Opioid overdose prevention with intranasal naloxone among people who take methadone. 

This paper reports on the implementation of an ‘overdose education and naloxone distribution’ initiative amongst people who had been taking methadone in the previous 30 days. It was based in Massachusetts over the period 2008 to 2010 and in total 1,533 participants received the intervention. It covered several different settings: 47% were doing an inpatient detoxification; 25% were on a HIV prevention program; and 17% were in methadone maintenance treatment programs.

The intervention consisted of overdose education involving education and techniques in overdose prevention and management. The naloxone kits included pre-filled syringes with mucosal atomisation devices. A questionnaire was completed when participants enrolled. If participants came back for a refill, to get more naloxone, then a further questionnaire was completed. As a result they were able to gather data on reports of 92 overdose rescues from 62 enrollees. The majority of the overdose victims were reported to be known to the participants - friends, partners or family. Only in 10 cases out of the 92 was it reported that the victim was a stranger.

Commentary: The authors concluded that people who take methadone tend to have multiple overdose risk factors and high exposure to witnessed overdose. The report on

the NTA pilot of naloxone was published in 2011 http://www.nta.nhs.uk/uploads/naloxonereport2011.pdf and involved 495 carers who were provided with the training and the naloxone. A total of 18 cases were reported where naloxone was used and two where basic life support was given. All of those survived.

Naloxone would seem like a no-brainer but the medical evidence doesn’t run very deep - it’s good to see better quality evidence along the lines of this American study that highlights the best use of naloxone. There is absolutely no moral justification for denying naloxone - but it has been argued that it is not necessarily what users want. That’s a flaw with the NTA pilot - it was carers involved rather than those at direct risk. For those who are at risk, naloxone may be a constant reminder and an unwanted association with addiction.

This study is valuable as it targets those still in treatment, on methadone, and this may well be a more appropriate group to target for a potentially valuable intervention.

Meta-analysis of naltrexone and acamprosate for treating alcohol use disorders: when are these medications most helpful? Maisel NC, Blodgett JC, Wilbourne PL, Humphreys K, Finney JW. Addiction 2012. Published online ahead of print.

This meta-analysis described its aim as being more nuanced - to examine when these medications might be most useful. Their results showed that acamprosate had a significantly larger effect size than naltrexone on the maintenance of abstinence. However, naltrexone had a large effect size on the reduction of heavy drinking and craving - though it
was noted that few acamprosate studies had data on heavy drinking outcomes so this did limit the power. In terms of issues of timing, the meta-analysis highlighted some issues. Notably, people who had their detoxification before medication administration had better abstinence outcomes compared with placebo. Similarly, for naltrexone a requirement for abstinence before the trial medication was also associated with better outcomes.

**Commentary:** Overall, this study has the potential to change how these medications are used. When acamprosate is compared to naltrexone across all drinking-related outcomes it is superior. However, breaking down the outcomes changed the picture a little. If maintaining abstinence is the priority then this meta-analysis suggests acamprosate to be superior - and the evidence suggests that both medications work better once the individuals are detoxified and abstinent. That said, if the patient’s goal is to reduce heavy drinking days then naltrexone may be superior.


This study delved into the issue of acquisitive crime in relation to drug use. Individuals who were seeking treatment within 94 of the 149 Drug Action Teams (DATs) across England completed a survey. It showed that 40% had committed acquisitive crime in the previous month. When subjected to regression analysis this showed that the acquisitive offending was associated with the use of crack cocaine, poly-drug use, sharing injecting equipment, unsafe sex, overdose risk, higher drug spend, unemployment, reduced mental wellbeing and younger age.

**Commentary:** In many areas it’s known as ‘grafting’ - the day-to-day grind of getting enough money to fund a significant habit. That is certainly a stereotypical view of drug addiction - but as the authors highlight it’s worth turning the numbers around. This study shows that the majority of users (60%) weren’t involved in acquisitive crime. It is not inevitable. The study also showed that although higher drug spend in acquisitive crime was a factor it wasn’t as strong as one might have thought - there is only a 3% increase in the chance of acquisitive crime for each £100 increase in drug spend.


This was, as the title states, a case-control study where they matched (by age and gender) non-injecting controls to a total of 432 individuals who had presented to a community health facility with injecting drug use. These individuals are the ones who make up the Edinburgh Addiction Cohort and they’ve been recruited over a 26-year period dating back to 1980. The follow up happened from October 2005 to November 2007. The cohort itself consisted of 794 participants at the start but only 571 were still alive at the time of follow up and 76% of these (n=432) were interviewed. Controls were recruited from the same primary care facility.

The main exposures and influences considered were: family structure, experience of public care, carer substance use, physical and sexual victimisation, and conduct problems. All of these were explored through personal interview. The researchers tried to ensure that all of the exposures (which were being considered as being potentially
causal) preceded the date of onset of injecting. So, for example, they only considered reports for some areas prior to secondary school age.

The findings showed that compared to two-parent families all other family structures were associated with increased risk of injecting drug use. The greatest risk was associated with public care. Violence, criminality and financial problems in the family were all associated with increased risk. Any carer substance use was also associated. The greatest increased risk was associated with markers of early conduct problems - school exclusion and contact with the criminal justice system. Overall, more than 70% of injecting drug use onset seemed to be attributable to the risk factors identified.

**Commentary:** One might wonder what impact one can have in primary care when it comes to early life influences. It’s worth bearing in mind that general practice is fundamentally about family practice. That is, after all, what the specialism is known as in much of the world. Knowing that these factors are potential risks is no good to us - now we need to see if interventions can make a difference. We can’t simply manufacture stable families but we can support children and we can support carers. It may be that appropriate interventions targeted at disadvantaged children could be effective.


This paper reported on a study that subjected 31 male anabolic-androgenic steroid (AAS) users to a battery of cognitive tests. They recruited 13 non-AAS-using weightlifters as controls. The cognitive tests included: Pattern Recognition Memory, Verbal Recognition Memory, Paired Associates Learning, Choice Reaction Time, and Rapid Visual Information Processing. The study was conducted in Middlesborough in May 2012.

The results showed that long-term AAS users had no significant differences from non-users on response speed, sustained attention, and verbal memory. However, on visuospatial memory AAS users performed significantly worse and there was a negative correlation with lifetime AAS dose. The authors commented on the size of these - on the Pattern Recognition test the AAS users were almost one whole standard deviation worse (p=0.036).

**Commentary:** This study offers new evidence that users of AAS may suffer from a cognitive deficit in the form of a marked visuospatial impairment. The authors put this in the context of recent lab evidence showing that higher doses of testosterone can induce apoptotic effects on neuronal cells. In other words, there is a plausible biomedical mechanism to explain these clinical findings. As ever, inferring a causal relationship needs to be approached cautiously. However, the association held good when factors such as education attainment were adjusted for. In addition, the variation within the AAS group was closely correlated to dose and is suggestive of a dose-response relationship.


This study recruited participants through nine methadone maintenance treatment sites in the USA. They were recruited as part of a smoking cessation study. In total 315 people went through
an initial 45 minute interview where the data for this study were collected. The results showed that among the persons prescribed methadone 19.9% reported sharing medication. Nearly 40% had used medications not prescribed to them. Analgesia, sleepers and sedatives were the most common drugs to be shared. Younger age was a predictor of both sharing and receiving medication, while financial hardship, and recent use of heroin or cocaine were independently associated with a significantly higher chance of receiving medication as well.


This short opinion piece in the New England Journal of Medicine puts together some of the dilemmas for doctors. It opens with the report that in 2010 there are up to 2.4 million opioid abusers in the United States with an increase of 225% from 1992 to 2000. Pain management is, of course, the main reason cited for ongoing high levels of opioid prescribing. The article discusses some of the cultural issues around pain. The belief amongst some patients and doctors that ‘all suffering is avoidable’; and untreated pain will result in a ‘psychic scar’ which will manifest itself as post-traumatic stress or other disorders. This leaves many doctors concerned that if they withhold opioids they are not only withholding relief but are also causing harm. In the USA, it is compulsory (since 2001) for physicians to complete a mandatory medical education course on pain treatment; no such course exists for addiction. The author comments that: ‘currently it is faster and pays better to diagnose pain and prescribe an opioid than to diagnose and treat addiction’.

**Commentary:** There is real concern about the extent to which we are going to run into serious numbers of people addicted to opioids. However, looking at UK general practice I’m not convinced we will develop the ‘epidemic’ that has been described in North America - one factor in our favour is that we don’t have a healthcare system that unintentionally promotes it. Sharing of medication could simply reflect problems with accessing healthcare.

In the USA, where this study was based, there are obviously different issues regarding insurance and medical costs that could contribute. However, we shouldn’t kid ourselves - the NHS may be free to all but there are still significant difficulties getting individuals in treatment to engage with healthcare.

The authors point out that the estimated rates of ‘ever having shared prescription medication’ in the general population have ranged from 17-23% and the rates of ever having received medication from 23-27%. In the wider population, the most common medications were allergy medications, antibiotics and pain medications.

It was also noted that college students had higher rates than this - with stimulants and pain medications most frequently shared. This is important - there is a risk that those in methadone maintenance are assumed to be blagging or abusing medications routinely.

The data in this study suggest that rates are broadly comparable to the general population. There does look to be some differences in the types of medications - sleepers and sedatives seem to feature more.

This British study wanted to assess how effective tailored cessation advice reports would be when compared to a control group who received a generic self-help booklet. The researchers mailed questionnaires to 58,660 current cigarette smokers throughout the UK. A total of 6,911 completed the questionnaire and 6,697 (11.4%) were included in the analysis. The intervention group received the standard self-help booklet but also got a computer-tailored advice report based on the information in the baseline questionnaire. This took into consideration factors such as educational level, daily reading, intention and motivation to quit, dependence, and a number of other factors.

The primary outcome was self-reported prolonged abstinence of at least three months at the six-month follow up. The results showed that quit rates were slightly better in the intervention group (3.2% vs 2.7%) - but they didn’t reach statistical significance. It was shown that a statistically significant higher proportion of intervention group participants made a quit attempt during the follow up period (32.3% vs 29.6%, p=0.026).


This systematic review looked at the acute effects of short bouts of physical activity on strength of desire and desire to smoke using individual participant data. The reviewers did a literature search and then contacted the authors of the individual studies to get the raw individual patient data.

The meta-analysis assessing the effect of physical activity on strength of desire to smoke showed an average standardised mean difference/effect size of −1.91. A similar analysis on the effect of physical activity on the desire to smoke showed an average standardised mean difference/effect size of −2.03. These were both highly significant with p-values of <0.001. Further analyses also showed significant craving reduction. The authors pointed out that despite a high degree of heterogeneity between studies all the effect sizes of all primary studies were in the same direction.

Commentary: These two papers from Addiction highlight a couple of potential interventions for smoking. The power calculation in the first study had been designed to detect an odds ratio of 1.42 or better. The actual difference (if true) shown in this study was an odds ration of 1.2. The authors point out that if that is the true effect then a sample of 30,000 would have been needed to achieve statistical significance. One would expect the difference in a study like this to be modest - there may still be merit in tailored advice and we shouldn’t get too hung up on the statistical significance (or lack of it) in this study.

The second study is impressive given it has gone back to the original study data and collated it all. The evidence for the effectiveness of short bouts of physical activity in reducing cravings is strong with some large effects. However, we need to put all this into some kind of clinical context. The interventions in the studies varied and included: moderate-intensity walking, running or moderate-intensity cycling. Perhaps the best we can do is to translate

This paper reported on the Hepatitis C Assessment and Testing Project (HepCAT) based around three primary care clinics in the Bronx, New York. They assessed two community-based interventions that had been designed to increase HCV testing. The two interventions had some common components.

Both included: educational sessions for primary care providers; regular communication between the research team and the clinical leadership; and what were called ‘environmental reminders’ which includes HepCAT badges, pocket cards and posters.

As well as this the project team also visited each clinic twice per week to put stickers on notes, encourage adherence to protocols and get feedback. The first intervention prompted clinicians to test if risk factors were present; the second one prompted to test based on birthdate alone (1945-1964).

Both of the interventions showed an increase in the proportion of patients tested for HCV. This rose from 6% at baseline to 13.1% in the risk-based screener period and 9.9% during the birth cohort period. (Both highly significant p<0.001.)


This report was also based on the HepCAT project but reported in more detail on the risk-based screening elements. It highlighted that among screened patients, 27.8% of them were found to have at least one risk factor. They managed to test 55% of those with any risk factors. There were seven factors that accounted for all the HCV infections identified: injecting drug use, intranasal drug use, elevated alanine aminotransferase, transfusions before 1992, ≥20 lifetime sex partners, maternal HCV, and existing liver disease.

Commentary: The project team clearly invested a great deal of time and resources into this study. And, they did show some improvement in testing. The addition of intranasal drug use as a risk factor is unusual in a screening tool. The study found that it wasn’t independently associated with hepatitis C infection, but it did identify almost 15% of cases. One difficulty with the study is that we can’t be sure if the changes will be sustained.

The problem with this intervention is how generalisable it all is - how do we improve things across the whole of primary care, in every single practice in the country? A risk-based screener sitting on every practice computer in the whole of the NHS? It would go a long way to identifying all those untreated HCV infections. Not all the way, as this study showed - they still only tested 55% of those with risk factors. There remains a reluctance to address HCV that we have to keep pushing against.