



Time to first treatment interruption in the Chinese methadone maintenance treatment programme[☆]



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ABSTRACT

Background: Methadone maintenance treatment (MMT) in China was established in 2004. The purpose of the present study was to estimate client retention and identify client factors associated with longer times in treatment.

Methods: Data were abstracted from the MMT Data System from April 2008 to March 2010. Clients were considered to have interrupted treatment when they missed 30+ days of treatment. The median time in treatment was estimated using Kaplan–Meier methods and factors associated with the duration of treatment were evaluated using accelerated failure time models.

Results: Among 107,740 clients enrolled in MMT between 2008 and 2010, the median time spent in MMT among clients was 155 days but the majority (69%) did not attend every day. Estimated probabilities for treatment interruption were 53% at 6 months, 66% at 12 months and 77% at 24 months. Longer time in treatment was associated with doses ≥ 60 mg (Time ratio (TR) = 2.12, 95%CI = 1.96–2.30) and having tested negative on their last urine opiate test (TR = 2.15, 95%CI = 2.03–2.27). The effect of continued drug use was significantly modified by attendance. Sensitivity analyses indicated a dose–response relationship.

Conclusion: Irregular attendance suggests there are barriers to accessing services that need further attention. The Chinese MMT programme needs effective strategies to improve its treatment durations.

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1. Introduction

Methadone maintenance treatment (MMT) has been shown to be an effective treatment to prevent the harms associated with opiate use and injection, including reduced risk of blood-borne diseases, particularly HIV, and reduced engagement in criminal behaviours (Gowing et al., 2011; Marsch, 1998; Mattick et al., 2003). It is now used widely as a key strategy for the control of HIV among drug users (MacArthur et al., 2012). The optimal duration of the maintenance period varies between patients, but long-term (years) maintenance treatment is generally more successful at helping opiate users to rehabilitate and maintain a healthy lifestyle when compared with short-term or abstinence-oriented programmes. Data from the US Drug Abuse Treatment Outcomes Studies (DATOS) suggest that at a minimum clients need one year of treatment to

achieve positive outcomes (Hubbard et al., 1997; Simpson et al., 1997). Thus, retention is among the most important goals for any methadone programme.

Overwhelmingly, the dose of methadone is the most commonly reported predictor of retention, with higher doses (60–100 mg/day) most effective at retaining clients (Bao et al., 2009; Faggiano et al., 2003). Doses exceeding 100 mg/day may have additional benefits but consensus has still not been reached on this issue (Fareed et al., 2011). However, many other factors also influence retention. Employment, living with family/partner, younger age, gender, participation in counselling/training, shorter distance to the clinic and realistic treatment expectations are associated with better retention, while clients who may find it difficult to remain in treatment include those with prior and higher involvement in crimes or with the criminal justice system, longer history of heavy opioid use, poly-drug use, and more severe psychological dysfunction (Bao et al., 2009; Ward et al., 1999).

China introduced MMT as an HIV control strategy in 2004 in response to the rapidly rising number of heroin users presenting with HIV infection (Sullivan and Wu, 2007). The programme has seen a dramatic increase in the numbers of clinics opened, from just 8 pilot clinics in 2004 to 738 clinics by the end of 2011 (Ministry of Health of the People's Republic of China, 2012). Scale-up was

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prioritised in areas of greatest need based on there being >500 registered drug users (Yin et al., 2010). Ideally, clinics have 300 to 500 clients and at least eight trained staff, but this varies and there are many barriers to finding and keeping well-trained staff (Lin et al., 2010a).

Ongoing evaluation has noted the high drop-out rate as being among the programme's major problems (Yin et al., 2010). Limited evaluation from some provinces has so far suggested that better retention is predicted by average doses above 60 mg/day, no history of forced detoxification, a maintenance goal, convenience of the clinic, the availability of ancillary services such as counselling, providing clients with incentives for participation and longer opening hours (Chawarski et al., 2011; Che et al., 2010; Gao, 2006; Li et al., 2007; Lin et al., 2010b; Liu et al., 2009; Yang et al., 2013). In addition, fear of arrest when accessing MMT services deters some clients from continuing or even commencing treatment (Cohen and Amon, 2008; Li et al., 2007). While these studies have provided important information for improving provincial programmes, there has been no evaluation of retention across the entire country. Such an evaluation would provide policy makers with a broad view of the impact the programme and permits comparison of the Chinese experience with that from abroad. Thus, the present study aimed to examine the average duration of treatment and factors associated with the time spent in treatment across China.

2. Methods

2.1. Data collection

Permission was granted by the internal review board of UCLA to conduct the study. Clients were accepted into MMT if they were aged at least 20 years, were registered as a local resident, met the Chinese Classification of Mental Disorders 3 criteria for drug dependence, had no contra-indications for taking methadone and agreed to the clinics rules (Sullivan, 2011; Yin et al., 2010). Upon admission to the programme, clients were required to provide demographic information and a brief drug-use history. Within the first week of treatment, a baseline questionnaire was administered in private by a member of staff to collect information on drug-use, sexual and criminal histories, and social functioning (i.e., involvement in crimes, employment and relationship with family and friends). Clients also provided a blood sample to assess HIV, hepatitis C and syphilis status, and a urine sample for opiate testing. During treatment, clients presented daily for their methadone dose and monthly urine-opiate tests were performed on a random schedule. The complete list of variables collected on patients can be found in table S1 of the supplementary material.¹ Staff received training in completion of data collection forms and conducting client interviews following the quality control measures outline in the programme's protocol, which was developed by the MMT Secretariat. A standard form was used across clinics and data were entered into the data system by a designated member of staff at each clinic. Paper forms were stored at clinics. Responses were checked prior to entry and data were cleaned prior to analysis.

Each day, the dose provided to the clients was recorded in the database. The absence of a dose for a particular day was assumed to indicate no dose was taken that day. No take-home doses were permitted. From this information, it was possible to calculate the median dose for selected periods (e.g., first week, last week, entire treatment episode) as well as measure day-to-day variation in dose and daily attendance. Clients whose records indicated they had received different doses within a week (e.g., from 50 mg to 80 mg) were classified as having changed their dose. Clients missing a dose during their last week were classified as having nondaily attendance. The attendance rate (%) across treatment was calculated as the number of days with a dose record among all days in treatment (last treatment date–first treatment date). Treatment interruptions were also identified from the daily dose record, where missing doses for 30 days or more were considered an interruption to treatment.

The data collected on all clients were maintained in the MMT data system, maintained by the National Centre for AIDS/STD Control and Prevention in Beijing. Since 2008, data have been uploaded in real-time, which led to dramatic improvements in the completeness of the data. For this reason, in this paper, analyses were restricted to clients who began treatment between April 2008 and March 2010. Although the clinics also maintained paper records with additional client information, only the information available from the data system was considered in these analyses due to the size of the dataset.

¹ Supplementary material can be found by accessing the online version of this paper at <http://dx.doi.org> and by entering doi:...

2.2. Statistical analyses

Baseline characteristics of clients were compared by dosage received (<60 mg/day versus ≥60 mg/day) by chi-squared test for categorical variables and by t-test for continuous variables. The duration of treatment was analysed using survival methods. Follow-up began on the date of entry, on or later than 1 April 2008 and ended when a client missed 30 days or more or on 31 March 2010. All treatment interruptions were considered negative outcomes, including voluntary (e.g., attempted abstinence) and involuntary withdrawals (e.g., incarceration, death). There was insufficient information in the data system to censor clients who left for reasons unrelated to the programme. Clients still in treatment at the end of follow-up were treated as censored observations.

Data were first reviewed using Kaplan–Meier survival analysis to estimate the median survival time and estimated probabilities of survival at different intervals (6, 12, and 24 months). Survival plots of treatment duration were generated, stratified by dose (<60 mg/≥60 mg), urine test result and attendance (daily versus non-daily) as these variables were considered *a priori* to be the most important.

To evaluate factors associated with treatment interruption an accelerated failure time frailty model was used. This is a parametric method which models the baseline survival function $S_0(t)$ of people in a cohort multiplied by an acceleration factor φ

$$S(t) = S_0(\varphi t)$$

where φ is a constant that stretches or shrinks the survival curve depending on the covariates

$$\varphi = \exp(b_1x_1 + b_2x_2 + \dots + b_px_p)$$

The exponentiated effects of φ are expressed as time ratios (TR), where shorter times until failure ($\varphi > 1$) suggest a longer time to event (e.g., TR = 1.5 suggests a 50% longer time until failure event) (Bradburn et al., 2003; Cox and Oakes, 1984 pp 64–70). As a parametric method, one must specify the distribution and a log-normal distribution was preferentially chosen because previous studies suggest that dropout from MMT is high early on and later levels off. Comparison with other distributions using the Akaike information criterion (AIC) suggested this distribution had the best fit (Cleves et al., 2008). Since it was expected that clients attending the same clinic would be more similar to each other than to clients attending different clinics, a frailty component (random effect) was included in the model to induce dependence between clients within clinics. Failing to do this would underestimate the standard errors. For clients who moved between clinics during a treatment episode, their clinic cluster was the clinic where they started treatment. Regression models were estimated in Stata with the *streg* function, using the *shared* option to identify frailties (Gutierrez, 2002; StataCorp, 2009). Given the large dataset we considered effect sizes of >2 (<0.5) to be meaningful rather than statistical significance.

The main effect of interest was the median methadone dose in the last week of treatment, categorised into <60/≥60, consistent with current treatment recommendations. We chose the last week of treatment as we believed *a priori* that the most recent dose would be a better predictor of dropout than the median dose throughout treatment. In a sensitivity analysis, the median dose was examined in 20 mg categories to see whether higher doses resulted in longer times in treatment, since evidence in this regard has been conflicting (see introduction). The covariates considered in the model included those previously identified as being associated with retention (as described in the introduction), including gender, ethnicity, employment, education, marital status, whether lived with family/partner or alone, length of commute (≤10 mins, 10–30 min, 31–60 min, >60 min), duration of drug use, continued opiate use while in treatment (based on last available urine test), history of criminal behaviour, attendance (categorised as <2 days/week, 3–4 days, ≥5 days), availability of counselling services at the clinic, and HIV and hepatitis C status. We explored several interactions among variables and retained only those showing a statistically significant effect ($\alpha = 0.05$).

Although no client was missing data for the main exposure (dose) or the outcome (treatment interruption and duration of treatment), some were missing data for one or more covariates. Therefore, we used multiple imputation to permit use of the entire dataset for regression models. Imputation was performed by chained equations to create 20 imputed datasets. Clinics missing the entire baseline record for more than 10% of their clients were excluded. Further description can be found in the supplementary material.¹ All statistical analyses were performed using Stata version 11 (StataCorp, 2009).

3. Results

Between April, 2008 and March, 2010 108,130 clients started MMT for the first time at one of 540 clinics included in the study. Of these, dose information was missing for 390 clients, implying these clients never received a dose of methadone. These clients differed from those who did have a dose record in some ways; a greater proportion were non-Han, had recently shared needles and were HCV-positive, while fewer had recently injected drugs (data not shown).

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