Report on the first government-funded opioid substitution programme for heroin users in the Western Cape Province, South Africa

G Michie,[1] BSc Hons, MB ChB, DA (SA), FCPsych (SA); **S Hoosain**,[2] BPsych, PGDip (Addictions Care); **M Macharia**,[1] PhD; **L Weich**,[1] MB ChB, MRCPsych, FCPsych (SA)

[1] *Department of Psychiatry, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa*
[2] *Sultan Bahu Treatment Centre, Mitchell's Plain, Cape Town, South Africa*

Corresponding author: *L Weich (lizew@sun.ac.za)*

Background. Although pharmacological opioid substitution treatment (OST) is a well-established treatment modality for heroin addiction, it is a relatively recent introduction in low- and middle-income countries.
Objective. To report on a pilot OST programme initiated in 2013 that was the only public-funded programme in South Africa (SA) at the time. Participants were offered standard care only (n=68) or, for the OST group (n=67), standard care plus Suboxone (Reckitt Benckiser), a synthetic partial opioid agonist, in a 12-week clinician-monitored programme.
Methods. Clinical records of 135 participants in the rehabilitation programme at Sultan Bahu Rehabilitation Centre in Mitchell's Plain, Cape Town, SA, from 1 January to 31 December 2014 were reviewed. Data collected included demographics and duration in treatment (retention) as well as number of urine samples provided, positive tests or self-reported use events and dates of first positive/negative tests.
Results. Significantly more participants in the OST group (65.7%) than controls (44.1%) completed the treatment (p=0.019). Among the non-completers, retention was higher in the OST group than in the standard care group (48.2 v. 30.1 days; p=0.001). The groups did not differ in respect of number of missed appointments and time to first positive test. However, the proportion of participants testing positive was higher in the OST group (80.6%) than in the standard care group (61.8%), although the former were tested nearly three times (18.3 v. 6.6 times) more. Consequently, the positive rate (proportion of positive tests) was substantially lower in the OST group (16.8%) than in the standard care group (23.3%).
Conclusions. The results demonstrate modest success of this pilot OST programme in terms of completion and retention and should argue for a move to increase availability of and accessibility to OSTs for the management of opioid use disorder.

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Globally, in 2010, there were an estimated 15.5 million opioid-dependent people, with opiate use disorder accounting for 9 million disability-adjusted life-years. North America, Eastern Europe and southern sub-Saharan Africa are among the countries most adversely affected.[1] The growing recognition of opioid misuse, especially of injectable opioids, has resulted in the need for effective, evidence-based strategies to reduce the growing burden.

Pioneered in the 1960s,[2] opioid substitution therapy (OST) has emerged as the pre-eminent treatment for heroin use disorder. The treatment involves prescribing controlled amounts of less euphoric long-acting synthetic opioid agonists or partial agonists, usually methadone or buprenorphine, to reduce cravings, prevent the euphoric effect of use and prevent withdrawal symptoms.[3] Being long-acting, the agonists can be dosed once daily, thus eliminating the need for multiple daily heroin doses. The intervention stabilises users' drug-using lifestyle, reducing criminal and other high-risk behaviour, including needle sharing and promiscuity that predispose to HIV and other diseases, and improving adherence to antiretroviral treatment for those living with HIV.[4] Much of the evidence for OST's effectiveness, however, has been generated in developed countries where such programmes are well-established components of HIV prevention and drug treatment strategies. Although sub-Saharan Africa accounts for 71% of the global HIV population[5] and an estimated 1 778 500 injectable drug users[6] (IDUs), only five of the 45 countries in the region have OST programmes accessible to the general public.[7] There is a need for evidence regarding outcomes of these programmes in the South African (SA) context in order to strengthen the case for scaling up of services.

The objective of this study was to report on the first, and at the time of submission of this article the only, public-funded OST pilot programme for heroin users in SA. No robust population-based data on the extent of the heroin use problem in SA are available, but there were an estimated 12 000 - 18 000 users in Cape Town in 2004, 23% of whom were IDUs.[8] The use of heroin in Cape Town as the primary substance of abuse among participants presenting for substance treatment increased from 2% in early 1998 to 12.7% in 2014.[9]

The treatment of drug addictions in SA is overseen by the Department of Social Development (DSD), with support services provided by medical practitioners, psychologists and trained drug counsellors. Many non-profit drug rehabilitation centres operate in- or outpatient drug rehabilitation services, generally consisting of an initial intensive phase followed by continuing care thereafter. With funding from the DSD, this pilot OST project was initiated in 2013 at Sultan Bahu Rehabilitation Centre (SBRC), a non-governmental organisation in Mitchell's Plain, Cape Town. Although the programme has treated 168 people in its first 2 years, the demand for the service is much greater. Given the high cost of Suboxone

(Reckitt Benckiser), the opiate analogue used, objective evidence of the programme's effectiveness will be a prerequisite to changing government service planning models.

Since addiction is a chronic condition and extended treatment has the best outcomes, the retention rate of participants in OST is often a key indicator of the effectiveness of such programmes.[10] We compared retention time and response to treatment (measured through duration until first use of heroin and number of positive tests during the treatment period) for heroin users receiving OST plus routine treatment and those receiving standard care only at SBRC during 2014.

Methods

Study design and population

This naturalistic retrospective study was approved by the Stellenbosch University Health Research Ethics Committee (ref. no. S15/02/031) and conducted according to locally and internationally accepted ethical guidelines. Records of all participants in the rehabilitation programme at SBRC from 1 January to 31 December 2014 were reviewed. All participants received the centre's standard care, which includes an intensive initial day programme based on the Matrix Model,[11] followed by an aftercare phase. The treatment (OST) group was additionally offered a fixed-dose combination of buprenorphine and naloxone (4:1) (the opiate analogue) in the 12-week clinician-monitored programme. The addition of naloxone is designed to prevent diversion and misuse of buprenorphine as it would precipitate opiate withdrawal if injected but not when ingested, because naloxone is poorly absorbed sublingually. Participants were accepted into the OST programme after detailed assessment by a multidisciplinary treatment team in accordance with local and international guidelines for psychosocially assisted pharmacological treatment of opioid dependence. The general goal of the investigation is to evaluate the participants' current and/or historical social, medical, psychological and legal profiles to aid in assessing motivation and treatment goals in order to formulate an effective treatment plan.

Data collection and analysis

Data were obtained from clinical case notes kept by the treating facility, which comprised an initial extensive clerking and records of positive urine tests and episodes of self-reported use. Prescriptions of the opiate analogue as well as dispensing information were recorded separately. Retention in the programme was measured from time of enrolment to the end of the programme or drop out. Also recorded were the number of urine samples provided, total number of positive tests or self-reported use events, and dates of first positive/negative tests. General demographic data including sex, race, highest educational level attained and debut of substance abuse were also collected, as well as voluntary data on HIV status including date of last testing where available.

Data were summarised as means (standard deviations (SDs)) and medians (25th - 75th percentiles or range) for continuous variables and as counts and percentages for categorical variables. Distribution of traits between the two treatment groups was assessed using *t*- and χ^2 tests for quantitative and qualitative traits, respectively. All statistical analyses were performed using SPSS statistical software (version 23, IBM Corp., USA) and the level of statistical significance was set at $p<0.05$.

Results

Population demographics

The analysis excluded 33 records with missing core data and those from participants on a self-funded OST programme. Of the 135 analysable records, 68 (50.4%) were from participants receiving standard care only and 67 (49.6%) from those also receiving OST (Table 1). All participants were non-injecting users. The mean (SD) age was 28.5 (6.5) years, there were more males (91.1%) than females, and the majority were single (74.8%) and unemployed (96.3%). The

Table 1. Summary of demographic data

Variable	OST + standard care (*n*=67)	Standard care (*n*=68)	Total (*N*=135)	*p*-value
Age (yr), mean (SD)	28.7 (6.8)	28.3 (6.4)	28.5 (6.5)	0.700
Gender (male), *n* (%)	60 (89.6)	63 (92.6)	123 (91.1)	0.742
Substance use debut age (yr), mean (SD)	15.3 (5.0)	15.3 (3.2)	15.3 (4.2)	0.978
Marital status, *n* (%)				0.229
Single	52 (77.6)	49 (72.1)	101 (74.8)	
Married	8 (11.9)	15 (22.1)	23 (17.0)	
Divorced	5 (7.5)	4 (5.9)	9 (6.7)	
Widowed	2 (3.0)	0 (0)	2 (1.5)	
Highest level of education, *n* (%)				0.915
Primary school	15 (22.4)	14 (20.6)	29 (21.5)	
High school	52 (77.6)	54 (79.4)	106 (78.5)	
Employment, *n* (%)				0.024
Employed	0 (0)	5 (7.4)	5 (3.7)	
Unemployed	67 (100)	63 (92.6)	130 (96.3)	
HIV status, *n* (%)				0.573
Known	58 (86.6)	61 (89.7)	119 (88.1)	
Unknown	9 (13.4)	7 (10.3)	16 (11.9)	
Gang affiliation, *n* (%)				0.017
None	51 (76.1)	54 (79.4)	105 (77.7)	
Past	7 (10.4)	0 (0)	7 (5.2)	
Current	9 (13.4)	14 (20.6)	23 (17.1)	
Previous arrests, *n* (%)	58 (86.6)	53 (77.9)	111 (82.2)	0.190

OST = opioid substitution treatment; SD = standard deviation.

highest level of education attained was high school (grades 10 - 12) for the majority (78.5%), and this was similar in both groups.

An overwhelming majority of the participants (82.2%) had been arrested previously, and 17.1% admitted to current gang affiliation. Of the participants, 119 knew their HIV status, and 37.8% had been tested within the past year.

The mean debut age for use of illicit substances was 15.3 years (range 8 - 36 years) and 74 participants (54.8%) reported current polydrug use, with the drugs most likely to be used together with heroin being methamphetamine (90.5%) and cannabis (39.2%) (Table 2).

Main outcomes

As shown in Table 3, significantly more participants in the OST group (65.7%) than controls (44.1%) completed treatment (p=0.019). Among the non-completers, the retention rate was higher among OST participants than in the standard care group (48.2 v. 30.1 days; p=0.001). Participants in the OST group had a non-significant 2 days longer median duration to first positive drug test or self-reported use. The proportion of participants testing positive was higher in the OST group (80.6%) than in the standard care group (61.8%), although the former were tested nearly three times (18.3 v. 6.6 times) more. Consequently, the positive rate (proportion of positive tests) was substantially lower in the OST group (16.8%) than in the standard care group (23.3%). The dose of the opiate analogue prescribed in the OST group ranged from 2 mg to 16 mg (median 4 mg).

Discussion

The study evaluated the performance of SBRC, the first public-funded opioid substitution programme in SA, by comparing retention time and response to treatment with that of standard care. While the two programmes did not differ with regard to duration of abstinence from illicit opiate use during rehabilitation, we found that individuals in the OST group remained in treatment significantly longer and were more likely to complete the programme.

The proportion of participants completing treatment was significantly higher (65.7%) in the OST programme than in standard care (44.1%). Retention rates in treatment reported in the literature vary widely, but it is generally estimated that >50% of patients leave or are withdrawn in the first 3 weeks of treatment.[12-14] After 6 months of treatment, one study reported retention of 79%,[15] but others noted much lower rates of 58%,[16] 46%[17] and 27%.[18] In another study, an average of only 44% of buprenorphine clients spent at least 3 weeks in an Australian treatment facility.[19] The only other evaluation of an OST programme in Africa reported a retention rate of 57% over 2 years,[20] although it utilised methadone, which differs from buprenorphine with regard to retention.[17] The rate for the OST group in our study was therefore relatively high. Even among participants who did not complete treatment, those in the OST programme remained on average 18 days longer (p=0.001) than in the standard group. These findings concur with previous reports providing evidence of improved retention rates in OST-based rehabilitation programmes.[10]

Response to treatment, denoted by a lower proportion of positive urine tests, was significantly higher in the OST group. However, abstinence from illicit opiates in this group was very low, as shown by the exceptionally high proportion of participants (80.6%) testing positive compared with other longer-term treatment programmes.[21-22] While this may reflect international experience that longer periods than the SBRC's 12-week programme are necessary for higher abstinence, a possible reason for the low rate could be the high rate (54.8%) of concomitant use of other potentially destabilising drugs, which often leads to impulsive use of heroin during rehabilitation.[17] In addition, so that more participants could be included in a setting where funding was limited, a lower dose of the opiate analogue was used (median 4 mg) than that required to suppress illicit opioid use. While any dose above 2 mg retains participants in treatment, at least 16 mg is necessary to suppress illicit opioid use.[23]

An encouraging finding was that the vast majority (88.1%) of the participants knew their HIV status, and more than a third had been tested within the past year. Similar positive findings were highlighted by South African Community Epidemiology Network on Drug Use (SACENDU) data[9] and may reflect successes made in community education pertaining to opioid use disorder as well as provision of access to confidential testing facilities. This is significant, as this population is at increased risk of contracting viral illness through high-risk behaviours such as unsafe sexual practices.

Study limitations

This study was limited by its retrospective nature, which precluded uniformity in terms of dosing, frequency of urine tests and client selection and restricted the range of variables assessed. The use of doses lower than those considered necessary to suppress illicit opioid use further limits the generalisability of the results. Future

Table 2. Comorbid substance use (N=74)

Substance used*	*n* (%)
Cannabis only	4 (5.4)
Methamphetamine only	36 (48.6)
Cannabis + any other	25 (33.8)
Methamphetamine + any other	31 (41.9)
Any two drugs	19 (25.7)
Any three drugs	13 (17.6)

*Substance used in addition to heroin.

Table 3. Main outcomes assessed

Outcome	OST + standard care	Standard care	Total	*p*-value
Completion rate, *n* (%)	44 (65.7)	30 (44.1)	74 (54.8)	0.019
Mean retention in non-completers (d), mean (SD)	48.2 (20.7)	30.1 (11.4)	36.9 (17.8)	0.001
Number of missed appointments, median (IQR)	4.0 (2.0 - 10.0)	4.0 (1.0 - 10.8)	4.0 (1.0 - 10.8)	0.755
Did not miss any appointments, *n* (%)	11 (16.4)	13 (19.1)	24 (17.8)	0.853
Days to first positive test, median (IQR)	5 (0 - 42)	3 (0 - 41)	3.5 (1.0 -14.8)	0.783
Participants testing positive, *n* (%)	54 (80.6)	42 (61.8)	96 (71.1)	0.022
Number of tests, mean (SD)	18.3 (7.4)	6.6 (4.0)	12.4 (8.3)	0.001
Positive rate (%)	16.8	23.3	18.6	n/a
Opiate analogue (Suboxone) dose (mg), median (range)	4 (2 - 16)	n/a	n/a	n/a

OST = opioid substitution treatment; SD = standard deviation; IQR = interquartile range; n/a = not applicable.

prospective studies should include further outcome measures such as relapse rate, mortality, criminality and client quality of life, in addition to addressing community and individual factors such as participant motivation that are likely to influence retention and interact with other outcome measures. Future studies should also consider increasing the dose of the opiate analogue to yield reliable abstinence data.

Conclusions

The results demonstrate a modest success of this pilot programme in terms of completion and retention rates and should argue for a move to increase availability of and accessibility to OSTs for management of opioid use disorder. This and future local programmes should consider extending treatment duration, as longer treatment is often required for long-term recovery from opioid addiction.[24] Future studies should evaluate performance of these extended programmes, and include the wider and more robust outcomes mentioned earlier, together with additional measures such as more intensive psychosocial support with possible penalties for early dropouts. The design of such studies should also allow for a more systematic collection of data where variables, such as frequency of urine tests, are uniform and consistent to allow better analysis, interpretation and utility for evidence-based quality improvement. More investments in financial and human resources will be needed to address comorbid drug use, gang affiliation and skilling participants to enhance prospects for gainful occupation. To improve retention, consideration can also be given to inclusion of employment assistance, as some authors have suggested.[25]

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