Opioid detoxification

Dijkstra, Boukje A G; De Jong, Cor A J; Wensing, Michel; Krabbe, Paulus; van der Staak, Cees P F

Published in:
American Journal on Addictions

DOI:
10.1111/j.1521-0391.2010.00033.x

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2010

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.
Opioid Detoxification: From Controlled Clinical Trial to Clinical Practice

Boukje A. G. Dijkstra, PhD,1,2 Cor A. J. De Jong, MD, PhD,1,2,3 Michel Wensing, PhD,4 Paul F. M. Krabbe, PhD,5 Cees P. F. van der Staak, PhD2

1Novadic-Kentron, Network for Addiction Treatment Services, Vught, The Netherlands
2Nijmegen Institute for Scientist-Practitioners in Addiction (NISPA), Radboud University Nijmegen, Nijmegen, The Netherlands
3Department of Clinical Psychology, Radboud University Nijmegen, Nijmegen, The Netherlands
4Scientific Institute for Quality of Healthcare, Radboud University Medical Centre Nijmegen, Nijmegen, The Netherlands
5Department of Epidemiology, Biostatistics and Health Technology Assessment, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Controlled clinical trials have high internal validity but suffer from difficulties in external validity. This study evaluates the generalizability of the results of a controlled clinical trial on rapid detoxification in the everyday clinical practice of two addiction treatment centers. The results show that rapid detoxification in everyday practice differs with regard to patient characteristics, enrolment, and completion rates (86.8% vs. 100%). However, abstinence rates after rapid detoxification in the controlled clinical trial (61.8%) were generalizable to everyday clinical practice (59.0%). Implementation factors that may have influenced the results, such as referral problems and treatment delivery, are discussed. (Am J Addict 2010;19:283–290)

INTRODUCTION

Randomized controlled trials (RCTs) are considered as the “gold standard” for assessing treatment efficacy and the impact of healthcare interventions. RCTs are particularly successful in reducing all kinds of biases and increasing internal validity. However, controlling for factors optimizing internal validity can reduce the clinical relevance and external validity (generalizability) of the findings of an RCT study. For instance, controlling for treatment delivery and outcome measurements could limit the conclusions of the RCT in their range of application and treatment programs. Second, inclusion and exclusion criteria are applied to control for sample characteristics, whereby large segments of the general patient population are excluded. Another controlling factor is the optimized conditions (e.g., research clinic, experienced and highly classified clinicians, no time constraints) through which the RCT may be unrepresentative of regular clinical practice. Apart from this, the participant’s awareness of participating in an RCT can affect the treatment results, as does the availability of treatment preference.

All in all, RCTs create an “ideal condition” to measure the efficacy of an intervention, but it is unclear if the intervention is equally effective under normal conditions. Making evidence from scientific studies available to clinical practice is expected to improve the quality of care. This expectation is not always realized due to the complexity of healthcare. As Black states, “Randomized trials generally offer an indication of the efficacy of an intervention rather than its effectiveness in everyday practice.” Victoria et al. report two types of effect modification that must be considered when the generalizability of RCT results is assessed: the first consists of factors affecting the dose of the intervention (e.g., changes in providers, promotion of compliance); the second consists of lower response due to the presence of other factors (e.g., other population criteria, other cointerventions, missing a critical cofactor, other causes of the outcome measure). Another factor to consider is treatment integrity, being the extent to which an intervention is implemented as intended or planned. This later function includes treatment adherence (how often the intended therapy is or is not provided) and competence (how skillfully or poorly the treatment techniques are applied).

Rapid detoxification has been shown to be an effective approach to the management of opioid withdrawal. In the Netherlands, an RCT was conducted in which the addition effect of general anesthesia was examined during rapid
detoxification induced by naltrexone. General anesthesia proved to be equally effective, although with less safety and higher costs. This was also confirmed by other studies.

In a reevaluation according to a naturalistic design, it proved that rapid detoxification produced convincing completion and abstinence rates at 1, 10, and 16 months. Abstinent patients displayed significantly improved health when compared to their baseline health state and to those in the relapsed group. As professionals and the Dutch Ministry of Health were convinced of the effectiveness of the rapid detoxification treatment, its implementation without anesthesia was started by clinical addiction treatment centers in 2003. However, it was not clear if the results of rapid detoxification from a controlled clinical trial could be transferred to everyday clinical practice. Thus, in this study we sought to determine the effectiveness of rapid opioid detoxification without anesthesia in two clinical addiction treatment centers in the Netherlands (implementation study), comparing the treatment outcomes with those from the previously mentioned controlled clinical trial.

Specifically, the goals of our study were to compare the results between the controlled clinical trial and the implementation of the same treatment protocol in everyday clinical practice on

1. patient characteristics;
2. patient enrolment and completion rates;
3. validity of self-reported opioid use; and
4. abstinence rates at 1-month follow-up.

Some implementation factors that could possibly influence the results are mentioned in the “Discussion” section.

METHOD

Study Design

This study comprises an observational evaluation of rapid detoxification in clinical practice (the implementation study) and a comparison of the treatment outcomes with those of a previously published controlled clinical trial of rapid detoxification (the controlled clinical trial). The implementation study was conducted from June 2003 to August 2007. It was approved by the Dutch Ethical Assessment Committee for Experimental Investigations on People. We chose to compare the outcomes of the implementation study to those of the controlled clinical trial because the latter study provided data allowing comparison with regard to the type of addiction treatment centers, the patient populations, and the rapid detoxification protocol.

The controlled clinical trial was conducted from September 1999 to August 2001 to determine whether rapid detoxification under general anesthesia results in higher levels of opioid abstinence than rapid detoxification without anesthesia. Only those patients treated without general anesthesia were taken into account for the purposes of outcome data comparison.

Patients

Patients were recruited on a voluntary basis. During the implementation study, opioid-dependent patients from five addiction treatment centers (Novadic, IrisZorg, Parnassia, Jellinek, and Kentron) were recruited for participation. Two centers provided the treatment (Novadic, IrisZorg) if the patients met the following criteria: diagnosed as opioid-dependent according to DSM-IV criteria, expressed the clear wish to become abstinent, were over 18 years of age, and had at least one nonopioid user in their social network. Exclusion criteria were severe somatic diseases or psychiatric disorders, pregnancy, and doubts about the patient’s willingness to cooperate. The doubts were based on the patient’s record of showing up at the intake appointments. Dependence on other drugs or current drug abuse was not an exclusion factor. Following a complete description of the study to the subjects, written informed consent was obtained.

During the controlled clinical trial, patients from four addiction treatment centers (Novadic, Jellinek, Parnassia, and Kentron) were recruited for participation. Three centers provided the treatment (Novadic, Parnassia, and Kentron) if they met the criteria described earlier. In addition to the inclusion criteria described earlier, two more inclusion criteria were applied for the controlled clinical trial, namely being familiar with the Dutch language and having made several previous unsuccessful attempts to abstain.

Enrolment

Patients interested in detoxification during the implementation study were informed about rapid detoxification by a professional responsible for assessment and referral. Those meeting the screening criteria underwent examination by a physician, who also took their medical history, to exclude individuals with severe somatic and psychiatric disorders. The assessment and referral committee made the final decision on whether a patient would be eligible for rapid detoxification and put him or her on the waiting list. On the day of admission to the treatment center, the patients were once again examined by a physician.

Compliance for the sake of enrolment was more promoted in the controlled clinical trial than in the implementation study by engaging research assistants during the assessment and referral procedure and offering the prospect of bypassing the waiting lists. The assistants were very active in the recruitment, as they received incentives for enrolling patients. Unlike the clinical trial, the implementation study did not provide staff incentives to encourage patient enrolment.

Treatment Protocol

The treatment protocol for the implementation study was exactly the same as that for the controlled clinical trial. In general, the program for rapid detoxification took 8 days—one for admission, three for detoxification, three for...
recovery, and one for discharge. Detoxification was induced on the second day by administering an opioid antagonist (naltrexone). Naltrexone was given orally at a dose of 12.5 mg (detoxification day 1), 25 mg (detoxification day 2), and 50 mg for the next 5 days. During the three detoxification days, the patients were treated for signs and symptoms of withdrawal according to a fixed schedule (see De Jong et al., for a detailed overview). During the 3 days of recovery, the patients were provided with a symptom-triggered treatment.

After discharge, the patients were treated as usual by the addiction care center. Aftercare consisted of a minimum of 3 months of naltrexone intake with supervision by a physician. This differed from the controlled clinical trial in which all patients followed the Community Reinforcement Approach protocol consisting of 23 sessions administered by physicians and psychosocial therapists.

**Implementation Interventions**

The implementation study applied the following interventions:

**Informing patients, healthcare professionals, and others.** To inform patients and members of the general population, the availability of the new treatment was announced in a press release, in local and free newspapers, and on the Internet. Brochures and posters were distributed among patients in methadone programs, and information sessions were given on request. Letters, brochures, and e-mails were sent to healthcare professionals at the participating addiction centers to inform them of the possibility for treatment and to educate them about the diagnostic criteria for rapid detoxification and the enrolment procedure.

**Informing healthcare professionals involved in the assessment and referral procedure.** Detailed educational sessions and a conference on rapid detoxification were organized for healthcare professionals working with opioid-dependent patients. Protocols and checklists were made available to the healthcare professionals responsible for the assessment and referral procedure, to members of the committee for assessment and referral, and to the administrator of the waiting list. All physicians were trained with regard to the medical screening, the study inclusion and exclusion criteria, and the side effects of naltrexone. They were also provided with detailed information on the rapid detoxification procedure and naltrexone maintenance.

**Informing and training healthcare professionals on the new treatment.** Nurses and physicians from the detoxification unit were trained in the rapid detoxification procedure for which detailed protocols were available. They received information about the side effects of medication used during rapid detoxification, about withdrawal symptoms, and about possible complications that may occur during rapid detoxification. Additional nurse training was given in blood pressure measurement, medication injection, and observation for dehydration. A nurse experienced in rapid detoxification supported the detoxification unit during the three detoxification days.

The implementation interventions were highly comparable for both studies, except for the assessment and referral procedure. Because special assignment was available in the controlled clinical trial (see “Enrolment” section), the healthcare professionals were only informed about the inclusion and exclusion criteria for patients and how to refer them to a research assistant.

**Outcome Measures**

Research assistants assessed patients at baseline (admission) and at 1-month follow-up. We compared the characteristics of the patients, patient enrolment, and treatment completion rates across the two studies. Patients were divided into four groups: included, not started, drop-out versus completed, and lost to follow-up (Fig. 1). Because of the considerable amount of missing urine specimens in the implementation study and the possibility of underreporting of opioid use by self-report, we carried out a check on agreement between self-report and urine test results to measure the validity of self-report. After that, an overall abstinence rate at 1-month follow-up was computed for those patients who had started rapid detoxification (regardless of completion).

Treatment results were measured with the EuropAddiction Severity Index (EuropASI) and urine specimens. The EuropASI measures the severity of addiction in eight domains: physical health, work/education/income, alcohol, drugs, legal problems, family/social relationships, psychological/emotional complaints, and gambling. The EuropASI was used for treatment entry scores, but also for self-report of opioid use at 30 days after detoxification. Urine specimens taken 30 days after detoxification were analyzed for psychoactive substances by an approved laboratory. Screening was performed on an Olympus AU 600 analyzer after immunoassays. The parameters screened for, the specific techniques used, and the cut-off values were as follows: for opiates—EMIT II, cut-off 300 ng/mL morphine; for methadone—CEDIA, cut-off 100 ng/mL EDDP.

**Data Analysis**

Differences in the baseline characteristics and in enrolment, completion, and abstinence rates between the implementation study and the controlled clinical trial were analyzed with the \( \chi^2 \)-test (Pearson) for categorical data and the independent \( t \)-test for continuous data.

A check on agreement between self-report and urine test results was carried out. Data from both studies was combined to make more data available for comparison. Opioid abstinence 1 month after detoxification was defined as a self-report of no heroin, methadone, or other opioid use in the last 30 days. If patients reported opioid use or had a positive urine analysis for opioids 1 month
after detoxification, they were defined as nonabstinent (Table 2).

All statistical tests were 2-sided, with a \( p \) value of .05 or less considered to indicate statistical significance. The statistical software package SPSS 15.0.1. was used for all the computations.

RESULTS

Patient Characteristics

Table 1 provides the sample characteristics of the two studies. Patients in the implementation study were significantly older (38.4 vs. 36.0 years), had higher educational levels (48.6% had secondary or higher education compared to 22.3% in the controlled clinical trial), used less heroin in the 30 days before admission (15.25 vs. 18.62), had lower EuropASI drug severity (5.71 vs. 6.24) and family/social severity scores (2.09 vs. 2.60), but had higher severity scores for work/education/income (2.73 vs. 2.10).

Patient Enrolment and Completion Rates

Over a period of 40 months, 121 patients were admitted for rapid detoxification in the implementation study. As this study did not record patient interest in rapid detoxification, it is unclear how many patients were interested in or met the inclusion criteria for rapid detoxification. Four patients (3.3%) did not start rapid detoxification: one because of the patient’s doubts, one because of anxiety, one because of intoxication (even though this was not an exclusion factor), and one for unknown reasons. Twelve patients (9.9%) did not complete the 3 days of detoxification (drop-outs) but 105 (86.8%) did (completers). No significant differences were found on any demographic characteristic between drop-outs and completers. The mean number of treatment days of all 117 patients who started detoxification was 7.19 (SD = 2.06), ranging from 2 to 14 days.

In the rapid detoxification group of the controlled clinical trial, a total of 135 patients were enrolled during 23 months. All 135 completed the 3 days of detoxification. The rates of completion were significantly different (\( \chi^2 = 19.04; \ p < .00 \)) between the implementation study (86.8%) and the controlled clinical trial (100%).

Validity of Self-reported Opioid Use

Defining opioid abstinence in terms of both negative self-report of opioid use and negative urine analysis was not possible for 49.2% of the patients. Given the possibility of underreporting, we carried out a check on agreement between self-report and urine test results. Data from both studies was combined to make more data available for comparison. Of both studies, only three patients (11.1%) with a positive urine analysis reported no opioid use. Thus, self-reported opioid use seems to be a valid method to define opioid abstinence (Table 2).

Abstinence Rates

Of the 121 patients in the implementation study, 45 (37.2%) were lost to follow-up at 1 month after rapid detoxification. Of the remaining 76 patients who started rapid detoxification, 61.8% could be rated as abstinent, whereas 27 (35.5%) were nonabstinent and two had missing values on self-report.
### TABLE 1. Baseline characteristics of patients by study

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Controlled clinical trial (n = 135)</th>
<th>Implementation study (n = 121)</th>
<th>Statistical significance test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean (SD)</td>
<td>35.99 (6.50)</td>
<td>38.37 (6.42)</td>
<td>(t = -2.95; &lt; .01^*)</td>
</tr>
<tr>
<td>Male (%)</td>
<td>81.5</td>
<td>81.0</td>
<td>(\chi^2 = .01; .92)</td>
</tr>
<tr>
<td>Country of birth (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Europe</td>
<td>82.5</td>
<td>92.0</td>
<td></td>
</tr>
<tr>
<td>Africa</td>
<td>6.1</td>
<td>3.0</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>6.1</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>Austr/Oce</td>
<td>.9</td>
<td>.0</td>
<td></td>
</tr>
<tr>
<td>Asia</td>
<td>4.4</td>
<td>3.0</td>
<td></td>
</tr>
<tr>
<td>Marital status (%)</td>
<td></td>
<td></td>
<td>(\chi^2 = 1.54; .46)</td>
</tr>
<tr>
<td>Married</td>
<td>18.0</td>
<td>13.9</td>
<td></td>
</tr>
<tr>
<td>Never married</td>
<td>65.6</td>
<td>73.3</td>
<td></td>
</tr>
<tr>
<td>Divorced/widowed</td>
<td>16.4</td>
<td>12.9</td>
<td></td>
</tr>
<tr>
<td>Employment (%)</td>
<td></td>
<td></td>
<td>(\chi^2 = 4.65; .10)</td>
</tr>
<tr>
<td>Full time</td>
<td>55.5</td>
<td>44.1</td>
<td></td>
</tr>
<tr>
<td>Part time</td>
<td>8.6</td>
<td>16.7</td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>35.9</td>
<td>39.2</td>
<td></td>
</tr>
<tr>
<td>Education (%)</td>
<td></td>
<td></td>
<td>(\chi^2 = 18.13; &lt; .01^*)</td>
</tr>
<tr>
<td>None</td>
<td>17.2</td>
<td>15.2</td>
<td></td>
</tr>
<tr>
<td>Lower</td>
<td>60.2</td>
<td>36.2</td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td>14.8</td>
<td>31.4</td>
<td></td>
</tr>
<tr>
<td>Higher</td>
<td>7.8</td>
<td>17.2</td>
<td></td>
</tr>
<tr>
<td>Opioid use in years, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age at first heroin use</td>
<td>19.87 (11.16)</td>
<td>18.01 (19.44)</td>
<td>(t = .90; .37)</td>
</tr>
<tr>
<td>Mean years of heroin use</td>
<td>12.14 (6.07)</td>
<td>12.13 (6.65)</td>
<td>(t = .01; .99)</td>
</tr>
<tr>
<td>Mean age at first methadone use</td>
<td>20.98 (21.17)</td>
<td>23.01 (20.85)</td>
<td>(t = -.72; .47)</td>
</tr>
<tr>
<td>Mean years of methadone use</td>
<td>7.35 (5.60)</td>
<td>7.75 (5.99)</td>
<td>(t = -.51; .61)</td>
</tr>
<tr>
<td>Opioid use in days, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heroin use last 30 days</td>
<td>18.62 (11.76)</td>
<td>15.25 (12.45)</td>
<td>(t = 2.10; .04^*)</td>
</tr>
<tr>
<td>Methadone use last 30 days</td>
<td>23.61 (10.08)</td>
<td>22.38 (11.53)</td>
<td>(t = .86; .39)</td>
</tr>
<tr>
<td>Number of previous drug detoxification</td>
<td>2.94 (3.37)</td>
<td>3.15 (3.55)</td>
<td>(t = -.46; .64)</td>
</tr>
<tr>
<td>treatments, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EuropASI Severity scores, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical health</td>
<td>1.12 (1.40)</td>
<td>1.18 (1.55)</td>
<td>(t = -.29; .77)</td>
</tr>
<tr>
<td>Work, education, and income</td>
<td>2.10 (2.29)</td>
<td>2.73 (1.97)</td>
<td>(t = -2.17; .03^*)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>.88 (1.69)</td>
<td>.98 (1.61)</td>
<td>(t = -.48; .63)</td>
</tr>
<tr>
<td>Drugs</td>
<td>6.24 (1.07)</td>
<td>5.71 (1.13)</td>
<td>(t = 3.48; &lt; .01^*)</td>
</tr>
<tr>
<td>Justice/police</td>
<td>1.65 (2.02)</td>
<td>1.78 (1.75)</td>
<td>(t = -.52; .60)</td>
</tr>
<tr>
<td>Family/social relations</td>
<td>2.60 (1.77)</td>
<td>2.09 (1.81)</td>
<td>(t = 2.11; .04^*)</td>
</tr>
<tr>
<td>Psychological/emotional problems</td>
<td>2.13 (1.92)</td>
<td>2.56 (2.04)</td>
<td>(t = -1.60; .11)</td>
</tr>
</tbody>
</table>

\(^*\) p-Value is statistically significant at the .05 level (2-tailed).

The controlled clinical trial had lost 18 (13.3%) patients at 1-month follow-up. The abstinence rate of the remaining patients (59.0%) was comparable to and not significantly different than that found for the implementation study. There were 43 nonabstinent controlled trial patients (36.7%), and five patients had missing values on self-report.

### DISCUSSION

In this study we sought to determine the effectiveness of rapid opioid detoxification in clinical addiction treatment centers (implementation study) by comparing the treatment outcomes with those from a controlled clinical trial. As treatment results, we included the patient...
characteristics, patient enrolment and completion rates, validity of self-reported opioid use, and abstinence rates at 1-month follow-up. The results show that rapid detoxification in everyday clinical practice differs with regard to patient characteristics, enrolment, and completion rates. Opioid abstinence rates after 1 month, however, were comparable to those from the controlled clinical trial. Some implementation factors that may have influenced the results will be discussed later.

**Patient Characteristics**

The first difference observed between the implementation study and the controlled clinical trial concerns the characteristics of enrolled patients. Despite broadening the inclusion criteria, some characteristics indicated less severe impairment among the implementation study population. This could not be explained by differences in environment. The older age of patients in the implementation study could be explained by the lower percentage of young opioid clients during recent years and the older age of the general population of opioid users in the Netherlands. Yet the age and gender of the implementation study population was representative of the opioid-dependent population in the Netherlands (80% being male and 42 years old in 2006). For patients in the controlled clinical trial, the drug problems were more severe than in our implementation study. This could be explained by exclusion of the criterion “several previous unsuccessful attempts to become abstinent” in the implementation study and the high motivation among the research assistants to provide a promising treatment for patients with chronic, severe drug problems. The other differences might be explained by the complex assessment and referral procedure of the implementation study. It may have proven especially challenging for patients with more family/social problems and lower educational levels, resulting in higher drop-out rates before admission.

**Enrolment**

Considering the longer duration of the implementation study, the lower enrolment of patients was striking. The inclusion criteria could not have had a negative influence on enrolment because they were less strict than in the controlled clinical trial. The difference in enrolment could probably be attributed to the participation of additional healthcare professionals in the controlled clinical trial, the differences in intervention delivery, and the measures taken to promote high compliance among patients. Compliance for enrolment in the controlled clinical trial was promoted by engaging research assistants in the assessment and referral procedure. Patients in the implementation study underwent the normal assessment and referral procedures, with their long waiting times and a good chance of getting unclear information. In the implementation study, rapid detoxification was not carried out continuously because of the required extra nurses and incurred additional costs. It was difficult to find a balance between enrolment and rapid detoxification delivery. In sum, the long waiting times during assessment and referral and the decrease in rapid detoxification delivery may have influenced the enrolment. As in the implementation study, the connection between waiting time and the high rate of “lost” patients has also been found in other studies, for example, Scheeres et al.

**Completion Rates**

Rapid detoxification in the controlled clinical trial obtained 100% completion rates. During the implementation study, 86.8% patients completed detoxification. This difference may be explained by the subject’s and/or clinician’s beliefs and treatment preferences and by the nature of the treatment offered. The principle of treatment preferences is often cited to explain why there is so little difference in outcome between groups. But in our case, we think that “treatment preference” could explain the 100% completion rate during the controlled clinical trial and the lower rate seen in clinical practice. During the controlled clinical trial, there was a high level of expectation from and a strong preference among the patients and clinicians for both experimental treatment and control treatment. After all, both options were “experimental” and thereby different.

---

**TABLE 2. Validity of self-report in the implementation study and the controlled clinical trial (n = 256)**

<table>
<thead>
<tr>
<th>Urine analysis</th>
<th>Negative</th>
<th>Positive</th>
<th>No data*</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-report opioid use last 30 days</td>
<td>Negative</td>
<td>88†</td>
<td>3†</td>
<td>28†</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
<td>15†</td>
<td>24†</td>
<td>20†</td>
</tr>
<tr>
<td></td>
<td>No data*</td>
<td>7§</td>
<td>8‡</td>
<td>63‡</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>110</td>
<td>35</td>
<td>111</td>
</tr>
</tbody>
</table>

*No data is the result of missing data or no follow-up response for self-report; for urine analysis it is the result of not submitting a urine specimen.
† Defined as opioid abstinent.
‡ Defined as nonabstinent.
§ Missing values.
∥ Lost to follow-up.
from the regular methadone-tapering program (ie, patients got a “special chance” to lead an abstinent life). By providing rapid detoxification in clinical practice with all of the above-mentioned implementation problems, the “novelty” may have been decreased and so may have the expectation level. Nevertheless, the completion rate, although not as high as during the controlled clinical trial, appeared to be quite satisfactory. Other rapid detoxification studies have found completion rates between 73% and 98%.20,27–33

Validity of Self-reported Opioid Use

For half of the patients it was not feasible to define opioid abstinence by the combination of negative self-report and negative urine analysis. However, self-report did prove to be a sufficiently reliable method for measuring abstinence in the patient population of both studies.

Abstinence Rates at 1-Month Follow-up

Because of the lower completion rates and the lack of a specified mechanism to ensure continuity of care between detoxification and aftercare programs (lower treatment integrity), it was expected that the abstinence rates would be lower in the implementation study than in the controlled clinical trial. This was not the case, however. For the patients in the implementation study who started rapid detoxification, opioid abstinence rates at 1 month (61.8%) were comparable to those from the controlled clinical trial (59.0%). This might be the result of less severe impairment in the implementation study population. Unfortunately, follow-up response in the implementation study (62.8%) was lower than in the controlled clinical trial (86.7%).

Strengths and Limitations of This Study

This study was a multicenter trial conducted in different clinical addiction treatment centers in the Netherlands. The implementation study was comparable to the controlled clinical trial with regard to the type of addiction treatment centers in which it was conducted, the patient populations in terms of their environment, and the rapid detoxification protocol utilized. Our study had the following limitations. First, it is unclear how many patients were lost during the assessment and referral procedures and why these patients did not start treatment. The second limitation is the lower follow-up response in the implementation study. There were several reasons for the loss to follow-up, but unfortunately we were not able to evaluate them in a consistent manner because the research was subordinated to the clinical practice. Yet as the lower follow-up response is directly related to the design of the study, we do not think this limitation could influence our results in a negative way.

Conclusion

In conclusion, the results show that rapid detoxification in everyday clinical practice differs from the controlled trial outcomes with regard to patient characteristics, enrolment, and completion rates. This could be the result of divergent assessment and referral procedures and different aftercare delivery. However, the completion rates for rapid detoxification in the implementation study were still comparable with those for the controlled clinical trial. Self-reported opioid use proved to be a sufficiently reliable method for ascertaining abstinence.

This study shows that abstinence rates after rapid detoxification in the controlled clinical trial were generalizable to everyday clinical practice and that rapid detoxification is an effective treatment option for opioid-dependent patients. In that light, assessment and referral procedures and treatment delivery should be optimized to provide rapid detoxification for more patients. Attention should be paid to completion rates and continuity of care between detoxification and aftercare treatment programs to ensure these positive results.

The Netherlands Ministry of Health, Welfare and Sports (VWS; The Hague, The Netherlands) and the Dutch Organization for Health Research and Development (ZonMw; The Hague, The Netherlands) funded this project under grants (31000060) for Novadic-Kentron, Vught, The Netherlands.

Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

REFERENCES
