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▶ Were the changes to Sweden's maintenance treatment policy 2000–06 related to changes in opiate-related mortality and morbidity?

Romelsjö A., Engdahl B., Stenbacka M. et al.

Addiction: 2010, 105, p. 1625–1632.

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Ironically, the fact that opiate substitute prescribing has been opposed and limited in Sweden has meant that country has been able provide solid evidence of its lifesaving potential. This study concluded that easing the restrictions was associated with and may have led to fewer opiate-related deaths.

SUMMARY Major changes between 2000 and 2006 in Sweden's national polices on methadone and buprenorphine maintenance treatment, and correspondingly substantial increases in the availability of these treatments, provided the opportunity to assess whether this expansion reduced illness and death due to opiate (mainly heroin) dependence and misuse.

From 1997 to at least 2004, the number of opiate dependent people in Sweden remained at about 10,000, but treatment policies progressively changed in a way which allowed and attracted more in to treatment. Up to 2004 admission criteria excluded patients who had been dependent for less than four years or who were not injecting, and set other treatment entry restrictions. However, the national ceiling on the methadone treatment caseload was raised from 800 in 1999 to 1,200 in 2003; about half the treatment slots were in the Stockholm County programme based in Sweden's capital city (from here on references to Stockholm include city and county). Buprenorphine became available in 1999 and the number of units prescribing this safer medication substantially increased.

A step change in policy came at the start of 2005 when the upper limit on the methadone caseload was abolished and the need for patients to have been dependent on opiates for at least four years was reduced to two. This latter restriction was also applied to buprenorphine, but still the policy change was expected to increase the availability of maintenance treatment.

Surveys of treatment units in 2003 and 2005 revealed that by 2005, very few had to freeze their intake, waiting times had halved, and retention improved (from 68% to 87% of patients retained for at least a year). From about 800 methadone patients in 2000, by 2006 there were 2,797 maintenance patients of whom about 54% were prescribed buprenorphine and 46% methadone. Fewer units commonly discharged patients for using illegal drugs (down from 30% to 17%), preferring instead to retain patients but adapt their treatment.

Key points

Restrictions in Sweden on maintenance prescribing of heroin substitutes such as methadone have provided an opportunity to reliably assess the treatment's lifesaving potential.

This study took advantage of a major expansion in provision and easing of restrictions between 2000 and 2006 to assess whether these reduced illness and death due to heroin misuse.

The authors concluded that these developments were associated with and may have contributed to declines in opiate-related deaths and hospitalisations.

Overall deaths declined despite a large proportional increase in deaths where methadone and buprenorphine were found in the body.

Since the end of the study's period deaths have risen, possible due to more patients being discharged for continuing to use illegal drugs.

Experience in Scandinavia and elsewhere shows that the degree to which substitute prescribing programmes save lives overall depends on striking the right balance between access and control, flexibility and regulation.

Data on sales of the medications confirmed the expansion in treatment. Per 1000 of the population, the number of typical maintenance doses sold increased over threefold between 2000 and 2006.

There were some possibly relevant differences between the Stockholm programme and typical programmes in the rest of Sweden. In 2005 in Stockholm, the average waiting time was shorter, 68% of treatment units (versus 42% in the rest of Sweden) allowed patients to take their medication away, buprenorphine doses were higher, more patients were offered psychosocial therapies, and there was a well established collaboration with social services, such as public centres for homeless people offering referral to maintenance treatment.

Main findings

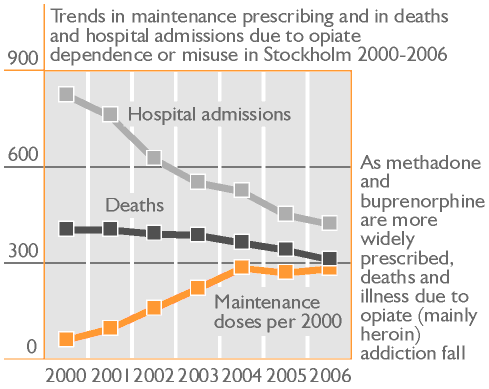
As maintenance treatment expanded there were statistically significant reductions between 1998–2000 and 2004–06 in the number of deaths registered as wholly or partly due to opiate dependence or misuse. This was seen across Sweden as a whole, but more especially in Stockholm, where they reduced by a third, and where there was also a statistically significant reduction of a third between 2000–02 and 2004–06; at about 16%, the reduction over this time period in Sweden as whole was substantial but not statistically significant.

The registration data reported above is available for almost all deaths. When a death is seen as

unnatural or violent, the great majority are also autopsied, affording data on the drugs found in the body. Deaths where opiates lie heroin were found (excludes methadone and buprenorphine) fell significantly by about 16% between 1998–2000 and 2004–06 and 30% between 2000–02 and 2004–06, but deaths in which methadone or buprenorphine were found increased from just 13 in 2000 to 53 in 2005 and 49 in 2006. Nevertheless, the net tally of drug-related deaths across Sweden (excluding tranquillisers, sedatives and hypnotics and dextropropoxyphene) fell significantly by about 12% between 2000–02 and 2004–06.

There were also significant and/or substantial falls in the number of opiate-dependent or misusing inpatients admitted to hospital, an indicator of trends in ill-health related to opiate use. Both between 2000–02 and 2004–06, and between 1998–2000 and 2004–06, in Stockholm the total fell by just over a third. Across Sweden between 2000–02 and 2004–06 the decline was over a fifth.

Another way to analyse the figures is to assess how closely year-on-year opiate-related deaths and illness mirrored the expansion in substitute prescribing, indicated by the number of typical maintenance doses sold. Between 2000 and 2006, for both Stockholm (▸ chart; doses converted to per 2000 of the population for clarity) and Sweden as a whole, the relation was very strong and statistically significant; as prescribing expanded, opiate-related deaths (registered and autopsy data) and hospital admissions fell. There was also a strong – yet not statistically significant – correlation in the other direction for deaths where methadone or buprenorphine were found in the body; as substitute prescribing expanded, these increased.



The authors' conclusions

Though a study of this kind can only demonstrate associations, not prove causality, on balance declines in opiate-related mortality and hospitalisations in Sweden in 2000–06 may be attributable to the large expansion in maintenance treatment, its greater availability, and a less restrictive access policy. This interpretation is supported by the direction of 14 of the 15 correlations between these variables, the co-occurrence of changes in treatment access with declines in opiate-related deaths and illness, similar relationships in France when maintenance treatment expanded there, and the fact that the declines in opiate-related mortality and hospitalisations were particularly large in Stockholm, which saw the greatest changes and expansions in treatment. Their beneficial impacts may have been even more noticeable had they not possibly been counteracted by the falling street price for heroin.

On the other hand, deaths where methadone and buprenorphine were found in the body increased markedly from a low number. However, in both France and Sweden these trends were definitively outweighed by the decline in deaths attributed to opiate dependence or misuse.

FINDINGS COMMENTARY The featured study adds to a considerable body of work indicative of the lifesaving potential of programmes which prescribe opiate-type drugs to patients dependent on heroin. Internationally and in Britain, being in opiate substitute treatment using methadone or buprenorphine has been associated with a substantially reduced risk of death. Nobody has credibly worked out the balance sheet of deaths contributed to versus prevented by methadone treatment, but the World Health Organization was convinced enough of the public health credentials of both methadone and buprenorphine to place them on the international list of "essential" medicines.

Since the last year of the study's period (2006) deaths related to drug dependence and misuse and those where traces of heroin/morphine and methadone or buprenorphine were found have all increased, as have the numbers treated for drug-related ill health. What caused these increases is unclear. Possibly in contrast to the featured study's period – during which retention in substitute prescribing programmes became very high – the European Union's centre for drug misuse notes that since 2005 some Swedish treatment centres "have introduced 'zero tolerance' against lateral drug use [ie, using illegal drugs], which leads to low retention rates". Aggravating the situation is that once thrown out, a patient cannot return for three months. While *being in* a substitute prescribing programme is highly protective, forced discharge creates a high risk of overdose death. Also, some of the highest risk opiate users – those also misusing alcohol or non-opiate drugs, including buprenorphine – are banned from substitute prescribing programmes. If these factors contributed to the increase in deaths in Sweden, it is an example of the fact that the impact substitute prescribing makes on the mortality rate is not automatic, but depends (▸ below) on how the programme is implemented.

Methadone and to a lesser extent buprenorphine are themselves dangerous drugs. In Britain and elsewhere there is concern that programmes which prescribe these drugs inadvertently result in some deaths, particularly when patients pass on their medication to other people. In the featured study deaths where buprenorphine or methadone were found in the body increased substantially, but there is no information on the degree to which these substances helped cause the deaths. When programmes are expanding, any opiate user tested – alive or deceased – will be more likely to be found to have buprenorphine or methadone in their system. However, the continuing increase since the end of the study period has left the tally of cases where methadone or buprenorphine was found exceeding that for heroin/morphine. There is no information on how the deceased got these drugs and whether they were patients being prescribed them.

Scandinavia's limits on maintenance help show its value

The featured study is one of several from Sweden and Norway, whose resistance to prescribing opiate-type drugs to heroin addicts has allowed its value to be more convincingly demonstrated than in countries which make such treatment easily available. In particular, restrictions on methadone maintenance in Sweden made it possible effectively at random to allow or deny this treatment. In countries such as the UK, how methadone patents fared compared to other opiate users might be due not to the treatment, but to pre-existing differences between those who choose methadone and those who do not. The Swedish situation permitted a level playing field between methadone and other

approaches which could not be created where methadone was widely available.

The single most important study tracked patients admitted to Sweden's national methadone programme before a five-year ban on enrolling new patients. Their fate was compared to that of addicts eligible for the programme, but who did not get in before the ban or had randomly been denied entry. All in this comparison group availed themselves of Sweden's well developed detoxification and drug-free treatment services, yet over on average the next six years, 4 in 10 died. Over about the same period, around 1 in 8 of the methadone patients had died, far fewer. Overwhelmingly, opiate overdose was the main reason for the difference. Another Swedish study found that the annual death rate was 1% while patients were on methadone but 2% among untreated opiate misusers. During an enforced break in treatment, hospital admissions rose only to fall again when the same addicts were allowed to return, strong evidence that treatment was an active ingredient in avoiding illness and death. The Swedish experience with methadone has been described in a Findings review.

The same message has come from neighbouring Norway, where a study found that even when some illegal drug use continues, being in methadone or buprenorphine treatment dramatically cut drug-related physical complaints requiring hospital treatment, and that such complaints rebounded when patients were forced to or chose to leave.

Another Norwegian study traded on the typically five or six months patients had to wait before they could get a slot in a methadone programme. All the study's participants had been assessed as needing and qualifying for treatment and had applied to enter a programme, yet many were forced to wait, enabling researchers to assess the impact of being denied immediate treatment and, by extension, to estimate what might have happened had there been no maintenance programmes for them to wait for. Unlike other studies, the study's design stripped away confounding variables like severity of dependence and motivation which influence whether someone seeks treatment, exposing the impact of the treatment itself.

The results implied that if 100 people are made to wait for treatment, an extra one or two will die per year compared to a situation where treatment was made immediately available. In line with other studies, the bounce back to pre-treatment overdose death rates after leaving treatment supports a view of methadone and other substitute prescribing programmes as an on-off switch. People in need of this treatment generally quickly improve when it is 'switched on' but rapidly relapse once it is off, and especially so if it is switched off against the patient's wishes. Despite this, over the span of the study, in-treatment gains overshadowed post-treatment reverses, leaving a substantial overall benefit.

Depends on the programme

Because take in so few patients, programmes in Sweden and Norway are not well suited to demonstrating a protective effect across a population of heroin users. In Spain this seems to have been clearly demonstrated by a low-threshold programme which in the 1990s contributed to a 21-year increase in the life expectancy of heroin users in Barcelona. It abandoned previous limits on doses and duration, stopped penalising patients who continued to use illegal drugs, and relaxed requirements to consume the medication under supervision. The latter might have led to more methadone deaths among non-patients, but the whole programme netted such a high proportion of the city's heroin users that this was unlikely.

Barcelona's experience and that in Scandinavia illustrate that it is not inevitable that any substitute prescribing programme will save lives overall, including among non-patients; it all depends on reaching the right balance between access and control, flexibility and regulation. Get this right and methadone and buprenorphine programmes make the greatest known contribution to reducing opiate-related deaths. Get this wrong, and there can be preventable deaths among non-patients due to medication passed on to them by patients, among dependent opiate users unable to access the treatment, among those who do but continue to use illegal drugs (perhaps due to inadequate doses), whose induction on to methadone has not been sufficiently well monitored, or who have been forced out or deterred by expense, onerous requirements, or unrealistic expectations of compliance and progress.

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