



## SMMGP CLINICAL UPDATE OCTOBER 2009

**Effectiveness of community treatments for heroin and crack cocaine addiction in England: a prospective, in-treatment cohort study.** *J Marsden, Eastwood B, Bradbury C, et al. Lancet 2009; 374:1262-1270*

This study scrutinises all adults in England with a heroin or crack addiction who were given pharmacological or psychosocial treatment starting between 1<sup>st</sup> Jan – 30<sup>th</sup> Nov 2008. In order to be included there had to be data submitted to the National Drug Treatment Monitoring System (NDTMS) and a total of 21075 adults were in the initial cohort.

The study uses the Treatment Outcome Profile (TOP) which was introduced in October 2007 to collate information of the effectiveness of all community treatments. This is not a randomised trial and there are no specific interventions being tested. It is simply an observational study of adults already in treatment. Unlike NTORS the study is limited to community level treatment and does not include residential programmes.

After 6 months in treatment the results showed that heroin users reduced their use by 14.5 days in a 28 day period and crack users reduced their use by 7.7 days in the same period. However, in those that used both drugs together the effects were less pronounced – there was a reduction in days of use but significantly less than those that used just one drug. This reduced effect was only seen in the group that received pharmacological treatment and there wasn't this disparity in the group getting solely psychosocial treatment. In addition, the study showed that psychosocial treatments, despite having a relatively weak effect in randomised controlled trials of cognitive behavioural therapies, reduced use in those using heroin, crack or both.

### **SMMGP comment:**

This really was a national study – every single PCT, bar one, was included and all mental health trusts in England. The numbers are huge and the statistical methods are almost as mind-boggling.

The authors acknowledge the weaknesses of the study. Ultimately, observational studies measure association and one has to be cautious when assuming causation. This is particularly important as there was no control group and so we have no idea of the natural untreated course of this cohort. TOP forms are usually completed with keyworkers who may have felt that they are a tool to measure their personal performance and this could have influenced their completion. Even with the best of intentions any unblinded study tends to show an increased effect and runs the risk of significant observer bias. The National Treatment Agency authors have openly declared their potential conflict of interest in this study and some critics have been quick to highlight this point.

A further gap is that there are TOP data missing for 26% at the review point - there were only 14656 analysed at the endpoint but 21075 were admitted to treatment. The authors feel that they have adjusted for this in their analysis and they stated: "the demographic and clinical characteristics of individuals with or without data did not differ, and weighting of the data to account for those without information did not change results".

This is simply the start of the analysis of enormous amounts of raw data. The authors highlight some of the areas that will be examined. These include analysis of drugs other than heroin and crack; the characteristics of the 2-3% of clients who increased their use during treatment; the regional variations in outcomes and how this relates to organisational differences; and even analysis of interventions other than pharmacological and psychosocial.

Overall, this is a massive study across the whole of England and it should be placed alongside the wealth of randomised control trials (RCTs) showing clinical benefits. It strengthens the evidence that the known benefits of clinical trials translate into real benefits in community based drug treatment services in England.

**Can we prevent drug-related deaths by training opioid users to recognise and manage overdose?** *Lopez Gaston R, Best D, Manning V, Day E. Harm Reduction Journal 2009; 6:26*

This study took 70 opioid users (66 in Birmingham and 4 in London) and trained them how to recognise and manage overdoses. In addition, they gave them a supply of 400mcg naloxone pre-filled syringes and they then followed them up after 6 months to see how they fared. The outcomes that the study looked at were, whether they had retained the information, whether they had witnessed any overdoses and if they still had the naloxone available and were willing to use it.

The patients were all given a 30 minute training session consisting of advice on overdose and advice on use of a pre-filled naloxone syringe. They were then issued with a naloxone minijet. The group received pre-test and post-test questionnaires and this questionnaire was repeated at the 6 month point. The study managed to follow up 65% of the sample (n=46) at the 3 and 6 month point. Phone interviews or face-to-face contact were arranged and consisted of a structured questionnaire assessing current drug use, whether the individual had experienced or witnessed an overdose and if so, what they did.

In the sample group 28.9% had previously experienced an overdose. After the six month period 9 users reported that they had witnessed a total of 16 overdoses. The scores on the questionnaire remained high at the 6 month test and the authors suggested that this demonstrated consistent retention of knowledge. There were no incidents where the naloxone had been used. Although the majority were still in possession of the naloxone most did not carry it with them.

**SMMGP comment:**

The significant mortality and morbidity associated with accidental overdose is not disputed. This study emphasises the challenges of assessing strategies to address overdose prevention. The discussion in this paper is a clear-eyed appraisal of the limitations of this study and an excellent discussion of many of the issues in this field.

Small numbers hamper the interpretation of these data and in all likelihood the study was never going to be big enough to pick up clear effects. The additional issues of missing data and drop-out further curtail the conclusions that can be drawn.

The authors point out some interesting areas of conflict for participants. They were all in a treatment setting and the carrying of naloxone could be seen as particularly contradictory to those striving for abstinence. They also discussed the stigma of carrying around a bulky minijet as well as concerns over police and paramedic reactions to the use of naloxone. Naloxone seems like an obvious remedy to help reduce overdose deaths but it may not be as easy as it first seems. We look forward to hearing the results from the NTA pilot of naloxone which started in June 2009 across 16 sites and involving about 950 family members and carers.

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**Self-reported health status, and health service contact, of illicit drug users aged 50 and over: a qualitative interview study in Merseyside, United Kingdom.** *Beynon C, Roe B, Duffy P, Pickering L. BMC Geriatrics 2009; 9:45*

This qualitative study interviewed 9 men and 1 woman who had used drugs on and off for the previous 30 years. The authors report that there are no previous qualitative studies looking at this group of drug users. The study was conducted in the Merseyside area where the proportion of users in treatment aged 50 and over has grown from 1.5 to 3.6% in men ( $p < 0.001$ ) over the period 1998 to 2005.

They conducted semi-structured interviews and used thematic analysis. The interviewees discussed high levels of both physical and mental morbidity. They discussed the issue of health service contact and although there was some positive experiences one predominant theme was the difficulty accessing care and hostile attitudes towards users in care. As a consequence interviewees in poor health had low expectations of healthcare. A common theme was the death of friends and this was associated with feelings of sadness and

depression. This deepened the isolation of the interviewees but the study also discussed some interesting adaptation to changing social networks with younger and older users forming a symbiotic alliance.

**SMMGP comment:** Caring for older users is already an increasing problem in general practice and it is going to grow and there is no better setting to manage the needs of the older drug user than in a system that is already highly adapted to provide care for chronic diseases.

The authors state that, in keeping with qualitative literature, they make no claim of generalisability. The interviewees were mostly white, male and in Merseyside. The authors may not feel they can make any claims but, in terms of UK practice, readers will feel it is perfectly reasonable that the issues of deteriorating physical health, particularly chronic obstructive airways disease from smoking, liver problems and mental health in older users will be highly applicable and increasingly relevant to their own local population.

The article concludes that ageing drug users continue to be a neglected group. Addressing the physical needs of drug users will become increasingly important as the demographic of the substance using population ages and chronic health issues become more prominent. There exists a great opportunity for primary care to address ongoing substance use while effortlessly slipping in chronic disease management to improve health outcomes in this vulnerable group.

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**Cocaine vaccine for the treatment of cocaine dependence in methadone-maintained patients. A randomized, double-blind, placebo-controlled efficacy trial.** Martell B, Orson F, Poling J. *Arch Gen Psych.* 2009; 66(10):1116-1123

The basic aim of this trial was to test the effectiveness of a cocaine vaccine that could be used to treat cocaine dependence. They selected cocaine dependent participants who were also opioid dependent as the retention in methadone programs is considerably better than primary cocaine treatment programs. The

aim is to reduce cocaine's effect of euphoria by using anticocaine antibodies to mop up circulating cocaine. Theoretically, those that received the vaccine would then be immune to the effects of cocaine.

The study explains how they made an anticocaine vaccine. They started with the cholera toxin B-subunit protein used in the cholera vaccine. It is safe and it is highly immunogenic so that when it comes into contact with the immune system the body will produce antibodies. By binding a small succinyl-norcocaine molecule to this cholera protein the body is suckered into producing antibodies that will subsequently recognise cocaine as an antigen.

In this study there were 115 patients who were eligible and were started on methadone maintenance. Of these, 57 were randomised to placebo (but only 47 completed 24 weeks) and 58 were randomised to vaccine (with 55 having the full course of 5 vaccinations).

The results showed that the vaccine can significantly reduce cocaine use in those subjects that achieved antibody levels over 43µg/mL. However, only 21 participants (38%) of those vaccinated got to these levels and they didn't get to them before week 8 and they were on the way down again between weeks 16-24. Overall, there was not a significant difference in complete abstinence for those that were immunised.

**SMMGP comment:** This study is a clever bit of science that may come as a bit of a surprise to those that were unaware that cocaine addiction is a disease that would respond to a vaccine. As it stands the vaccine is simply a novel method of delivering a longer-acting blocker.

The delivery of the intervention might be elegant but the vaccine was short-lived and not highly effective. The authors have buffed up the results by analysing this sub-group with improved levels but clearly this is not currently an option for normal therapeutic practice.

This study does suggest the method shows promise and it will be an interesting area to watch. The authors set out their aim to develop longer-acting vaccines. Currently the clinical situation is akin to the use of short-term opiate

blockade using naltrexone with a similarly limited evidence base for its use. However, if the future can produce anticocaine vaccines that have long or even permanent effects this could prove to be an intervention that will have far-reaching consequences.

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**Adverse health effects of non-medical cannabis use.** *Hall W, Degenhardt L. Lancet 2009; 373:1384-91*

This review published in the Lancet discusses the current evidence on the adverse health effects of cannabis. Initially, they quote the UN Office on Drugs and Crime who estimate that 166 million adults (3.9% of the world's population) aged 15-64 years used cannabis in 2006.

They then set out on a whistle-stop tour of the consequences of using non-medical cannabis. They give some information on the experience for the user before considering both the acute and chronic effects. The acute effect of anxiety, panic reactions and psychotic symptoms are detailed but the authors also take the time to discuss the concerns around cannabis use and driving. The authors highlight that while cannabis use is probably not as bad as using alcohol and driving there is good epidemiological evidence to support increased risk of accidents.

Some of the chronic physical effects discussed include chronic bronchitis and increased risk of myocardial infarction. Cannabis may be an independent risk factor for lung cancer but teasing this out from tobacco smoking is challenging. A dependence syndrome may exist in as many as one in ten.

Other effects include psychotic symptoms in heavy users, impaired educational attainment in regular adolescent users and subtle cognitive impairment in those who have used daily for more than 10 years. As for cannabis and mental health they state that cannabis use has been associated with increased risk of psychiatric disorders. This association persists in many studies even when confounders have been considered.

**SMMGP comment:** This is a narrative review and the paper should be read with that in mind. However, it is a useful summary of the current known position on the adverse effects of cannabis. While the media in the UK may frequently focus in any debate about cannabis on its legal status it is clear that there are adverse effects across a wide range of areas.

The Advisory Council on the Misuse of Drugs (ACMD) [report on cannabis](#) in 2008 may have come to the recommendation that cannabis should remain Class C (which the government ignored) but they did make 20 other recommendations to address the public health concerns and stated "in the face of widespread use a concerted public health response is needed to drastically reduce its use".

It is undeniable that cannabis is associated with mental illness. Whether this is causal remains a contentious point but many of the studies do seem to show some persistent association even after controlling for confounders. There are also clear physical adverse effects and we shouldn't be distracted from the fact that although the public health issues from cannabis are perhaps mild compared with alcohol, tobacco or heroin they do still exist.

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**A randomised clinical trial of methadone maintenance for prisoners: results at 12 months post release.** *Kinlock TW, Gordon MS, Schwarz RP et al. Journal of Substance Abuse Treatment, 2009; 37:277-285*

This study in the USA took prisoners with a pre-incarceration history of heroin dependence and looked at the impact of prison-initiated methadone. There were 204 male prisoners who were randomly assigned to one of three treatment arms: either counselling only with referral to treatment on release; counselling with transfer to methadone maintenance treatment on release or; counselling and methadone maintenance in prison which was then continued in the community on release.

The counselling involved 12 weekly sessions and a meeting just prior to release. Those that received methadone were started at 5mg and increased by 5mg every 8 days up to a

maximum of 60mg. The doses were so cautious as prisoners were opiate naïve. The primary outcomes measured were numbers of days in treatment in the community, urine results for opioids and urine results for cocaine. The secondary outcomes were self-reported measure of substance use and crime.

The most significant result was the difference in retention in treatment. The counselling only group remained in community treatment for a mean of 23 days. The counselling with transfer group for 91 days and the counselling with methadone in prison group for 166 days. All of these pairwise comparisons were statistically significant. In the urine testing for opioids 65.6% were positive in the counselling group, 48.7% in the counselling and transfer group while 25.0% were positive in the counselling and methadone group. This group also had significantly less positive tests for cocaine at 12 months. The urine testing results had 89 out of 204 participants missing from the analysis.

**SMMGP comment:** The most striking finding was the massively increased engagement that users had with treatment services. A cynical interpretation might be that participants were compelled to attend as they faced an awkward and uncomfortable withdrawal from methadone. While this might be the case earlier in the study it seems rather less likely after a year.

However, there are limitations in the findings. The study didn't show any reduction in criminal activity in the first 12 months and although urine testing showed significant differences the self-reported levels of use did not show significant differences.

One compelling statistic from this study is related to the mortality on release. The disastrously high mortality rate of substance users leaving prison is well documented and is a key driver for the Integrated Drug Treatment Service in the UK. There were 4 deaths out of the 64 participants who received no other intervention other than counselling. The other two arms of the study had no deaths at all. Methadone may not be appropriate for everyone in prison but this study provides further evidence of the potential benefits for some.

Two important new guidance documents related to treating young people who have problems with substance use have been published this month. They were developed by the Department of Health, together with the NTA, working with an expert group:

- **Guidance for the pharmacological management of substance misuse among young people - and**
- **Guidance for the pharmacological management of substance misuse among for management of young people in secure environments**

In brief, key points from the documents include that pharmacological management of substance misuse:

- should be in line with recommendations made in the National Service Framework for Children, Young People and Maternity Services (2004)
- is only one component of addressing substance-related needs
- should be based on a holistic assessment of the child or young person's needs and tailored to those needs (not one-size-fits-all)
- should be delivered alongside specific psycho-social interventions to provide comprehensive care for substance misuse
- and alongside mental health services for those children and young people with mental health needs and
- should be delivered in the context of a clear clinical governance framework.

The documents are available on the DH website [http://www.dh.gov.uk/prod\\_consum\\_dh/groups/dh\\_digitalassets/documents/digitalasset/dh\\_106429.pdf](http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_106429.pdf) and will be further discussed in next month's SMMGP Policy Update.

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