▶ BAP updated guidelines: evidence-based guidelines for the pharmacological management of substance abuse, harmful use, addiction and comorbidity: recommendations from BAP.

Lingford-Hughes A.R., Welch S., Peters L. et al.

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Practitioner-friendly review from the British Association for Psychopharmacology on drug-based treatments for substance dependence offer authoritative, evidence-based guidance to prescribers and others; they also demonstrate the limitations of trying to cure over-use of drugs with drugs.

SUMMARY These guidelines running to 54 pages are freely available and intended to be read by practitioners who are not necessarily experts in drug-based treatment of substance dependence. Rather than repeating the already summarised and practitioner-friendly contents, this account describes the intention and remit of the guidelines and then in the commentary picks up particularly interesting issues.

The first guidelines from the British Association for Psychopharmacology on drug-based treatments for substance misuse, addiction and comorbidity were published in 2004. This substantial revision retains a focus on providing helpful and pragmatic guidance for clinicians such as psychiatrists and GPs involved in prescribing to people with substance abuse, harmful use or addiction, alone or with psychiatric comorbidity. They cover the management of problems related to the use of alcohol, nicotine, opioids, benzodiazepines, stimulants, cannabis, 'club drugs' and the 'polydrug' use of several drugs together, and focus on dependence rather than 'harmful use' or 'abuse'. Sections are devoted to mentally ill and personality-disordered patients, children and young adults, the elderly, and treatment during pregnancy.

The guidelines are not intended to be a manual on how to safely prescribe the pharmacotherapies they assess, for which readers are referred to sources such as the British National Formulary and the Summaries of Product Characteristics provided by the Electronic Medicines Compendium, as well as expert colleagues.

Treatment goals should be set and agreed between the patient and prescriber. In dependence, medications may be used to:
• ameliorate withdrawal syndromes;
• prevent relapse and maintain abstinence;
• reduce harms associated with illicit drug use by prescribing substitute drugs, such as in methadone maintenance; and
• prevent complications of substance use, such as the use of thiamine to prevent Wernicke's encephalopathy and Korsakoff's syndrome in alcohol-dependent patients.

FINDINGS COMMENTARY This commentary picks up on a few interesting and/or possibly contestable comments in the review. It should not be read as a criticism of the review as a whole, which provides a valuable, thoughtful and comprehensive summary of the evidence.

Limits of pharmacotherapy

Though about the uses of drugs to treat dependence on other (or the same) drugs, the guidelines are also a testament to the limitations of medications and the primacy of psychosocial influences.

For some drugs of dependence like alcohol, opiates, and tobacco (not covered in this account), the guidelines see a proven and valuable role for medications not just as an aid to withdrawal, but as a treatment to promote and sustain the overcoming of dependence. That leaves swathes of the illicit and/or recreational arsenal of drugs entirely or largely outside the ambit of drug-based treatments, and their dependent users reliant on treatment based on human interaction in the form of counselling and psychosocial therapies.

There is, say the guidelines, "no convincing evidence supporting the use of pharmacological treatment for amphetamine and cocaine abuse and dependence," and "no clear evidence base for pharmacological treatment of cannabis withdrawal and no pharmacological treatment can be recommended." Also noted is an "absence of any evidence for a role for pharmacotherapy in treating ecstasy dependence or withdrawal." For non-medical users of benzodiazepines, "Maintenance prescribing in illicit drug users cannot be recommended."

Even for alcohol, medications are in practice a minor component of treatment which usually makes only a small extra contribution to psychosocial approaches. Best established are approaches to heroin and other forms of opioid dependence which rather than helping remove the need for these types of drugs, replace one type with another which is safer and more likely to form the basis for a productive life free from crime and the exigencies of reliance on an illicitly obtained drug.

Such limitations can be seen as an indirect commentary on the 'brain disease' vision of substance dependence with its accompanying expectation that eventually pharmacological or other physical therapies will prove a solution. At best this has yet to happen despite decades of trying, at worst, it is chimera which absorbs resources but can never deliver the anticipated benefits.

Drug treatment the norm for alcohol dependence?

By far the biggest potential application (and from the manufacturer's point of view, market) for medications in drug and alcohol dependence is for the treatment of dependent drinking. Here the guidelines go a step further than the NICE recommendations they cite, which advise prescribers to "consider" prescribing acamprosate or oral naltrexone for moderate and severe alcohol dependence, and for less or non-dependent problem drinkers who have not done well with psychosocial approaches alone or who ask for medications.

Endorsing this recommendation, the featured guidelines interpret them as saying that "pharmacotherapy should be the default position" in these circumstances, suggesting the drugs should be prescribed unless there is a reason not to. The NICE formulation instead implies that *considering* prescribing should be the default position, not prescribing itself. If implemented, the huge difference BAP's formula would make can be appreciated from the fact that in England only about 1 in 10 specialist alcohol treatments involve

medications. In practice, these seem to be used not as frontline approaches, but as a minor fallback option, or one reserved for the "more complex patients" beyond which the BAP guidelines wanted to extend their use.

Not all science when it comes to methadone; role of psychosocial therapy

Interestingly, these highly science-based guidelines recognise that in respect of methadone maintenance, "Opinions and practice are strongly influenced by political/social context." In their recommendations on maintenance prescribing for opiate dependence, they drew heavily on previous systematic reviews, including those conducted for the Cochrane collaboration under its rigorous rules for what counts as evidence and how it should be assessed. These rather mechanistic procedures have, however, their limitations. Those seem to have carried through to the guidelines' conclusion that "There is no clear evidence of enhancement of agonist maintenance treatments by specific psychosocial treatments."

From the data presented in the cited Cochrane review, this is the inevitable conclusion, but a more nuanced analysis of relevant studies (see our commentary on the review) might have softened this judgement.

Most studies on which it was based derived from the USA, where generally patients are required to attend the clinic almost daily to take their methadone – already more potentially therapeutic staff contact than many British patients experience, contact which extra therapy might find hard to improve on. In the studies usually patients volunteered to be randomly allocated to therapy or not. If they did so because they did not care much either way, it perhaps comes as no surprise that on average they did as well with therapy as without. Commonly studies excluded psychologically unstable patients, the very ones whom some US studies suggest might have benefited from psychotherapy – or at least, from the extra quality and quantity of therapeutic contact entailed in therapy.

No recommendation on long-acting naltrexone

Taken daily by mouth, the review saw a role for the opiate-blocking drug naltrexone among "opioid-dependent people who are highly motivated to remain abstinent", but declined to make any recommendations for or against naltrexone implants and injections which block the effects of heroin for up to several months. Instead the reviewers simply posed the question, "What is the role for injectable or depot naltrexone?"

Yet there seem arguments for suggesting (resources allowing) that implants and injections would have a more extended role than the oral form of the drug. Both products avoid the need to take medication daily, in theory overcoming the main shortcoming of oral naltrexone – that patients usually stop taking the tablets and resume heroin use. Official US guidelines see numerous roles for the injections among patients at risk of resuming opioid use immediately after detoxification, including patients who have not done well on or don't want methadone or allied treatments, or who have tried them and done well and still want the support of medication, but from a drug which does not have opiate-type effects.

At Findings we noted that among caseloads prepared to accept this treatment, long-acting naltrexone seems a major advance on oral naltrexone in safety because it protects from overdose during the life of the injection or implant and has not been associated with the high risk of overdose after cessation seen with the oral drug. It has also proved more effective then the oral form in curbing illicit opiate use. We saw the clearest candidates for the treatment as patients who are motivated (perhaps due to employment or other pressures) to return to a life without opiate-type drugs including prescribed substitutes, who have the resources, stability and support to sustain this, are unlikely simply to use other drugs instead, but who when free to experience heroin and allied drugs, cannot resist using them. Other candidates might include those unwilling or unable to accept daily supervised consumption if this is a requirement of being prescribed substitute medications.

Though the depot injection has been approved in the USA and Russia, neither product is approved for medical use in the UK.

With money at stake for pharmaceutical companies and others, it is important that pharmacotherapy guidelines have been formulated through a process demonstrably free from commercial and other non-scientific influences. The featured guidelines do not itemise possible conflicts of interest of the authors or expert reviewers, but say, "Declaration of interests of the participants are held by the BAP office." A consensus meeting which initiated the revision of the guidelines was part-funded by "charging participating pharmaceutical companies, some of whom sent representatives ... and had the opportunity to comment on these guidelines."

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