

A Multi-Centre Efficacy Trial of
Naltrexone Maintenance Therapy in
Hong Kong

Executive Summary

1. Study Background

1.1 In May 1999, upon the recommendations of the Action Committee Against Narcotics (ACAN) Sub-committee on Treatment and Rehabilitation, a Working Group was formed to conduct a comprehensive review of the Methadone Treatment Programme (MTP).

1.2 In December 2000, the MTP Review Working Group recommended more research to fully assess the effectiveness of naltrexone in relapse prevention of detoxified opiate dependents.

1.3 Naltrexone is a pure opioid antagonist that blocks the pharmacological actions of opioids. It has been administered to detoxified opiate addicts to reduce their risk of relapse. Naltrexone has no opioid agonist properties, and therefore is not associated with the development of dependence. Clinical studies showed that administration of naltrexone at the recommended doses did not lead to any predictable profile of serious adverse events. However, since the blockade effect produced by naltrexone is surmountable, patients who attempt to overcome the antagonist effect by taking heroin may suffer fatal overdose.

1.4 The efficacy of naltrexone as a maintenance medication has been reported in a number of overseas and Chinese studies. The double blind controlled studies in US and Europe suggested that naltrexone

could reduce relapse and the number of drug using days. In China, several uncontrolled and retrospective studies had been conducted, which generally showed an inclination of positive outcomes for patients maintained on naltrexone.

1.5 The efficacy of naltrexone maintenance treatment was systematically examined and analysed in a Cochrane evidence-based review. Reviewers commented that final conclusions on whether naltrexone treatment was considered effective in maintenance therapy could not be drawn from the evidence available so far. More studies were needed before making a clear decision on further application of naltrexone. Nevertheless, a trend in favour of treatment with naltrexone had been observed for certain target groups, particularly those who were highly motivated.

2. Study Design and Methodology

2.1 The initial proposal of the study was an open trial design. With the involvement of the Substance Abuse Clinics (SACs) of the Hospital Authority and interested drug treatment and rehabilitation agencies, a total of 150 recently detoxified opiate addicts would be recruited to receive naltrexone maintenance therapy, and be categorized into 3 sub-samples according to the level of supervision, namely family/institution supervision, clinic supervision and self-supervision. No control group would be formed for outcome comparison.

2.2 However, in order to pursue for a higher standard of scientific

rigour, the research team complied with the request of the Monitoring Group by converting the initial open trial study into a randomized controlled trial (RCT) design. In such design, 160 recently detoxified opiate addicts would be randomly assigned to treatment or placebo arm in 1:1 ratio. These participants would undergo 4-month naltrexone/placebo maintenance treatment with counselling services on fortnight basis. In order to ascertain the treatment completion rate under unsupervised context, an independent cohort of 20 participants would also be recruited to receive 4 months of naltrexone maintenance treatment in the absence of family/institution or clinic supervision. Following then, all participants would be followed up for 6 months to monitor outcomes of the treatment.

2.3 The research team initiated a pilot trial for the RCT in September 2003. A total of 16 eligible participants were approached and 6 agreed to participate in the pilot study. Two eventually completed the 4-month naltrexone treatment, and one of them further proceeded to and eventually completed the 6-month follow-up phase for outcome monitoring.

2.4 The research team had encountered several problems when conducting the pilot study. First, it was difficult to recruit participants for the RCT since potential addicts were reluctant to join a trial entailing a possibility of placebo. Second, participants who found out that they were not receiving naltrexone saw no point to stay in the trial, resulting in an unfavourable attrition

rate. Last but not least, potential risk of heroin overdose existed among the local drug addicts who were ready to go for experiment to test the medication.

2.5 To resolve the difficulties found in the pilot study, the research team raised the issues at the Monitoring Group meeting, and finally concluded to revert the study design into open trial. In the revised open trial design, the participants would be stratified by their sources of referral, mode of supervisions, previous experience with naltrexone and so forth. There would be 160 participants without control comparison.

3. Rethinking of the Study Status

3.1 The research team applied for ethics approval with the Clinical Ethics Committee of the Chinese University of Hong Kong for the reversion of the study design to open trial. In response to our modifications of the study design, the Committee raised some concerns of the unusually large sample size and the absence of control arm for comparison.

3.2 Further to the Committee's concerns, the research team consulted experts on research methodology and trial design. A number of alternative designs have been considered and discussed with the Monitoring Group. It included comparing the results of naltrexone treatment with benchmark data of other relapse preventions services, comparing with past treatment data of participants, comparing with a control group without any treatment, and conducting an open trial study of small scale. After thorough discussion, it was found that none

of these alternatives were feasible in the local context.

3.3 The research team was particularly concerned about the risks of the study. The study was predominantly conducted on an outpatient basis, it was thus difficult to keep participants away from high-risk environment. Moreover, as a result of the common myths and misunderstandings about the effects of naltrexone, there were worries about the danger of heroin overdose as an experimental attempt to overcome naltrexone effects.

3.4 Therefore, the research team found that neither was it feasible to conduct a randomized controlled trial, nor was it possible to identify control comparison for an open trial. Last, whatever design to take, the risk of naltrexone maintenance therapy would be substantial.

3.5 Given that no appropriate study design could be carried out in the local context, and the potential risks were unavoidable in a practical setting, the Monitoring Group concluded that the study should be wound up at this juncture for the safety of the study participants.

3.6 In conclusion, based on the available evidence and experience accumulated from the present study, subsidized naltrexone maintenance therapy is not recommended to be provided in Hong Kong.