The role of opiate substitute prescribing

Scottish drugs Forum

September 2011

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Opiate substitute treatment

- Rationale for treatment
- Range of pharmacological agents and treatments available
- Evidence for benefits
- Limitations of interventions
- Political and public opinion affecting treatment policy

Substitute treatment (OST) for chronic opiate dependency

- Methadone Maintenance
- Buprenorphine maintenance
- Codeine derivatives (Dihydrocodeine)
- Hydromorphone (dextromoramide, Dilaudid)
- Heroin (Diamorphine)
- Morphine
- Detoxification with above agents

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Aids explosion forecast in Glasgow

By STUART TROTTER
Political Correspondent

GLASGOW is on the precipice of a great Aids disaster, an MP claimed yesterday as the Government announced new measures, including a £20m public information campaign, during a Commons debate on the disease.

Liberal Health spokesman Archy Kirkwood said there were 2000 Aids carriers from Edinburgh now travelling to Glasgow to get their heroin.

Although there were only 154 identified carriers in the city itself there was an estimated drug community of between 8000 and 12,000 to whom the disease could be spread by the sharing of infected needles, he said.

With Ministers still undecided

registered addicts and condoms to homosexuals and others at risk, Mr Kirkwood appealed to the Scottish Office to mount a pilot scheme in Glasgow to assess the effectiveness of such measures.

Health Minister Tony Newton praised Scottish MPs for their "impressive contributions" to a grave debate in which Ministers warned that Aids could spread widely among heterosexuals as well as homosexuals if it was not controlled.

Mr Kirkwood said after the debate that he believed that if the Government did not act in Glasgow within the next two or three months the chance of controlling the disease would have gone.

Mr Newton said the public should not treat Aids carriers like

Editorial Comment: Page 6

Government's clear medical advice is that you cannot get the Aids virus from normal social contact with someone who is infected.

"You can't get it from shaking hands. Nor is there any risk of anybody being infected through kissing. There is no danger in sharing cups and cutlery nor can you catch it from public baths and toilets."

Tory MP Sir Nicholas Bonsor protested that it was "not safe" for the Minister to make these comments "since the state of medical knowledge is not conclusive." But Mr Newton said his statement was "based on clear-cut medical advice from

Opening the debate Mr Norman Fowler, Health and Social Services Secretary, said a special health authority would be set up from April 1 to deal exclusively with Aids.

The Scottish part of this authority wil be the Scottish Health Education Group, a body to which there is no English equivalent, which alreay reports directly to Ministers.

A special Scottish working party of officials and health board representatives will be set up to work out the resources each health board is likley to need to treat Aids victims and report, if possible, by the end of the year

that extra funds will be made available.

The national leaflet campaign will begin in the new year and in addition a special booklet advising employers on how to treat Aids-carrying employees will be launched on Monday. Mr Newton emphasised there should be no witch-hunt against carriers and no sacking them from their jobs.

In Scotland two further leaflets will be distributed in the spring through doctor's surgeries, pharmacies, clinics, and other health centres. One will be a general information leaflet, the other will be entitled "Safe sex for heterosexuals."

As earlier reported in the Glasgow Herald the Government

experts on the disease early next year.

Mr Fowler warned MPs: "The virus is spreading. Unless we all act to protect ourselves it will not be long before we find the numbers infected rising as high here as in other countries."

He said the broadcasting organisations had agreed to transmit special Aids public health advertisements. The first priority was public education and this would be tackled on a large scale.

The language used would have to be explicit and would offend some people. "I regret that, but I have to say that I believe the greatest danger is that the message does not get over."

At present the infection was

relatively small groups but there was a danger it would "spread widely into the heterosexual pupulation."

Advertising would seek to get over the following messages, he said. On sexual habits — stick to one partner; if you don't, use a condom. For drug users — don't inject drugs, but if you can't stop, don't share equipment.

He promised Dr Gavin Strang, Labour MP for Edinburgh East, that a Government decision on providing free needles and syringes to registered drug addicts would be reached "relatively quickly."

Mr Fowler said there were practical difficulties about screening foreign visitors for Aids. Dr Strang suggested that

children should be screened. Mr Anna McCurley, Tory MP fo Renfrew West and Inverclyde suggested screening of doctors dentists and health workers, an those handling food.

Mr Roger Sims, Tory MP fo Chiselhirst, said patients dying o Aids should be asked to identify their contacts, and convicte rapists who might commit the crime again should be screened.

Mr Patrick Cormack, Tory MP for North Staffordshire, suggested that condoms should carry a Government health warning "sex can damage your health."

Mr Michael Meacher, Shadow Social Services Secretary, said the minimum adequate budget fo preventive measures against the

HOW MANY PEOPLE WILL GET IT FOR CHRISTMAS?

Every day, more and more people are catching the AIDS virus.

Up until now, it's been confined mainly to small [illegible] people. But it's spreading all the time

before they start looking ill. And during all this time they can still pass the virus on to you.

So in the future, sleeping around is quite simply risking your life. It's best to have sex with as few people

Deadly warning . . . one of the posters

£20m war on AIDS

THE government yesterday stepped up the fight against AIDS into a £20 million crusade.

Health Secretary Norman Fower announced that a special health education authority will be set up in April next year to co-ordinate a nationwide campaign against the disease.

And he revealed during a special Commons debate that £20 million will be available for a public information campaign — four times the original suggested figure.

The advertising campaign will spell out in explicit language the threat posed by AIDS, which has already killed 284 people in Britain.

The 12-month campaign starts in newspapers on Sunday and will be stepped up over Christmas.

There will also be posters in 1500 sites around the country, a youth campaign using magazines, radio and cinema and a New Year leaflet drop to 23 million households accompanied by TV and radio advertising.

FOWLER'S CRUSADE: SEE PAGES 4 AND 5

opiate substitute treatment: prevention of infectious diseases

- Estimates indicate that around 200,000 people in England are chronically infected with hepatitis C – yet only 38,000 diagnoses have been reported. *Hepatitis C – Action plan for England 2003*
- Between 1982 and 1986 around 3000 people were infected with HIV infection from sharing injecting equipment *(Heroin Addiction and Drug Policy OUP 1994)*
- Between April and September 2000, 60 injecting drug users in Scotland contracted Clostridium Novyii infection, 19 died *(Epidemiol. Infect 2005, 133: 193-234)*
- Between December 2009 and December 2010 drug users were infected with Bacillus Anthracis. 208 suspected anthrax cases had been formally investigated; 119 patients were classed as anthrax cases, classified further as: 47 confirmed cases; 35 probable cases; and 37 possible cases based on the strength of microbiological evidence; 89 suspected cases were classed as not having anthrax (anthrax negative). Fourteen cases died (13 confirmed, 1 probable). *A report on behalf of the National Anthrax Outbreak Control Team 2011*
- An Evolving public health crisis: HIV infection among injecting drug users in developing countries *(Wodak. A, Fisher/ R, Crofts. N 1992)*

opiate substitute treatment: risk/harm reduction

- **Drug related deaths**. On the basis of the definition used for these statistics, there were 485 drug-related deaths registered in Scotland in 2010, 60 (11 per cent) fewer than in 2009. However, this was the third-highest number ever recorded, 30 (7 per cent) more than in 2007 and 193 (66 per cent) more than in 2000. The number of drug-related deaths has risen in six of the past ten years *(General Register Office for Scotland 2011)*
- **Bacterial infections**. Other health considerations bacterial infections such as TB, cellulitis and septicaemia, malnutrition, cardiac and respiratory problems and premature chronic diseases *(Drug Misuse and Dependence, UK Guidelines on Clinical Management Departments of Health 2007)*
- **Social and domestic problems**
- **Collateral damage** to partners, families and all of us
- **Cost to society**, prison, violence, medical expenses


GENERAL PRACTICE Primary care team
Cardiovascular
Endocarditis
Cardiomyopathy
Methadone toxicity
Respiratory
Lung cancer
COPD, Pneumonia
Smoking cessation
Renal and hepatic medicine
Hepatitis C
Cirrhosis
Hepatoma
Pregnancy, contraception
(short and long acting)
termination of pregnancy
Non-statutory sector
Benefits
Advocacy
Sudden death
Infectious diseases
Immunisations
HIV/HCV/HBV
TB, Anthrax
Pneumonia
Social work
Child care
Legal and court work
Orthopaedic surgery
Fracture reconstruction
Care of the elderly
Patient as carer
Patient as elderly
Family and partners
Surgery
Abscess at injection sites
Trauma
Plastic surgery

Edinburgh Addiction Cohort

A follow-up study of survival & long term injecting cessation

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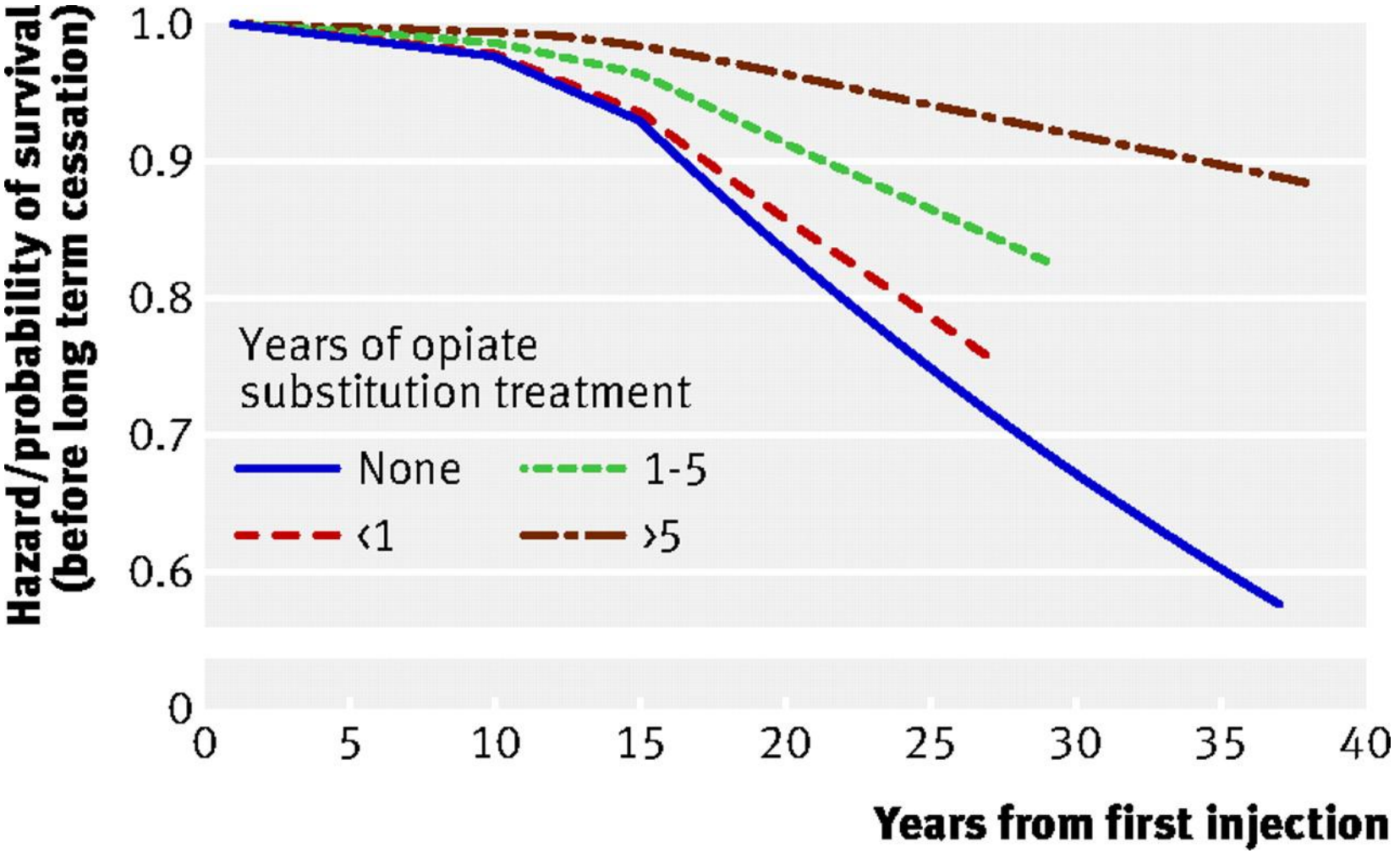
Primary cause of death in EAC: numbers (%)

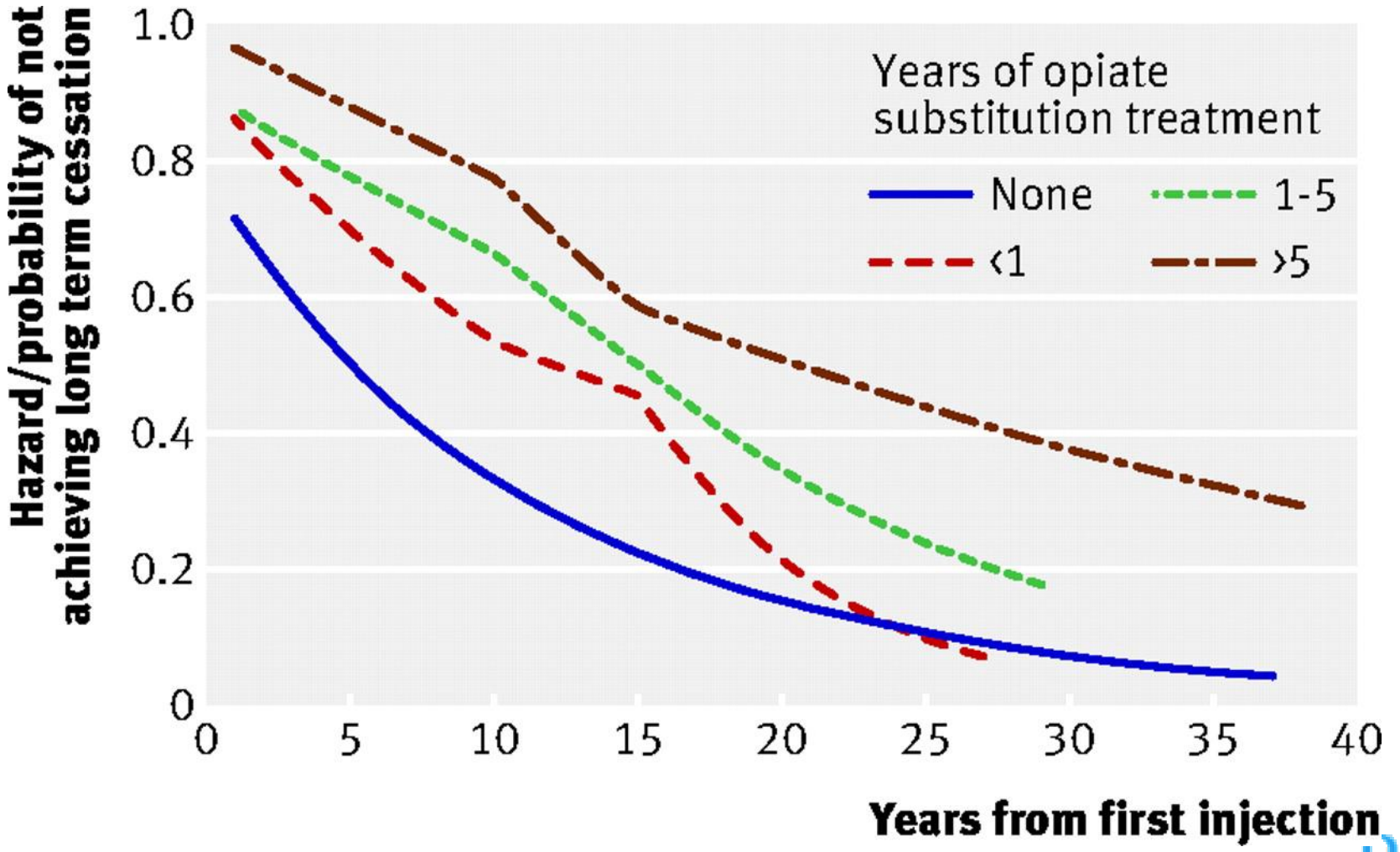
	All deaths (n=228)	Deaths before long term cessation (n=112)
HIV	102 (45)	43 (38)
Injury:		
Drug overdose[1]	55 (24)	43 (38)
Suicide[2]	15 (7)	8 (7)
Homicide	1 (<1)	0
Liver:		
Liver disease	26 (11)	8 (7)
Alcohol related	11 (5)	2 (2)
Other causes:		
Cardiovascular	7 (3)	4 (4)
Injecting related	2 (1)	2 (2)
Lung/throat cancer	2 (1)	1 (1)
Respiratory disease	2 (1)	0
Unascertained	2 (1)	1 (1)
Other	3 (1)	0

Fig 2 Survival: probability of not dying before long term cessation by exposure to opiate substitution to treatment.



Kimber J et al. BMJ 2010;341:bmj.c3172

Fig 3 Injecting duration: probability of achieving long term cessation by exposure to opiate substitution treatment.



Kimber J et al. BMJ 2010;341:bmj.c3172

Overview of findings

- Opiate substitute treatment protective against death
- Continued injecting common but less frequent and less risky
- Premature death
  - 20 years from their first injection, 50% were dead
  - HIV and drug overdose main causes
- High levels of morbidity/co-morbidity
  - HIV, HCV
  - Tobacco, alcohol problems are common
  - Poor mental health, low quality of life were prevalent

Conclusions from this study

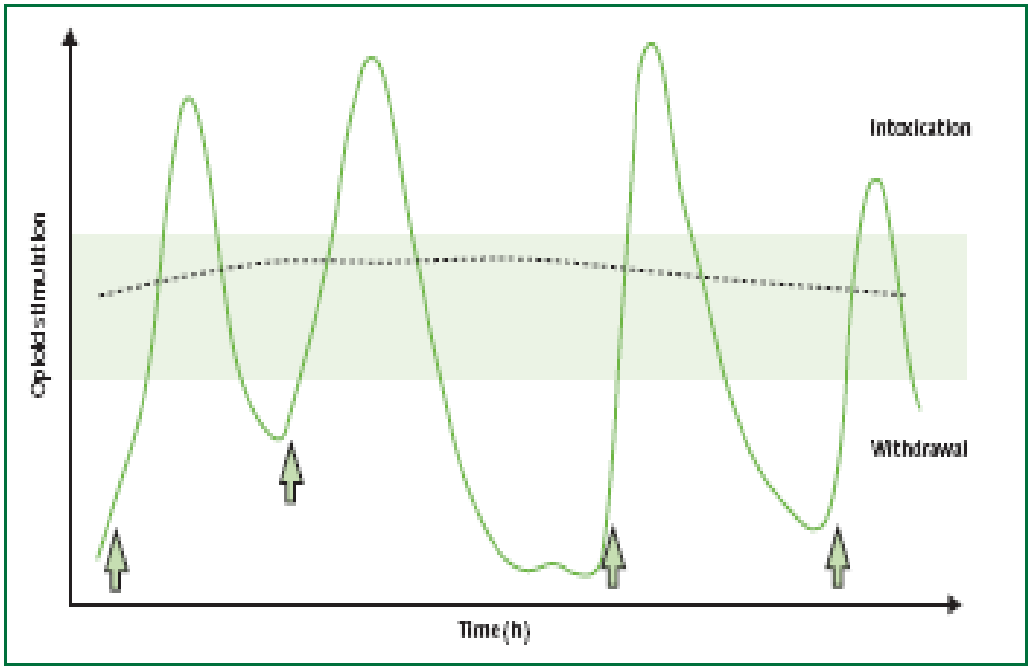
- Excess mortality among EAC participants mainly due to AIDS and overdose of drugs
- Blood borne viruses and overdose were the main preventable causes of death
- Opiate substitute prescriptions are important and maybe required for many years or decades
- Recovery is slow and cumulative in survivors
- Drug injecting remains a major problem worldwide in relation to HIV transmission

Methadone

- Used in treatment clinics since the 1960's as standard therapy for opiate dependency
- Long term use established, and effective
- Best in conjunction with psychosocial supports
- Saves lives, prevents infections and improves lifestyles
- Best retention compared to other pharmacological preparations
- Overdose potential especially during induction and in combination

Figure 2: Principle of opioid maintenance treatment

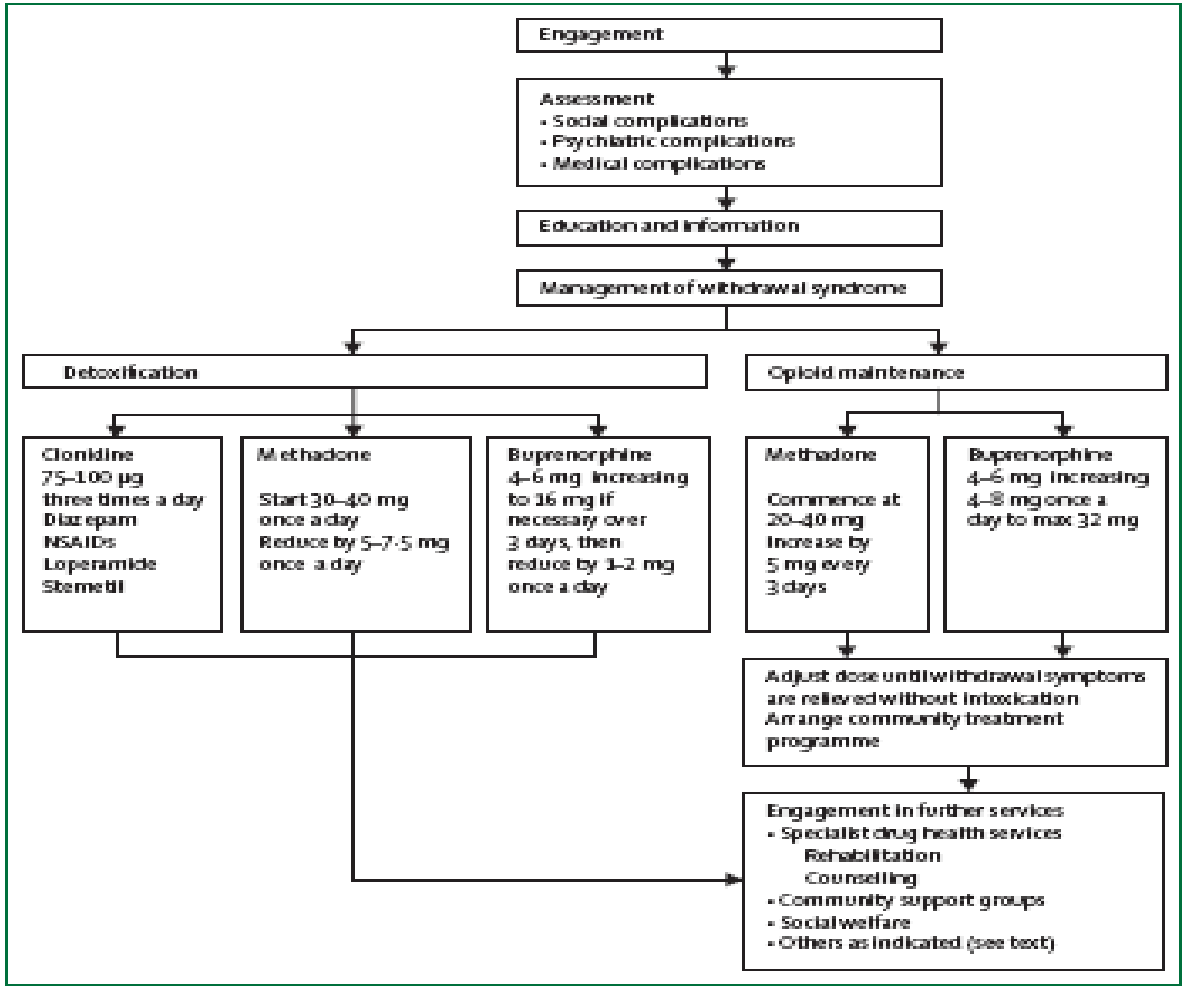
A narrow window of opioid stimulation separates symptoms of withdrawal from intoxication in established opioid dependence (green band). Injection of shortacting opioid drugs (solid line) leads to cycles of intoxication followed by withdrawal that are relieved by further drug use when available (upward arrows). Maintenance treatment (dashed line) involves an orally active longacting preparation (methadone or buprenorphine) that avoids both excessive stimulation and subsequent onset of withdrawal. When successful, the patient feels comfortable and functions normally.



Management of the hospitalised injecting opiate user

Paul S Haber, Abdullah Demirkol, Kezia Lange, Bridin Murnion

Lancet 2009; 374: 1284–93



Evidence base for methadone

- Many randomised controlled trials in many countries, mostly outside UK demonstrate efficacy and especially reduced injecting and retention in treatment (Cochrane, NICE etc.)
- Follow up studies show long term benefits but adherence variable
- Guidelines drawn up by experts endorse evidence
- Clinical experience and personal testimony

Dihydrocodeine as an opiate substitute treatment

RANDOMISED CONTROLLED TRIAL OF DIHYDROCODEINE AND METHADONE IN THE TREATMENT OF OPIATE DEPENDENCE SYNDROME

Dr Roy Robertson, Dr Malcolm Bruce, Professor Gillian Raab, Mr James McKenzie, Helen Strokey

- **Outcome** measures included survival, retention in treatment, continued drug use (particularly injecting), criminal behaviour, and physical and psychological health
- **Results** were similar on both treatments, both groups showing improvement in illegal drug use (using less) and criminal behaviour
- There was one death in the methadone group.

Conclusions

- Dihydrocodeine was found to be as good as methadone using the internationally accepted outcomes and there were indications of improved retention in some subgroups on dihydrocodeine
- Getting the dose right important
- Dihydrocodeine should be considered as an option in the treatment of opiate dependent patients.

Heroin as a substitute

- Trials in Canada, England, Switzerland and Netherlands all confirm benefits of injectable heroin (sometimes with methadone) over oral (or sometimes injectable) methadone
- All conclude risks make it feasible only in secondary care settings with close supervision

Heroin as a substitute

Wim van den Brink, Vincent M Hendriks,Peter Blanken, Maarten W J Koeter, Barbara J van Zwieten, and Jan M van Ree, Medical prescription of heroin to treatment resistant heroin addicts: two randomised controlled trials *BMJ. 2003 August 9; 327(7410): 310*

Results Adherence was excellent with 12 month outcome data available for 94% of the randomised participants. With intention to treat analysis, 12 month treatment with heroin plus methadone was significantly more effective than treatment with methadone alone in the trial of inhalable heroin (response rate 49.7% *v* 26.9%; difference 22.8%, 95% confidence interval 11.0% to 34.6%) and in the trial of injectable heroin (55.5% *v* 31.2%; difference 24.3%, 9.6% to 39.0%). Discontinuation of the coprescribed heroin resulted in a rapid deterioration in 82% (94/115) of those who responded to the coprescribed heroin. The incidence of serious adverse events was similar across treatment conditions.

Conclusions

Supervised coprescription of heroin is feasible, more effective, and probably as safe as methadone alone in reducing the many physical, mental, and social problems of treatment resistant heroin addicts.

Strang. J, Metrebian.N, Lintzeris.N, Potts.L, Carnwath.T, Mayet.S, Williams.H, Zador.D, Evers, Groshkova.T, Charles.V, Martin.A, Forzisi.L

Randomised Injectable Opiate Treatment Trial (RIOTT)

Lancet 2010; 375: 1885–95

- A randomised trial for opiate dependent patients
- Open to addicts in England after persistent failure in orthodox treatment
- Supervised injectable heroin or injectable methadone versus optimised oral methadone as treatment for chronic heroin

THE UNIVERSITY OF EDINBURGH

Interpretation of RIOTT trial

- Treatment with supervised injectable heroin leads to significantly lower use of street heroin than does supervised injectable methadone or optimised oral methadone.
- UK Government proposals should be rolled out to support the positive response that can be achieved with heroin maintenance treatment for previously unresponsive chronic heroin addicts.

Other opiate substitute treatment studies

- Hydromorphone found to be effective in short follow up study in Australia (where heroin is not available) Mitchell et.al.
- Codeine derivatives commonly used in custodial situations until introduction of methadone into prisons
- Morphine trial in UK aborted because of methodological issues
- Case reports and individual experience wide reported

Findings from trials of opiate substitute treatments

- Trial patients may have better outcomes
- All “optimised” treatments are better than standard
- All trials show improved outcomes independent of trial drug when compared with placebo or standard opiate substitute treatments
- There are collateral benefits for participants in trials

Political and policy landscape – confusing to say the least

- Most political parties and policy statements endorse opiate substitute treatment, sometimes under the guise of clinical freedom
- National guidelines and NICE appraisals reinforce efficacy and, relative, safety *(DoH 2007, NICE 2007)*
- Recovery agenda has introduced confusion, probably unnecessary confusion
- A change in the law in 2003 made it lawful to provide injecting drug users with other equipment used when injecting, e.g. spoons and filters, to reduce further the risk of infection (Home Office. Statutory Instrument 2003 No. 1653)

The Lancet

"Drug users around the World face stigma, discrimination, mistreatment, and the systematic violation of their human rights"

See comment page 543

Vol 378;9791 August 13-19, 2011

Joseph Amon, Human rights watch.

General conclusions about opiate substitute treatment

- Methadone better for retention but overall less safe in overdose
- Better coverage maybe available with buprenorphine
- Claims for increased benefits (better in pregnancy, less sedative, better in withdrawals) so far unsubstantiated
- Other possibilities either limited in range (heroin due to safety margin) or never tested in community services
- Maximum coverage maybe most important in preventing serious epidemics
- Long term outcomes depend upon retention in treatment
- Modalities important but trials of infrastructure is equally important for example delivery systems (Methadone dispensing in A+E in St Vincent's, community care choices)

end

- The American Society of Addiction Medicine (ASAM) has released a new definition of addiction highlighting that addiction is a chronic brain disorder and not simply a behavioural problem involving too much alcohol, drugs, gambling or sex. *(2011; www.asam.org)*