A National Study of the Retention of Irish Opiate Users in Methadone Substitution Treatment

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Background: Retention in treatment is a key indicator of methadone treatment success. The study aims to identify factors that are associated with retention.

Objectives: To determine retention in treatment at 12 months for Irish opiate users in methadone substitution treatment and to indicate factors that increase the likelihood of retention. **Methods:**

National cohort study of randomly selected opiate users commencing methadone treatment in 1999, 2001, and 2003 ($n = 1269$). **Results:** Sixty-one percent of patients attending methadone treatment remained in continuous treatment for more than 1 year.

Retention in treatment at 12 months was associated with age, gender, facility type, and methadone dose. Age and gender were no longer significant when adjusted for other variables in the model. Those who attended a specialist site were twice as likely to leave methadone treatment within 12 months compared with those who attended a primary care physician.

The most important predictor of retention in treatment was methadone dose. Those who received <60 mg of methadone were three times more likely to leave treatment. **Conclusion:** Retention in methadone treatment is high in Ireland in a variety of settings.

The main factors influencing retention in methadone treatment was an adequate methadone dose and access to a range of treatment settings including from primary care physicians. **Scientific Significance:** Providing an adequate dose of methadone during treatment will increase the likelihood of treatment retention. Methadone treatment by the primary care physician is a successful method of retaining opioid users in treatment.

Keywords: methadone, opiate dependence, addiction, treatment, treatment retention, treatment setting

INTRODUCTION

Problematic opiate misuse has caused significant morbidity and mortality in Ireland since the 1980s (1). In Ireland, methadone is the most widely available opiate substitute for the maintenance of opiate-dependent persons (2). The aim of methadone maintenance therapy is to replace illicit opiate misuse with a licit oral medication in order to provide the individual with a stable lifestyle and to reduce the harms associated with opiate misuse. Methadone maintenance involves the daily administration of (the oral opioid agonist) methadone as a treatment for opiate dependence. There are currently over 8000 people receiving treatment in Ireland in a number of settings, including specialist addiction outpatient service, prisons, and primary care setting (3). A large majority (90%) are receiving treatment in the greater Dublin area.

Methadone substitution treatment has been shown to reduce the overall illicit drug use, reduce high-risk HIV-related behaviors, and reduce incidence of drug and property-related crime (4–9). Some studies have demonstrated the additional effects of methadone therapy, such as a stable lifestyle and reduced likelihood of negative health consequences (including overdose and death) (10). In Ireland, a recent cohort study reported similar findings (11).

Retention in methadone treatment is a key indicator of methadone treatment success (5,12,13). Ward and colleagues report that the retention levels in good quality community-based methadone maintenance programs were greater than 50% at 12 months after initiating the treatment (14).

Studies have found several factors, both pretreatment attributes of patient and in-treatment variables, that increase the likelihood of treatment retention (15). The patient variables include cessation of street opiate and cocaine use (16), female gender (17), and being a parent

(18). The in-treatment variables include methadone dose (19), greater treatment satisfaction (20), and psychosocial support in addition to medical therapy during treatment (21). A recent article examining retention categorizes several factors such as patient factors, program factors, and community factors (17).

Methadone dose has been found to have a dose-response effect with higher doses of methadone associated with better retention in treatment (19,22). In addition, methadone given at higher doses of between 60 and 100 mg/day has been found to be more effective than lower doses of under 40 mg/day in retaining opioid users in treatment (19,23). There is variability in the literature between countries and methadone maintenance programs of the dosages given and recommended (24,25). High levels of retention have been found in some studies, where average doses were 100 mg/day (18). Other studies have found a decrease in illicit opiate use during treatment with high versus moderate doses of methadone, but no difference in retention rate when measured at 6 month (26).

Some attention has been paid to setting and components of treatment in addition to medical therapy (21,27–29). Primary care physicians are increasingly becoming involved in the treatment and longer-term care of drug users (30–32). Studies have largely concentrated on the acceptability and feasibility of transferring care to the primary care physicians (30,31,33). Some outcome studies have found similar improvements at follow-up between primary care physician-treated patients and the clinic-treated ones (7,32,34) and better outcomes in some (35). The issue of retention in treatment services has not been addressed in relation to any differential between primary care and clinic settings.

Internationally, policy on the provision of methadone maintenance in a primary care setting differs. In Ireland, the provision of methadone treatment by primary care physicians is central to the drug treatment system. Since the setting up of a legal basis for methadone prescribing in 1998, and the central methadone treatment list (CTL), the health authorities have facilitated and supported training of general practitioners to enable them to get involved in the methadone prescribing protocol. Some primary care physicians expressed interest in having a substantial amount of involvement in the program and were willing to undergo training to enable them to initiate methadone prescribing. The training was overseen by the Irish College of General Practitioners. For many other doctors, particularly in areas where drug use was prevalent, they did not want to get involved in great detail in the methadone program but were happy to prescribe methadone for existing patients or take on new patients who had been stabilized. These doctors also underwent training from the Irish College of General Practitioners. Currently, one-third of patients receiving methadone maintenance treatment get this from a primary care physician.

In Ireland, data on retention rates at 12 months and relapse rates during the first year of treatment are not routinely available for a random sample of the population in treatment or as a trend over time. Irish and international

longitudinal outcome studies have used 12 months as a cutoff period for measuring retention in treatment (9,13,36), and improvement observed at 12 months has been shown to be maintained at 3 years (15).

In this study, we seek to determine retention rates in the national methadone maintenance program in Ireland at 12 months, for the years 1999, 2001, and 2003. Factors associated with higher levels of retention including, gender, treatment setting, and methadone dose are identified and discussed.

METHODS

In order to complete the retention study, we took a retrospective random sample of new entries of patients registering with the CTL for the years 1999, 2001, and 2003 with 1999 as the first year, as this was the first year for which there were complete figures. The numbers of patients commencing treatment (registering on the CTL) in these years were 3916, 5378, and 5497, respectively. This number was 71% of the number of patients on the treatment register for the years in question, 29% carrying over from previous years.

The international literature was reviewed to determine the appropriate sample size calculations. Studies indicate that about half of those who enter treatment will leave within the first 12 months of treatment (14). We expected that 50% of entrants each year will be retained in methadone treatment and used this as the anticipated population proportion of those retained in treatment. Using confidence levels of 95% and an absolute precision of five percentage points, the required minimum sample size for the 3 years was 1152 (8% of those commencing treatment).

The CTL is a real-time register of all patients who were prescribed methadone for opiate dependence in the Republic of Ireland. Data held include name, date of birth, gender, address, date of entry onto the list, and date of exit, with reason for exit. The list is maintained in the offices of the Drug Treatment Center Board (a national addiction clinic in Dublin) and is managed by the Health Service Executive, which is the national statutory health authority for the Republic of Ireland. Three staff maintain the list on a daily basis and report to the chairperson of the Methadone Prescribing Protocol Implementation Committee, one of the authors (JB). The list is a stand-alone list and is maintained with appropriate security arrangements, where security levels are constantly updated and are audited by an external security company. Data can be compressed into a zip file, and then encrypted and password protected before it is transmitted. Patients who leave treatment are exited from the list and are reentered for each new treatment episode. If the gap between the exit and reentry is less than 1 month, it is classified as continuous treatment.

Ethical approval for this study was granted by the Drug Treatment Center Board Ethics Committee. We sought the randomly selected clinical records for 1875 patients commencing treatment. The sample of entries was then

validated as to treatment status. The completeness of exits and accuracy of the exit information recorded on the CTL was compared with clinical notes. The accuracy of recording was good for demographic variables and moderately good for other variables. This has been reported elsewhere (37). The validated data from charts were used in this study. A number of records were not included; 273 (14.6%), 62 (3.3%) patients were in methadone treatment since the preceding year (not newly entered onto system and therefore excluded), 29 (1.5%) had incomplete exit data recorded, and 242 (12.9%) were attending a methadone detoxification program, a separate modality reported elsewhere (38). In total, 1269 of the selected patients attended the methadone maintenance program. This included 398 in 1999, 419 in 2001, and 452 in 2003; this was in excess of the number required for the minimum sample size.

We developed a data collection instrument that included the variables collected using the CTL entrance and exit forms as well as factors identified as being important from the literature to retention in treatment. Using the data collection instrument, we extracted data from each of the clinical records, and where patients were transferred to another treatment site, hospital, or prison, we followed the patient's record to ascertain the total period of continuous treatment. Each patient's name, address, date of birth, gender, date commenced on methadone, type of methadone treatment, prescribing doctor, date of last exit, and the reason for exit are recorded on the CTL. In addition to these data, we collected each patient's reported main problem drug, use of more than one drug, use of alcohol, use of benzodiazepines or cocaine prior to this treatment, injecting and sharing status, methadone treatment status, frequency of dispensing, and dosage at 3 months and 1 month prior to exit or the completion of 12 months in treatment. An average methadone dose was then constructed and used for further analysis.

In Ireland, there are various locations where methadone treatment can be delivered. They represent a tiered approach to the problems ranging from primary care up to specialized drug treatment centers. There is one national specialized treatment center (open 7 days a week) catering for the most complex patients. This center is staffed by a multidisciplinary team headed by addiction psychiatrists and would be in a position to provide a broad range of psychological inputs delivered by psychologists and counsellors in addition to psychiatrists in training. Community drug treatment centers are either large centers providing dispensing on site 7 days per week or smaller centers where multidisciplinary inputs are provided twice per week, and dispensing is in a community-based pharmacy. The large community drug treatment centers have a multidisciplinary team on site with medical care provided by primary care physicians and nurses, and psychosocial inputs provided by counsellors. In addition, these centers also receive support in terms of liaison psychiatric sessions under the supervision of addiction psychiatrists. The smaller community drug treatment centers are based in varied locations in the community with a team from the drug

treatment services attending twice per week. This team provide limited psychosocial inputs from a counsellor. Those patients attending primary care are considered, in general, to be the less severe end of the spectrum, and many have been stabilized in larger drug treatment centers prior to transfer to primary care. Those patients attending primary care would not have ongoing access to psychosocial interventions as many practices do not have counsellors attached.

When analyzing the data, we calculated the length of stay by recording retention of the patient in treatment at 1 year or by subtracting the date of exit (if less than 12 months) following admission from the first date of treatment for the treatment episode recorded on the clinical record. This provided the time (in months and days) in continuous treatment for each patient. The retention rate at 12 months for each annual cohort was calculated so as to track changes over time and 95% confidence intervals were calculated. Independent *t*-tests were conducted to determine whether there was a difference in the mean age and methadone dose, by time in treatment.

Retention at 12 months was modeled using logistic regression. Three groups of variables were considered for inclusion in each model: demographic characteristics, drug use and injecting practices, and treatment experience. To determine if these characteristics influence retention in treatment, the relationship between the variables and the treatment outcome was measured using chi-square tests. The independent variables analyzed were age group, gender, place of residence, drug-using characteristics, type of service provider, and average methadone dose.

RESULTS

The study population was 68.6% male and young with a mean age of 26 years. Seventy-five percent of the cohort was under the age of 30 years. There was not a significant difference in mean age by time in treatment ($F = 1.6, p = .20$). Almost three quarters of patients, 942 (74%), had injected drugs. Over half of these admitted to sharing drug injecting equipment. This was the first methadone treatment episode for 363 (28.6%) of patients. Many of the drug users, 913 (72%), had used more than one drug, in the month prior to the commencement of treatment. These drugs include benzodiazepines 623 (49%), and cocaine, 233 (18%). The use of alcohol was poorly recorded in clinical notes, but 101 patients (8%) indicated use in the previous month.

Methadone was dispensed daily to 1201 (95%) patients of the cohort in our study. The average dose was 58 mg/day, 20.9 SD. There was a significant mean difference in average dose by time in treatment ($F = 3.1, p = .05$). The average daily dosage of methadone was calculated for the three settings. The differences are small but statistically significant ($p \leq .01$): 60 mg/day in the specialist center, 59 mg/day in the community clinic, and 53 mg/day in the primary care setting.

Of the 1269 patients attending methadone treatment, 770 (60.7%) remained in continuous treatment for more

than 1 year. There was a statistically significant increase in the proportion of patients retained in treatment over the study period, with 223 (56%) in 1999, 261 (62%) in 2001, and 286 (63%) in 2003 (chi-square test for trend = 4.52, $p = .03$).

Of the 499 (39%) patients who exited treatment before the end of 12 months, the exit reason was recorded in 40% of cases. Most were recorded as treatment failure. Treatment failure includes: returning to opiate use, no longer resident in Ireland, no contact for 1 month, and being asked to leave treatment. Other reasons for nonretention of patients included patients moving to a detoxification modality (61) and being sent for medication-free therapy. Five patients in the cohort died. Though we have no further information of the deaths, the number of deaths among patients on the CTL has been found to be low (3).

Retention in methadone treatment at 12 months was independently and positively associated with an older age group, female gender, attendance at a primary care physician, and a methadone dose of 60 mg/day or higher (Table 1). Factors that were not associated with retention were year of treatment, place of residence, use of more than one drug, use of benzodiazepines, cocaine, alcohol or injecting status, sharing injecting equipment, or first treatment episode.

A logistic regression model was used to determine factors that would predict retention in treatment at 12 months. When age was adjusted for in the model, it was no longer an independent factor in retention. Gender continued to be a significant factor, with men more likely to leave methadone treatment before 12 months (Table 2). Those who attended a specialist addiction treatment service site were two times more likely to leave methadone treatment within 12 months compared with those who attended a general practitioner. The most important predictor of retention in treatment was methadone dose. Patients who received <60 mg/day of methadone were three times more likely to leave treatment than those who received 60 mg/day or more.

Daily methadone dosage was the strongest predictor of retention in treatment. Average dosage was grouped using several cutoff points, and odds ratios (ORs) were calculated using chi-square test for trend (61.43, $p \leq .001$): <20 mg (OR = 1.00 baseline), 21–40 mg (OR = 2.99), 41–60 mg (OR = 7.10), 61–80 mg (OR = 9.52), and 81–100 mg (OR = 11.38). The cutoff points were selected to represent the clinical practice in Ireland. It was noted that increase in dose was associated with increasing retention in treatment (Figure 1). This increasing trend in retention remained when the data were stratified by gender and type of treatment facility.

DISCUSSION

Retention in methadone treatment is high in this study (61%) and consistent with data from studies in Ireland. Irish research indicates a higher retention in methadone treatment (79%) (9) than the 50% suggested by Ward and Hall (10). Moreover, across settings, the Research

Outcome Study in Ireland (ROSIE) study found a similar dropout/exit rate from methadone treatment (of 20%) (29). The main factors influencing retention in methadone treatment in this study were the average methadone dose while in treatment, gender, and access to treatment from primary care practitioners.

Age was found to be a predictor of retention in treatment in this analysis but not when covariates of treatment and average methadone dosage were taken into account. This may be due to the young age of the cohort overall. Gender has been associated with better retention in treatment with females more likely to be retained (17,39). This was consistent with our results, and though reasons in the Irish cohort are not clear, Kelly (17) found that males scored lower on the readiness for treatment scale.

Our finding that higher methadone dosage (>60 mg/day) predicts long-term retention in treatment replicates the work of others (19). In addition, our study shows a dose response in which retention rates increase as methadone dose increases to a ceiling of 100 mg/day. Most gains in treatment retention are seen between the 20–40 mg and the 41–60 mg cutoffs with only modest gains after that. The implication of these findings are that adequate clinical dosages of methadone after stabilization are important for maintaining patients in treatment and that recommended guidelines should be considered.

There has been a general movement in Ireland to provide services including addiction services in the primary care sector. The treatment of opiate users by primary care physician is shown in this study to be a highly effective policy in terms of retention of drug users in treatment. This setting has the potential to deliver treatment in a less stigmatizing environment (40) and to increase satisfaction with treatment (32) by tailoring treatment to individual needs (20).

The analysis indicates a small but significant difference in the average daily dose of methadone across the three settings. This variation should be further explored as it is not possible to determine from our data why the settings differ in terms of their methadone dosage practice. This variation may be due to variation in patient characteristics, prescribing, or different clinical approaches. There are no standard clinical practice guidelines in Ireland, though the UK guidelines are widely followed.

It must be noted that specialist centers in Ireland often have a client base that is more chaotic in their drug use, including drug users who are of no fixed abode or who have comorbidities and would not be suitable for treatment in a primary care setting. It is a limitation of this study that we were not able to control for these potentially confounding factors. In Ireland, drug users are often transferred from the specialized clinics into the community drug treatment centers and general practice when a particular degree of stability has been attained. This could be an important factor, and therefore further study should be considered to determine what factors influence these patients pathway.

The CTL is a national administrative database and it was not established as a clinical database and has limited clinical information. This is a limitation of this study as

TABLE 1. Demographic, drug using, and treatment characteristics of the sample by length of time in continuous treatment, 1999 to 2003.

	Time in treatment				Total	Test of association
	More than 12 months in continuous methadone treatment		Less than 12 months in continuous methadone treatment			
	<i>n</i> = 770, <i>n</i> (%)		<i>n</i> = 499, <i>n</i> (%)			
Year (<i>n</i> = 1269)		1999	223 (56.0)	175 (44.0)	398	
		2001	261 (62.3)	158 (37.7)	419	
		2003	286 (63.3)	166 (36.7)	452	χ^2 trend 4.5, <i>p</i> = .03
Age in years (<i>n</i> = 1269)		13–19	63 (51.2)	60 (48.8)	123	
		20–29	507 (60.7)	328 (39.3)	835	
		30–39	150 (61.7)	93 (38.3)	243	
		40–59	50 (73.5)	18 (26.5)	68	χ^2 trend 7.2, <i>p</i> = .007
Gender (<i>n</i> =1269)		Male	509 (58.5)	361 (41.5)	870	
		Female	261 (65.4)	138 (34.6)	399	χ^2 trend 5.5, <i>p</i> = .02
Ever injected (<i>n</i> = 1238 ¹)		Yes	564 (59.9)	378 (40.1)	942	
		No	189 (63.9)	107 (36.1)	296	χ^2 trend 1.5, <i>p</i> = .22
Facility type at start of treatment (<i>n</i> = 1269)		Specialist addiction treatment center	76 (49.7)	77 (50.3)	153	
		Community drug treatment center	524 (61.1)	334 (38.9)	858	
		Primary care setting	170 (65.9)	88 (34.1)	258	χ^2 trend 10.8, <i>p</i> = .005
First time ever prescribed methadone (<i>n</i> = 1129 ¹)		Yes	228 (62.8)	135 (37.2)	363	
		No	455 (59.4)	311 (40.6)	766	χ^2 trend 1.2, <i>p</i> = .27
Average methadone dose (<i>n</i> = 973 ¹)		59 mg or less	317 (65.5)	167 (34.5)	484	
		60 mg or more	411 (84.0)	78 (16.0)	489	χ^2 trend 44.4, <i>p</i> < .0001

¹Data were not available for all variables in the clinical records, therefore some answers do not add to 1269 cases.

TABLE 2. Factors associated with retention in treatment at 12 months using a logistic regression model.

	Total*	Adjusted odds ratio (95% CI)	p-Value
Gender			
Male	870	1.4 (1.0–2.0)	.03
Female	399	1	
Facility type			
Specialist drug treatment center	153	2.0 (1.2–3.5)	.01
Community drug treatment center	858	1.2 (.8–1.7)	.4
Primary care setting	258	1	
Average methadone dose			
59 mg or less	484	3.0 (2.2–4.0)	.0001
60 mg or more	489	1	

Initial models included age, injecting drug use. Significant factors were retained in the final model.

For whole model, χ^2 trend = 56, $p < .0001$.

*Numbers do not always add up to total because not all respondents answered all questions.

FIGURE 1. Methadone doses in milligrams by retention in treatment at 12 months.

contextual information is not always recorded in detail and variables are limited when data are gathered for administrative purposes. It is however a mandatory reporting system and has high levels of completeness. We accept that recording of some variables, especially alcohol and to some extent polydrug use, were most likely underreported. Further research needs to be undertaken to indicate which factors most contribute to an increase in retention of opiate users in treatment, whether individual, treatment, or setting. Patient satisfaction, readiness for treatment, and treatment setting should be further investigated.

In conclusion, delivering treatment to opiate users in settings suitable to their needs, including by individual

primary care physicians, with moderate to high daily dosage of methadone has the potential to increase the retention of patients in methadone substitution treatment.

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Declaration of Interest

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

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