent of any benefits or harms on the mental or physical health of those receiving dexamphetamine.*
- *To contribute to the development of guidelines for best practice in the management of amphetamine dependence.*

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## Policy Relevance

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After cannabis, amphetamine is the second most widely used illicit drug in the UK. Most amphetamine use is recreational but a proportion of amphetamine users develop significant dependence. Amphetamine is often injected and injectors have been shown to be at higher risk of infection with blood-borne viruses than heroin injectors. Amphetamine dependence is also associated with high levels of criminality. Several generic and symptomatic treatments are potentially of relevance to amphetamine users, but there is little research into treatment effectiveness and services have generally failed to attract users into treatment. If parallels can be drawn between amphetamine and opiate dependence, then prescribing dexamphetamine as a substitute treatment could confer benefits similar to methadone, the benchmark treatment for heroin dependence.

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## Introduction

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Evidence suggests that dexamphetamine is widely prescribed for the treatment of addiction. In England and Wales between 900 and 1,000 amphetamine users are prescribed dexamphetamine and 60% of specialists in drug dependence consider that dexamphetamine has a role in treating amphetamine dependence. There are a small number of studies from the UK and Australia on prescribing dexamphetamine to amphetamine users. They have shown that treatment results in increased retention in treatment and reductions

in illicit amphetamine use, injecting and offending behaviour. The potential to receive a prescription for dexamphetamine also encouraged amphetamine users to present for treatment. Prescribing dexamphetamine remains controversial because benefits have not been demonstrated in randomised controlled trials and because of the possible risks to physical and mental health.

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## Research Design and Methodology

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The study was a randomised two-centre (Manchester and Cardiff) parallel group design comparing the effect of dexamphetamine prescribing and best available treatment (DEX) to best available treatment alone (BATA) for the treatment of amphetamine dependence. Study participants provided written consent and the study had local ethical approval.

BATA included provision of literature on amphetamine, motivational style interviewing, review of recent behavior using a retrospective drug diary and discussion of cues, coping and lapse management, advice on healthy lifestyles, harm minimisation advice including advice on safer injecting and use of syringe exchange schemes, referral to appropriate non-drug agencies for other health or social issues, symptomatic prescribing for depression, anxiety and insomnia and the possibility for inpatient admission for detoxification if clinically indicated. The DEX treatment arm included all the above and dexamphetamine tablets up to 100 mg daily, dispensed on a daily basis through a community pharmacist.

After treatment randomization, participants received weekly clinical appointments for the first 4 weeks and then fortnightly clinical appointments until 7 months, at which point the treatment phase of the study finished. During the first 4 months DEX participants received maintenance dexamphetamine prescribing. After four months participants in the DEX group were gradually withdrawn from dexamphetamine according to a predefined schedule over the next 3 months. Independent research assessments took place at entry into treatment, 1 month, 4 months, 7 months and 9 months i.e. two months after treatment ended. The research interviews included standardised questionnaires on drug use, physical and psychological health, social functioning and quality of life, offending behavior and satisfaction with treatment.

The two treatment groups were compared during the course of the trial based on research interviews and clinical monitoring data. For the research data this involved two sets of statistical analyses, the first of

early outcome combining assessment for months 1 and 4 (equivalent to the dexamphetamine maintenance phase), and the second of longer-term outcome using assessment at 7 and 9 months (dexamphetamine withdrawal phase). A similar approach was used with the clinical monitoring data, analysing responses for the first 16 weeks and weeks 17-28 separately. Statistical analysis followed the principle of intention-to-treat, i.e. data was analysed according to the way we intended to treat participants, not the way in which they were actually treated.

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## Findings

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Fifty-nine individuals fulfilling DSM IV criteria for amphetamine dependence were recruited from the 2 centres in Manchester and Cardiff. Randomisation was computerised and eligible participants were allocated to DEX or BATA using minimisation controlling for treatment centre, gender and injecting status. Thirty-two participants were randomised to DEX and 27 to BATA. Amongst the study sample, 71% were male, 56% were injecting on entry to the study, the mean illicit amphetamine use was 19.3 grams over the previous 7 days and polydrug use was common with alcohol, tobacco and cannabis being the most frequently used other substances.

DEX participants attended a median of 7 of 16 scheduled clinic appointments and BATA clients a median of 5. Research interview follow up rates were 78% at 1 month, 69% at 4 months, 56% at 7 months and 59% at 9 months.

Prescribing dexamphetamine did not significantly reduce illicit amphetamine use compared with BATA with both groups reporting reductions. Dexamphetamine did not have a positive impact on reducing injecting behaviour compared with BATA. There was evidence to support reduced polydrug use in the late outcome period ( $p = 0.08$ ) for those prescribed dexamphetamine.

Participants prescribed dexamphetamine showed significant improvement in physical health outcomes during the first 4 months of treatment (maintenance phase) ( $p = 0.01$ ) with some evidence to support this being sustained over the later outcome period ( $p = 0.08$ ). There was a statistical trend showing improvements in psychological health in the DEX group compared with the BATA group in both the early and late outcome periods.

Blood pressure was increased in the DEX group during weeks 17 to 28 of clinical monitoring but the mean

blood pressure for the DEX group remained within the normal range. Body weight reduced in the DEX group compared with the BATA group during maintenance treatment (weeks 1 - 16) and increased during the reduction phase (weeks 17 - 28). Overall both groups gained weight.

Prescribing dexamphetamine did not have adverse effects on the physical or psychological health of participants. There was only one episode of psychosis when a participant was in receipt of a dexamphetamine prescription. This was in the context of severe emotional stress and during the dexamphetamine reduction phase.

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## Future Research

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Future randomised controlled trials into the treatment of amphetamine dependence based on the methodology of the current study should be achievable within clinical settings. They must be designed using power calculations based on more modest outcomes than previously expected, and will have to overcome the difficulties in recruiting and retaining participants encountered in this study.

There are likely to be subsets of amphetamine users who benefit more from dexamphetamine prescribing than others and this should be considered by future research. Psychosocial treatments also clearly require further research, both as treatments within their own right and as components of an overall treatment package that includes dexamphetamine prescribing. The management of stimulant dependence in clients with severe and enduring mental illness is a particularly difficult therapeutic area that also requires further research.

There is pressing need in the UK for effective interventions for crack use and combined crack and opiate use. Dexamphetamine may have potential as an agonist therapy in the treatment of cocaine dependence.

The need for a larger randomised controlled trial, that provides definitive outcomes and allows comparisons of subgroups, should not detract from further uncontrolled studies, but these should use more stringent and better-validated outcome measures than hitherto has been the case.

With regard to best practice in managing amphetamine dependence, the study provides modest support for the benefits of prescribing dexamphetamine. Concerns that dexamphetamine confers significant risk to the physical and mental health of patients were not

substantiated. The study also showed that amphetamine users will present for treatment when there is no certainty that they will receive a prescription for dexamphetamine and that they can engage in treatment and benefit substantially from such treatment.

The evidence supports the Department of Health's current clinical guidelines that dexamphetamine substitution should remain a specialist treatment intervention carried out by experienced practitioners. When offered, dexamphetamine should be part of a complete treatment package incorporating psychosocial interventions and providing clinical monitoring procedures that include urine drug screening with the ability to differentiate prescribed from illicit amphetamine, blood pressure checks and mental state reviews. ■