Heroin maintenance for persons with chronic heroin dependence

This is an excerpt from the full technical report, which is written in Norwegian.

The excerpt provides the report's main messages in English.

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Systematic review

kunnskapssenteret

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Norwegian Knowledge Centre for the Health Services summarizes and disseminates evidence concerning the effect of treatments, methods, and interventions in health services, in addition to monitoring health service quality. Our goal is to support good decision making in order to provide patients in Norway with the best possible care. The Centre is organized under The Norwegian Directorate for Health, but is scientifically and professionally independent. The Centre has no authority to develop health policy or responsibility to implement policies.

We would like to thank all contributers for their expertise in this project. Norwegian Knowledge Centre for the Health Services assumes final responsibility for the content of this report.

Norwegian Knowledge Centre for the Health Services
Oslo, July 2010

Key Messages (in English)

Background: This report addresses the following research question: Are there differences in effect between heroin assisted maintenance (diacetylmorphine) versus the traditional substitution maintenance treatment (methadone, buprenorphine) for persons with chronic heroin dependence?
Methods: We based our systematic review on a literature search in relevant databases for previous systematic reviews of high quality and randomised controlled trials. We synthesised and critically appraised the included documentation after they met our pre-defined inclusion criteria. We extracted results from the following outcomes: mortality, retention in treatment, use of illegal drugs, quality of life and serious adverse outcomes.
Results: We included eight randomised controlled trials. The oldest study was published in 1990 and the most recent was from 2010. Two of the studies were performed in the Netherlands, two from England, and one each from Switzerland, Spain, Germany and Canada. In one of the trials the participants were heroin smokers whereas the other studies predominately concerned injecting heroin users. Participants in the studies were mainly adults (+35 years) and had a history of chronic, long term heroin addiction, and many had previously failed attempts in traditional treatment programs (without and with methadone substitution and maintenance). All studies reported outcomes for mortality and retention in treatment. Whilst for the other outcomes only five and six of the studies presented effect sizes. The results were not quantitatively combined due to heterogeneity. The quality for this documentation is graded. Grading the studies separately for a Norwegian audience led us to the category very low quality. The results must therefore be interpreted as uncertain.
Conclusion: The existing documentation does not give an adequate foundation to answer the question of effectiveness of heroin assisted maintenance treatment compared to traditional maintenance (with methadone) for persons with chronic heroin dependence for the outcomes mortality, retention in treatment, use of illegal drugs, severe adverse outcomes and quality of life. Even though the quality, from a Norwegian perspective, is graded to be very low, others can argue that the intervention is effective and promising for patients in other countries. We need research in Norway to answer the question of effectiveness for a Norwegian context.

Executive summary

Heroin maintenance for persons with chronic heroin dependence

BACKGROUND

Norwegian Knowledge Centre for the Health Services summarizes and disseminates evidence concerning the effect of treatments, methods, and interventions in health services, in addition to monitoring health service quality. Our goal is to support good decision making in order to provide patients in Norway with the best possible care. The Centre is organized under The Directorate of Health, but is scientifically and professionally independent. The Centre has no authority to develop health policy or responsibility to implement policies.

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Heroin maintenance for persons with chronic heroin dependence is not an available treatment option in Norway. In several other western countries heroin maintenance is made available for a limited group of heroin addicts. Heroin addicts have an elevated risk for drug overdose, death caused by drug overdose, health problems, and infectious diseases such as hepatitis C and AIDS. Norway has a high rate of deaths caused by drug overdose among opiate users compared to other European countries. Approximately 200 persons die each year as a result of drug overdose. Treatment for opiate addicts has the purpose of saving lives, to improve the health condition and to end the craving for illicit drugs. Some patients have a long history of addiction and are regarded as chronic addicts. Up to 10% does not seem able to succeed with the help of conventional maintenance treatment. The short term aim of ending the use of opiates seems futile. This assumption combined with the hope for a dignified life has lead to the idea of pharmaceutical substitution treatment. The aim is to reduce, or stop the use of illicit drugs. In this report we set out to answer the question of the effectiveness of heroin assisted substitution (HAB) for persons with chronic heroin addiction compared to methadone, buprenorfine or any other pharmaceutical as-

sisted treatment. Our research question is: Can HAB increase the treatment retention rate and reduce overdose related deaths? Is HAB an effective intervention for reducing use of illicit drugs and increasing quality of life? Are there any known serious adverse events related to HAB?

METHODS

We performed a systematic search for relevant scientific literature on the predefined research question. Two persons read through all identified titles and abstracts to search for possibly relevant trials. Data from included trials were extracted and presented. Included trials were critically appraised by two persons working independently using existing checklists for examining risk of bias. Information about methodology in the included trials were gathered and presented in the report. The included documentation was graded for each study individually. A draft was reviewed by two employees at the Knowledge Centre for the Health Services. Thereafter three external referees commented on a revised draft. The revised report was then reviewed and approved by the management team in the Knowledge Centre for the Health Services.

RESULTS

The eight included randomised controlled trials dealt, primarily with persons with long term, chronic heroin or opiate addiction. The trials were from Spain (N=62), Germany (N=1015), Canada (N=251), Netherlands (two trials N= 174 and N=256), Switzerland (N=51) and England (two trials N=96 and N=127). The participants, predominantly adult males, had a history of (several) previous unsuccessful treatment attempts in ordinary pharmaceutical substitution facilities. In seven out of eight trials the intervention participants injected heroin, and the control group in all studies received traditional (methadone or buprenorfin) substitution treatment (MAB). In total most of the data stemmed from trials of low to unclear risk of bias. Meta-analysis was not feasible due to heterogeneity in the material. All studies reported measurement of our predefined outcomes, namely retention in drug abuse treatment, and mortality/serious adverse outcomes. The results are ambiguous for mortality and retention but points mainly in favour of heroin maintenance. For the other outcomes, not all studies presented effect sizes. For quality of life / welfare the evidence does not allow us to make a judgement of what type of maintenance is the best. In our material there are several reports of serious adverse events in both treatment groups. However, epileptic seizures, overdoses, and respiratory failure are predominantly reported in the groups receiving heroin maintenance. Ambiguous results are also presented about use of illegal drugs, but there is a trend favouring heroin maintenance over methadone maintenance especially for reduced use of illegal street heroin. The quality of the included material is graded down to very low, due to unclear items in risk of bias / limitations, publication bias, imprecision and

indirectness (for our patient population in a Norwegian context) and all effect sizes must be interpreted with caution.

DISCUSSION

We included material from four randomised controlled trials stemming from a high quality Cochrane systematic review published in 2005. In addition we found and included four recently published randomised controlled trials. We aspired to include all existing trials, but we found no unpublished trials. Results from studies indicating no effect could remain unpublished. Thus, there is a possibility that the results in our material may be skewed.

The material stemming from other European countries and Canada made it difficult to transfer the results to a Norwegian clinical context. Most of the research was performed in experimental conditions and in the absence of a pragmatic trial it is difficult to assess how the intervention would affect the daily clinical practice.

CONCLUSION

Available documentation gives an inadequate foundation to answer which maintenance treatment option is the best for persons with chronic heroin dependence. The total documentation for the pre-defined outcomes retention in treatment, illegal drug use, quality of life, and serious adverse events such as death and overdose is of very low quality using the grade approach.

Using our standard way of presenting results from single studies of low quality our conclusion is that:
For the varied heroin assisted maintenance treatments compared to traditional methadone maintenance treatment for persons with chronic heroin dependence the quality is too low for us to be certain whether mortality, retention in treatment, use of illegal drugs, severe adverse events or quality of live is affected.

Even though the quality, from a Norwegian perspective, is graded to be very low, others can argue that the intervention is effective and promising for patients in other countries.

We conclude that we have insufficient documentation to support or refute the use of heroin assisted treatment for persons with chronic heroin dependence. The conclusions could be altered if new research material becomes available. We support the conclusion from the included systematic review from 2005 where more research was called for. We need research in Norway to answer the question of effectiveness for a Norwegian context.