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▶ Mortality prior to, during, and after opioid maintenance treatment (OMT): a national prospective cross-registry study.

Clausen T., Anchersen K., Waal H. Request reprint

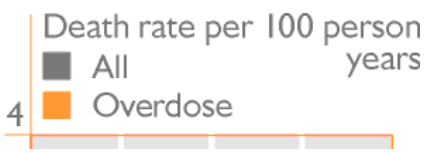
Drug and Alcohol Dependence: 2008, 94(1–3), p. 151–157.

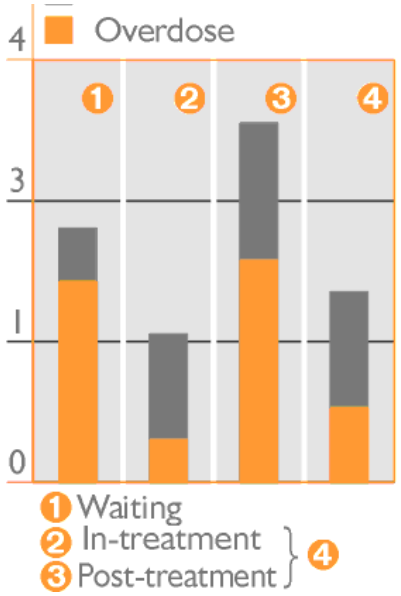
Limited access to opiate substitute prescribing in Norway opened a window on its powerful lifesaving potential, a view obscured in countries where barriers create a confounding selection effect or where everyone who needs and wants this treatment can quickly get it.

Abstract At the time of the study Norway's substitute prescribing programme for opiate addiction was designed to recruit severely addicted heroin users aged 25 and over who have not benefited from other types of treatment. Priority was given to applicants also suffering from other severe physical or psychiatric illnesses. The featured study investigated mortality reductions associated with entering this programme, drawing on national registry data on the treatment careers of all 3789 opioid-dependent patients accepted for this treatment at any time in the seven years from 1997 to 2003 inclusive. This was cross-linked with data from the national deaths registry on deaths up to the end of 2003. On average each patient was tracked for nearly three years.

Death rates were calculated during:
- **Waiting time** The typically five or six months patients had to wait between being assessed as qualifying for treatment and starting their programmes.
- **In-treatment time** Total number of days in the programme whether during one or several episodes, typically about two years. Sometimes referred to below as 'during' treatment.
- **Post-treatment time** Number of days out of treatment within the study period, whether between successive treatment episodes, or following a single or the last episode.

Combining the last two periods afforded an estimate of the change in death rate after entering treatment, regardless of whether the patient remained in the treatment or had left.





While waiting, per year 2.4% of the would-be patients died. This fell to 1.4% during treatment and rose to 3.4% after leaving. Combining the last two periods, the death rate fell from 2.4% before treatment to 1.8% after starting it ▶ chart. A more sophisticated analysis indicated that the risk of death after entering treatment (whether still in it or after leaving) was 60% of the risk while waiting, and that while still in treatment, patients were half as likely to die as while they were waiting.

Given the priority afforded to ill applicants, many deaths might have been due to preceding illnesses which could not be prevented by the treatment. Overdose deaths offered a more direct indicator of the impact of starting treatment. The overdose death rate fell from 1.9% a year while waiting to 0.4% during treatment, and rose to 2.1% after leaving. Combining the last two periods, the overdose death rate fell from 1.9% before treatment to 0.7% after starting it. Again a more sophisticated analysis quantified the relative risks run by patients in the different phases of their treatment careers. Waiting for treatment, patients were three times more likely to suffer a fatal overdose than after starting treatment. While still in treatment, overdose deaths were cut to a fifth of their pre-treatment level.

Though studies which sample only patients still in treatment may overestimate mortality reductions, the authors concluded that their study shows reductions remains significant and substantial, even when patients who have left are included in the calculations.

FINDINGS This study takes us closer to an answer to the question, 'How many more people dependent on heroin would die if there were no substitute prescribing programmes?' Its most important feature was a by-product of the time patients had to wait for treatment as the programme came to terms with the workload revealed when the new service became available. At the time participants started contributing data to the study, all had already been assessed as needing and qualifying for treatment and had applied to enter the programme. The fact that many had to wait enables us to assess what happens when such people are forced to wait, and by extension, to estimate what the impact might have been had there been no maintenance programmes for them to wait for. Unlike other studies, the study's design strips away confounding variables like severity of dependence and motivation which influence whether someone seeks treatment, exposing the impact of the treatment itself.

What it implies is 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 many 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. Over the span of the study, in-treatment gains overshadowed post-treatment reverses, leaving a substantial overall benefit.

The Norwegian context at the time does however limit the findings to patients failed by non-prescribing approaches, turning the spotlight on the adequacy those approaches. Had these been better developed, these patients may never had got as far as the doors of a prescribing service and as many lives may have been saved. For Norway this seems unlikely, as drug-free treatment aimed at achieving a drug-free life is the mainstay of the treatment response; maintenance prescribing is a late and relatively peripheral addition. Nevertheless, in 2003 about 30% of the established and severe cases of opiate addiction in the country were in substitute prescribing programmes. Nine out of ten injected, exposing them to the highest risk of overdose. This caseload gives the programmes great scope to demonstrate their power to reduce this risk, but also concentrates the most difficult to treat addicts in the clinics. The study also reflects the results of a tightly controlled programme with an avowed rehabilitation objective (highlighting housing and − generally unsuccessfully − employment), entailing supervised consumption, frequent urine tests for unauthorised drug use, and discharge of patients who do not progress sufficiently, divert medication, or do not comply with the requirement for frequent attendance. Despite this stringency, the programme has very high retention, possibly aided by most provision being in the hands of local GPs, and by methadone doses averaging well over 100mg and buprenorphine doses averaging 16mg daily, very high average levels. While the 'all deaths' figures are unambiguous, deciding what is or is not an overdose death is less straightforward.

Neighbouring Sweden also has a programme with restricted access. As in Norway, this has provided insights in to the lifesaving potential of substitute prescribing obscured in other countries. Based on expected death rates for Swedes of a similar age, one seminal study showed that patients eligible for maintenance treatment, but denied it and offered detoxification and drug-free services instead, were eight times as likely to die as those admitted to the maintenance programme. These and other studies have been reviewed for Drug and Alcohol Findings.

Because of their restricted access, studies of such programmes 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 '90s contributed to a 21-year increase in the life expectancy of heroin users in Barcelona.

It is not however 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 − perhaps even more so buprenorphine programmes − make the greatest known contribution to reducing opiate-related deaths. Get this wrong, and deaths due to

diverted medication, among patients unable to access the programme, who continue to use illegal drugs 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, can all become a concern.

Partly as a result of such research, access to Norway's substitute prescribing programme is no longer as restricted both in terms of intake criteria and waiting times.

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