



Welcome to the latest SMMGP Clinical Update (to June 2015). Highlights include:

- Fatal poisoning by methadone or buprenorphine in England and Wales.
- Femoral ultrasonography for promoting cessation of groin-injecting behaviour.
- Injection into the femoral vein among people who inject drugs in urban areas of England.
- Women's injection drug practices in their own words: a qualitative study.
- Long-term self-treatment with methadone or buprenorphine as a response to barriers to opioid substitution treatment: the case of Sweden
- Diversion of opioid maintenance treatment medications and predictors for diversion among Finnish maintenance treatment patients.
- Adulteration, adverse effects and drug use transitions during the 2010/2011 United Kingdom heroin shortage.
- Methadone continuation versus forced withdrawal on incarceration in a combined US prison and jail
- Designer drugs 2015: assessment and management.

The relative risk of fatal poisoning by methadone or buprenorphine within the wider population of England and Wales. *Marteau D, Macdonald R, Patel K. BMJ Open 2015;5:e007629.*

This study has used the drug-related mortality data available from the Office for National Statistics and data on the number of prescriptions of methadone and buprenorphine compounds available from the NHS for the period 2007 to 2012. These have then been combined and presented as the overdose rate per 1000 prescriptions allowing the relative risk ratio of methadone to buprenorphine to be determined.

Over the period 2007 to 2012 there were 2366 deaths related to methadone and 52 deaths related to buprenorphine. In the same period there were over 17 million methadone prescriptions and just over 2.6 million buprenorphine prescriptions. In the authors' outcome measure this gives an overall rate of 0.137 deaths per 1000 prescriptions of methadone and 0.022 deaths per 1000 prescriptions of buprenorphine-containing compounds. This gives a relative risk of 6.23 (95% CI 4.79 to 8.10).

Commentary: This relatively simple study uses two sources of data, available in public databases, but it needs to be unpicked with care as it poses some complex questions. It's certainly no revelation that methadone is a more dangerous compound than buprenorphine - expressed, if nothing else, in the different legal class and schedule in which they sit. I'm not convinced we've got nearly enough data in this paper alone to make convincing suggestions on policy changes - there are just too many questions left unanswered. Firstly, the nature of methadone- or buprenorphine-related deaths is a very broad church and association does not necessarily imply causation in all cases and it's also an area where reporting bias may feature. The authors suggest the "treatment sector needs to reappraise its relationship with methadone" which in effect comes down to a couple of options: prescribe more buprenorphine or increase supervision of methadone.

Our knowledge of the people dying is limited and not available in this dataset. Previous studies in the UK have suggested that only 36% of deaths associated with methadone involve people who were prescribed it at the time. If it's not people with addictions then that's a very different public health imperative and quite possibly one where effective supervision does become very important. However, if the people who died had addictions but weren't in treatment, which on the face of it seems more likely, then that screams out a failure in engagement - one in which onerous supervision policies may well exacerbate the problem. And it is possible that those who were in treatment were inadequately dosed and self-treating with street methadone. It's notable that the average dose of methadone across the six years was 46.6mg per day compared with a mean average dose for buprenorphine preparations of 10.4mg per day. All of these lead to very different scenarios and one where it won't be easy to come up with blanket assertions on policy.

Other papers covered in this Clinical Update also highlight the complexities of diversion and illicit use. We need treatment services that keep people in treatment - something we know methadone does well in comparison to buprenorphine. Clinical experience suggests that the most complex patients, the ones most likely to overdose, are more challenging to manage with buprenorphine. In addition, they may move in and out of prison - where buprenorphine is less likely to be available in IDTS programmes and disgraceful prison policies of forcible reductions will lead to disengagement with services creating a market for illicit methadone and buprenorphine. So the complexities build up. Clinically, this is an important reminder of the risks associated with methadone, if you needed it, but I'd pause before we make wholesale changes to practice on the basis of this paper alone.

Evaluation of femoral ultrasonography as a tool for promoting cessation of groin-injecting behaviour. *Senbanjo R, Strang J. Eur Addict Res 2015, Apr 21;21(4):204-10.*

In this case-control study there was a total of 348 participants spread across 11 clinics in the south-east of England who were receiving opiate substitution therapy (OST). The 'cases' were the 174 consecutive attendees at an ultrasound clinic and they were recruited from July 2006 to November 2011. These were matched to 174 controls on the basis of gender, age, OST medication, time in treatment and they were categorised as 'persistent groin injectors' or 'former groin injectors'. Those who were given an ultrasound were screened for any arterial or venous damage and changes in blood flow at the groin injecting site. Each person was then given feedback, described as: "personalised descriptive and visual feedback on that the images portrayed". Follow up data were then collected.

The results showed that there were no significant differences between cases and controls in the prevalence of groin-injecting behaviour for the 12-months before baseline or at baseline. After baseline in weeks 0 to 4, groin-injecting prevalence went from 56.9% to 36.2% in the cases. Controls had no change in behaviour (56.9% to 56.3%). Overall, over a period of 12 months after scanning groin-injecting did drop off in both groups - the rate of decline is similar in cases and controls. However, the sharp initial drop in groin-injecting in cases ensured that, overall, the reduction in prevalence of groin-injecting persisted over a 12-month period.

Going into the groin: Injection into the femoral vein among people who inject drugs in three urban areas of England. *Hope VD, Scott J, Cullen KJ, Parry JV, Ncube F, Hickman M. Drug Alcohol Depend 2015, Apr 9*

Participants were recruited into a cross-sectional survey between 2006 and 2009 in Bristol, Leeds and Birmingham. They all had an interview and dried blood spot sampling. They used respondent driven sampling (RDS) and that involves starting with some initial recruits, 'seeds', who then recruit through their social networks.

In total 855 people were recruited across the three sites and 53% (n=450) reported having *ever* injected into their groin. There was no association with age or gender but there was an association with injecting for longer - a mean of 11.4 years compared to a mean of 9.7 years in those who hadn't groin injected. The mean period of time between first injection and first groin injection was 6.5 years. It was found that 10% used groin injecting at the start of their injecting history.

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Current use: in the past month 41% (348 out of 855) reported having used their groin. In the multivariate analysis the factors associated with recent groin injecting included: those people who always swabbed injection sites; those saving filters for re-use; those currently on opiate substitution therapy. It was less common amongst people using only two body areas for injection (compared to those using one or three or more sites); and it was less common in those people who got their needles and syringes from other people.

The study, although not qualitative, did capture a little bit of context and the reasons why people groin injected. These included: *“Can’t get a vein elsewhere”* - 68%; *“It is discreet”* - 18%; *“It was how I was shown to inject”* in 13% of women compared to 5.7% in men; and *“It is quicker”* - 18% in the over 30s where it was more common.

Commentary: The Hope et al study emphasises just how common groin injecting is - with over half having ever groin injected and just over 40% groin injecting in the past month. There’s no doubt about the potential harms and I’ve commented before on the much neglected topic of chronic venous insufficiency and leg ulcers in injecting drug users. Groin injecting often reflects, in a large number of cases, though not exclusively, a long career with injecting drug use. That means there are no veins elsewhere and that also leads to difficult phlebotomy with all the problems of health care avoidance and stigma that can bring.

So what can we actually do? That’s where the Senbanjo and Strang paper comes in - could femoral USS be a valuable intervention? Ignoring the methodological issues for one moment the overall message from this study seems initially to be fairly encouraging - if we send people for USS of the femoral veins and then give them feedback on the basis of this it seems to have a positive effect on reducing groin injecting. If we accept that then we might ask: do they switch sites and inject elsewhere? Apparently not - these data in graphical form suggest that the injections into other sites don’t increase in compensation.

However, we need to be careful as this study is framed to suggest that femoral USS is an effective intervention - but using a case-control study to test an intervention is a very long way indeed from ideal. The best we can hope for is to highlight associations, yet at one point the authors state that this gives an NNT of 3 to stop one person groin-injecting within 4 weeks. I’m not sure we can legitimately generate NNTs from this type of study and it underscores the methodological confusion here. Also worryingly for the overall conclusion, one I would dearly like to be true, is that the study design could lead, as acknowledged by the author, to considerable selection bias. It seems that all groin injectors were offered the chance to attend the ultrasound clinic and they then volunteered

and attended - which strongly suggests considerable motivation in itself. They've then been matched with controls who didn't attend which adds up to a big difference between the two groups from the very start. I'd be delighted if this proves to be an effective intervention - what we sorely need now is a randomised controlled trial.

Women's injection drug practices in their own words: a qualitative study. *Tuchman E. Harm Reduct J 2015;12(1):6.*

They recruited 26 women who inject drugs in New York in late 2012 into 2013. The sampling was very much purposive, the women weren't necessarily in treatment, and injecting drug use was confirmed at recruitment. The average duration of injecting drug use was 18.2 years. They were interviewed in-depth using a topic guide. The research used a grounded theory approach with the aim to understand the concerns, actions and behaviours of the women.

The results were presented in three main themes: *Transitioning from non-injection to injection drug use*. The reasons for moving into injecting were complex. Non-injectors were given advice by their peers on the benefits of moving into injecting e.g. the need for less drugs so less expense and an improved high. Many thought it would be a way to get control of their habit. The researchers found it was common for current women injectors to encourage their peers to inject. For others it was more about curiosity and gratification - and it was noted that women weren't necessarily passive in this. *Patterns and variations of initiation into injecting*. Usually the first time of injection it was prepared and given by someone else. In more than half the time it was another woman - these women acting as "instructors". *Shifting towards autonomy or reliance on other*. Most women were self-injectors and they identified within themselves a strong independence and autonomy. Those who needed help to inject described the experience of being "second on the needle" and the risks they ran from being injected by someone who was intoxicated, as well as the obvious infection risks of HIV and hepatitis C.

Commentary: The received wisdom about women and injecting is that it is something that they often don't have control over, they are passive partners being injected by males, putting them at higher risk of BBVs and other injecting related complications. As a paper using grounded theory approach it is more about generating hypotheses - not testing existing ones - and this certainly raises some interesting points that could illuminate consultations with women who inject. Perhaps one of the most pragmatic suggestions is the importance of female peers and the authors suggest an area for services should consider: "Development of peer-driven experiential interventions with

strong female representation with the aim to dissuade woman from transitioning to IDU and increase their personal capability to self-injection is needed". Absolutely.

Long-term self-treatment with methadone or buprenorphine as a response to barriers to opioid substitution treatment: the case of Sweden. *Richert T, Johnson B. Harm Reduct J 2015;12(1):1.*

This qualitative study involved interviews with 27 opioid users who had self-treated with methadone or buprenorphine for at least three months. The self-treatment period varied from 5 months up to 7 years. Three major themes explaining why people self-treated emerged: *Difficulties in gaining access to opiate substitution treatment (OST)*. Many didn't meet the criteria set out in Sweden - which included a requirement to have a documented history of at least one years' duration. *Difficulties remaining in OST*. Again, this doesn't seem to be an easy thing to do in Sweden with several reasons that allow for involuntary discharge including any ongoing use of illicit drugs. One user, a 53-year-old woman, was discharged for using benzodiazepines, and it took a year to get back into the programme. During that period she used illicit methadone to self-treat and she stated the illicit methadone "had been her salvation". *Ambivalence about or reluctance to enter OST*. This was often related to the label of being an addict and being stigmatised. There were also concerns expressed about the control measures and they found self treatment an escape from this. People who had been self-treating also expressed challenges with this approach: there was a high cost with getting illicit medication and access to it was frequently a problem.

Diversion of opioid maintenance treatment medications and predictors for diversion among Finnish maintenance treatment patients. *Launonen E, Alho H, Kotovirta E, Wallace I, Simojoki K. Int J Drug Policy 2015, Apr 1.*

This paper reports on a cross-sectional study that took all patients in Finland on opiate substitution therapy (OST) as their sampling frame. They used an anonymous questionnaire and got a 60% response rate. Out of the 1508 people who responded they found that 7% admitted to selling their medication and 12% had given it away. The factors that were associated with diversion were: being on buprenorphine-naloxone, low buprenorphine-naloxone dose (<9.0mg/day), IV use within the last six months, and longer time on OST. There was no association with age or unsupervised prescribing of buprenorphine-naloxone.

Commentary: This Scandinavian pair of studies offers a more nuanced perspective on the topic of diversion. Only buprenorphine-naloxone and methadone are available in Finland and it's interesting to note how, despite its anti-misuse spin, buprenorphine-naloxone is still being abused. A curious finding from the study is that unsupervised treatment didn't result in any more diversion. One of the notable findings is that there was more diversion in those on lower doses - perhaps we should be particularly careful about ensuring adequate treatment doses.

What the Finnish study doesn't get into is what people do with that diverted medication and the Swedish study offers a particularly novel view and one which has good face validity for those working in services. We all meet people who have managed to get hold of some illicit methadone or have a few buprenorphine tablets tucked away to tide them over some missed pick ups or a gap in treatment. And, of course, we should be careful about attributing misuse of medication to people with addictions. It seems to be part of normal human behaviour: who takes all their BP medications exactly as prescribed and how many people don't finish courses of antibiotics or start them from packets left in the cupboard? There has been a rise in methadone-related deaths associated with increased diversion in Sweden. However, this paper presents the case that part of the problem in Sweden is a treatment system that is unreasonable and stigmatising has opened up a self-treatment 'market'.

"It's Russian roulette": Adulteration, adverse effects and drug use transitions during the 2010/2011 United Kingdom heroin shortage. *Harris M, Forseth K, Rhodes T. Int J Drug Policy 2015, Jan;26(1):51-8.*

This qualitative study used a sample of 37 people who injected drugs in 2010-11. The average age was 40 and they had an average of 20 years of injecting. The data collected were longitudinal life histories and narrative interviews. The participants were recruited through low threshold opiate substitution services.

Despite the reductions in purity and worsening adulteration the majority of the participants were able to get hold of heroin and continued injecting. It was also common to move toward poly-drug use during the heroin shortage and this increased the risk of overdose as well as other drug-related harms (such as severe damage to veins and soft tissue infections). Participants came up with their own harm reduction strategies to manage these risks - though not necessarily successfully. One 51-year-old woman stated:

I don't usually sell my methadone, I take it all, but I know a lot of people that have never taken it and have always sold it and nobody has anything to sell at the moment because everybody's taking it.

Commentary: So what happens when there isn't enough heroin on the streets? Law enforcement agencies would doubtless proclaim this as a triumph and commonsense might dictate that it can't be anything but good. This paper takes a look at the impact on the lives of London-based heroin users. Ultimately, it didn't stop people using and although they had a variety of strategies to cope there were definitely increased harms. There's an interesting dynamic here across several of the papers in this Clinical Update: the interplay between illicit and prescribed drug availability, its diversion, and its use and abuse are complex and inter-dependent. This paper highlights the need for clinicians and services to be responsive to changes in supply in local markets - we need to be flexible enough to be able to step up care provision when there is a shortage of heroin on the street.

Methadone continuation versus forced withdrawal on incarceration in a combined US prison and jail: a randomised, open-label trial. Rich JD, McKenzie M, Larney S, Wong JB, Tran L, Clarke J, et al. *The Lancet*. Published Online 29 May 2015.

This study, based in the United States, randomised inmates who were already on methadone in the community to either continuation of their methadone treatment or to usual care - which in the US happens to be a forced tapered withdrawal. The prisoners that were included were serving sentences varying from one week to no longer than six months.

The outcome measures used were: engagement with methadone maintenance clinics after release and time to engagement with methadone maintenance treatment. This was all assessed at one month after release. In total there were 114 people in the 'continued-methadone' group and 109 in the 'forced withdrawal' group. Those in the continued-methadone group were more than twice as likely to return to a community methadone clinic (hazard ratio 2.04, 95% CI 1.48-2.08). There was no difference in serious adverse events between the two groups.

Commentary: I do wonder if this study could run into some difficulties in getting past a research ethics committee in the UK given the forced withdrawal nature of one group. Overall, the conclusions are straightforward: continuing with methadone could lead to better treatment engagement after release. An immoral approach to prisoner health in relation to drug misuse is a global problem. A recent Cochrane highlighted the importance of pharmacological interventions in prisoners with addictions and the WHO recommends that methadone or buprenorphine are provided for people dependent on opioids.

The principle of equivalence between prison and community health care is one enshrined in the NHS, and, for that matter in international law - yet, in many prisons in the UK, people are still struggling to avoid forcible reductions or they don't have the option of either methadone or buprenorphine.

Designer drugs 2015: assessment and management. *Weaver MF, Hopper JA, Gunderson EW. Addict Sci Clin Pract 2015;10(1):8.*

This paper offers an overview of the clinical management of several of the new psychoactive drugs. These include: substituted cathinones such as mephedrone ("bath salts"); synthetic cannabinoids such as Spice; and synthetic hallucinogens such as N-bomb. For each of them it gives a brief paragraph of the pharmacology, the acute clinical effects, adverse psychiatric effects, and adverse physiologic effects.

Commentary: I have to admit to frequent sensations of being somewhat overwhelmed by the whole novel psychoactive drugs scene. They don't present too frequently into community drug team setting where the staple diet remains heroin and crack. That said, those working in the local young persons' service have become quite familiar with several of these. We have had particular problems with synthetic cannabinoids in Blackpool that led to a local prohibition order banning their sale. This paper is a useful overview of the three main categories - the synthetic cathinones (which have a shared biochemical heritage with khat); the cannabinoids; and the synthetic hallucinogens (which I freely admit I haven't come across at all yet). I think one of the key factors is not to get too bogged down in the myriad of brands and try to get a feel for the class of compound. If getting up to speed on the new designer drugs is on your Personal Development Plan for this year then look no further - this paper is accessible in a couple of senses: in terms of its content and, importantly, as an open access journal there is no paywall to negotiate.