The Post-Rehabilitation Recovery Effect of a Peer Mentoring Programme among Opiate-addicted Patients in England

CID:02073239

ABSTRACT

Background

Prevalence of opiate drugs misuse and unsatisfying post-rehabilitation recovery calls for opiate rehabilitation services optimization in England. The identification of new intervention methods to reduce drug relapse and facilitate restoration of social function after discharge is on demand.

Methods

A randomised controlled trial was initiated. Opiate-addicted patients were recruited, and all were under treatment of initial standard rehabilitation. After completion of treatment and discharge, patients were randomly allocated to peer mentor support programme or standard of care procedure and followed up for two years. The primary effectiveness outcome was days post-therapy of first relapse. The secondary outcome was a comprehensive social wellbeing score estimating the general social functions of patients one year after discharge.

Results

864 patients were included in the study. The overall hazard ratio of relapse for peer mentor programme compared to standard of care was 0.72 (95%CI 0.59 to 0.88). The hazard ratios of relapse for peer mentor programme relative to standard of care were different for the first four months (hazard ratio, 0.90; 95%CI 0.69-1.17) and four months to two years on treatment (hazard ratio, 0.54; 95%CI 0.40-0.74). The mean change of the social wellbeing score for the peer mentoring group compared with the standard of care group was 0.658 (95%CI -1.17 to 2.48). Sensitivity analysis showed robust results.

Conclusions

The peer mentor support programme effectively reduces relapse for opiate addiction patients; however, it does not promote their social function after one year. Longer trials are required to investigate social wellbeing in the long run.

INTRODUCTION

An enormous number of dependence and abuse of prescription opiate drugs is emerging in England. A recent investigation suggests that over half of drug-related deaths involve opiates in England[1]. In addition to opioid-related death trends, the expanding epidemic of opiate misuse and addictions are primary outcomes of chronic intake of opiate drugs[2]. Repeated exposures to opiate drugs can result in opioid use disorder (OUD), a psychiatric disorder detrimental to the patient's central nervous system, causing sustained behavioural changes[3], which could lead to adverse social impacts such as increased homelessness or criminal activities. To manage this, opiate drug rehabilitation and recovery have been provided by NHS alcohol and drug treatment services to people suffering from OUD. Conventional treatments include behaviour therapy and opioid-substitution therapy; however, the high prevalence of relapse after discharge is a significant concern for OUD patients[4]. Thus, there is an urgent need for the exploration of successful intervention methods to achieve positive post-rehabilitation treatment outcomes.

From 2017 to 2019, a randomised controlled trial has been conducted by NHS England to explore the contributing factors of rehabilitation treatment success and assess the effectiveness of a peer mentor support programme after completion of the rehabilitation therapy in England. We evaluated the effectiveness of this method on the reduction of opiate-abuse relapse and discussed its long-term influence on OUD patients' integration back into the local community.

METHODS

Trial Design

Patients are recruited between April and August of 2017. The study enrolled opiate-addicted patients presented for drug rehabilitation treatment in centres across four regions of England: Northwest, Southeast, West Midlands, and Northeast. Upon entry to rehabilitation therapy, patients were randomly assigned with a 1:1 ratio to peer mentor support programme group or normal standard of care group after completion and discharge from treatment. For patients in peer supporting group, each of them was assigned a rehabilitated addict residing in the same local neighbourhood as their peer mentor. Baseline data were collected upon completion of initial rehabilitation, including demographic characteristics, treatment entry characteristics, and initial treatment program success. Patients and their peer mentors were matched and introduced following discharge, and then they scheduled weekly meetings and monthly participation in social activities. The follow-up procedure started at the initiation of the peer mentor programme and lasted for 720 days before closing in July 2019. Follow-up encounters with patients were arranged every three months.

Assessment of Clinical Characteristics

Duration of previous opiate use was defined as the number of months of regular opiate use before entering initial therapy programme, rounded up to integer. The number zero represents that the duration of taking opiate was less than half a month. Injection history groups are categorised by the patient's injection status prior to initial therapy. Two groups were defined according to their injection status at baseline: patients were included in *no previous injection history* group if they had never injected; patients were categorised to *with injection history group* if they had previously injected or were injecting. Initial treatment results were defined according to whether patients remained abstained from opiate through the duration of rehabilitation therapy.

Outcomes

The primary clinical outcome was the number of days from being discharged from initial treatment programme to the day when the first relapse occurred. Relapse was measured during routine visits on a quarterly basis (every 90 days), and patients would be asked whether they had relapsed to taking opiate. If participants did not relapse at every visit before the study completion, no relapse would be recorded.

The secondary effectiveness outcome was the social wellbeing score. A study interview occurred at the twelfth months' visit, when the social wellbeing was measured. Social wellbeing score was a standardised continuous composite score that was constructed by capturing four aspects of the subjects' quality of life: employment, residence, social relationships and connections, and mental health.

Statistical Analysis

864 patients were followed up according to trial protocol. Some subjects were excluded in the analysis due to missing outcomes when lost to follow up happened. Comparisons based on randomised treatment assignments were performed with the use of intention-to-treat analysis. Descriptive summaries of baseline demographic and clinical characteristics were compared for each randomised treatment group. Continuous baseline variables were presented as median with interquartile ranges, and categorical variables were summarised with frequencies and percentages.

Factors associated with initial treatment programme success were analyzed with complete data. A logistic regression model was used to generate the odds ratio of initial treatment success for each additional month of opiate use prior to treatment, with p value and 95% confidence interval reported. Gender, age, and socioeconomic status (SES, represented by residence and housing status) were added as covariates in the adjusted logistic regression model. The proportion of initial treatment programme success is compared for patients with injection history and those without. The results were presented with risk difference and risk ratio estimates with p value and 95% confidence intervals.

Relapse-free survival for the primary effectiveness outcome was displayed by the Kaplan-Meier plot. The median relapse-free survival months and one year relapse-free survival rates were computed in each group by Kaplan-Meier estimates. Relapse-free survival were compared by log-rank tests, followed by Cox

regression to examine the hazard ratio comparing peer mentor group with standard of care group, with 95% confidence interval and p value reported. Participants lost to follow up before a relapse event arose or did not develop relapse event at the end of the study were defined as censoring. As there were noticeable numbers of patients lost to follow-up, gender, age, SES, injection history, duration use, and initial treatment success were considered confounders and were added as covariates in the Cox regression model. The proportional-hazards assumption was checked for the randomised treatment groups and all the covariates using Schoenfeld residuals test. Time-splitting cox-regression were performed according to prior specification, to examine whether the effect of the peer mentoring intervention on relapse differed for the first four months post-rehab and longer than four months after rehab. Subgroup comparisons were conducted by adding interaction terms between prespecified factors and intervention group. Gender and injection history were included in subgroup analysis according to prior assumption, stratified hazard ratios were presented with p value denoting statistical significance of interaction. Comparison of social well-being one year following treatment discharge in the two trial groups was conducted using a linear regression model, with p value and 95% confidence interval reported. Adjusted linear regression models were applied to control for gender, age, SES, injection history, duration use and initial treatment success.

Sensitivity analyses were applied to assess robustness of results to potential underreporting of outcomes due to loss of follow-up. In sensitivity analysis, all censoring cases were assumed to have experienced the relapse outcome when they were censored. Hazards of relapses were compared using the same Cox regression model as in initial analysis. Likelihood ratio tests were used to compare models. The overall significance level was at alpha equals to 0.05. All analyses were performed with R, version 4.1.1.

RESULTS

Patients and Baseline Characteristics

Overall, 864 patients were eligible and agreed to participate the trial during enrolment from April 2017 to August 2017 (Fig. 1). 433(50.1%) and 431(49.9%) were allocated to peer mentoring programme and standard of care group, respectively. A total of 658 (80.5%) had complete data on study outcomes (i.e., they completed the entire study, or left the study after endpoint relapse event occurred with wellbeing scores assessed). A total of 206(23.8%) lost to follow up at certain time points during the study, among which 37(4.3%) left the study with complete data, 76(8.8%) left after one year, and 49(5.7%) left the study at the beginning and never participated in any encounter visits. The number of patients left the study and the number of patients with complete ascertainment of study outcomes were equally distributed between the two groups ($p = 0.35$).

The demographic and clinical variables for patients at baseline are summarised in the two groups (Table1). At baseline, the median age was 39 years, 73.6% were male and 26.4% were female, respectively. 73.1% of patients lived in urban areas, 24.9% in Northeast, 23.4% in Northwest, 25.5% in Southeast, and 26.3% in West Midlands. The majority (60.7%) of the participants had no housing problem, whereas 38.7% had varying degrees of housing problem. The median duration of previous opiate use was 12 months. For injection history, 1.6% of the values were missing due to incomplete record. Those who had never injected accounted for 40.7%; the rest 57.6% had injection history, with 25.3% injecting continuously at baseline 32.3% injected previously. Among all patients, 483(55.9%) completed the initial treatment successfully with no substance use.

Influencing Factors of Initial Treatment Success

For all patients, the median and mean duration of opiate use was 12 and 18.3 months. The odds of initial treatment succuss for a patient with mean duration of drug use was 1.26(95%CI 1.11 to 1.45). For each additional month of opiate use, the odds of initial treatment succuss decreased by 0.989 times (95%CI 0.982 to 0.997, $p = 0.005$). Adjustment for age, gender and SES did not change the odds ratio ($p = 0.728$).

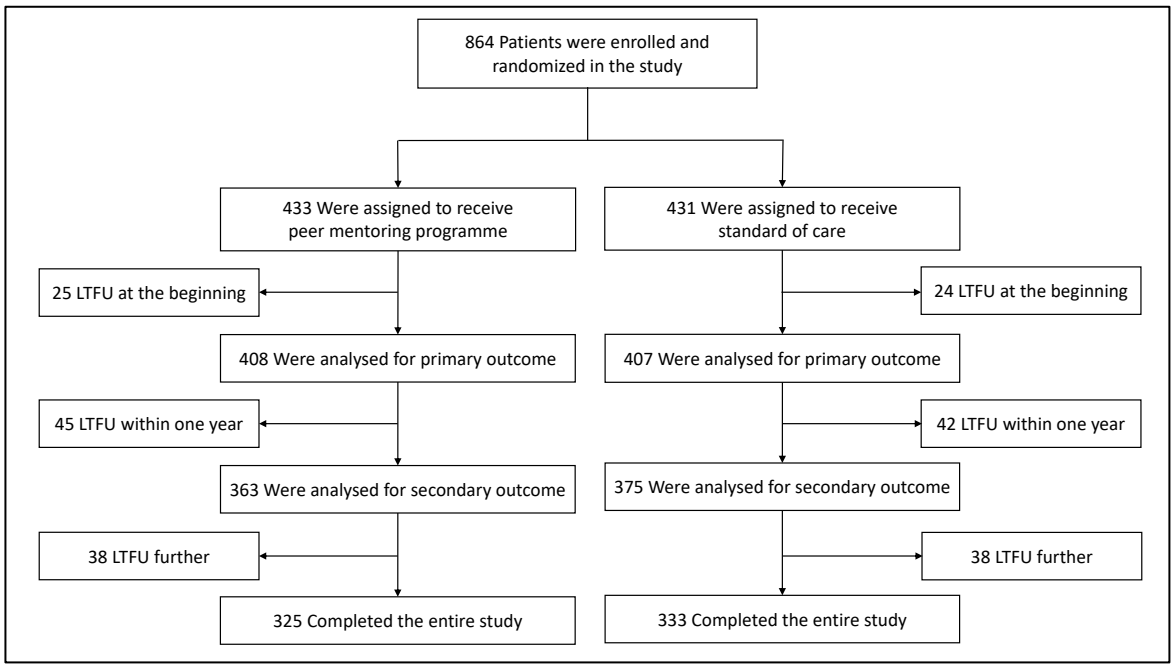

Figure 1. Enrolment, Randomization, and Follow-up. LTFU: lost to follow up.

Table 1. Baseline Characteristics of Trial Population with Respect to Baseline Variables

Characteristic	Peer mentoring programme group (n=433)	Standard of care group (n=431)
Demographic		
Median age (IQR *) – years	39(33-46)	38(32.5-45)
Female sex – no. (%)	111(25.6)	117(27.1)
Residence region – no. (%)		
Northeast	108(24.9)	107(24.8)
Northwest	101(23.3)	101(23.4)
Southeast	110(25.4)	110(25.5)
West Midlands	114(26.3)	113(26.2)
Residence urban – no. (%)	316(73.0)	316(73.3)
Housing status – no. (%)		
No problem	275(62.5)	250(58.0)
Housing problem	78(18.0)	78(18.1)
Urgent housing problem	77(17.8)	101(23.4)
Other	3(0.7)	2(0.5)
Clinical		
Duration of opiate use (IQR *) –months	12(5-24)	14(6-26.5)
Injection status – no. (%)		
Currently injecting	116(26.8)	103(23.9)
Previously injected	138(31.9)	141(32.7)
Never injected	172(39.7)	180(41.8)
Missing	7(1.6)	7(1.6)
Initial rehabilitation success – no. (%)	249(57.5)	234(54.3)

*IQR denotes interquartile range.

The successful rate of rehabilitation treatment for patients with previous injection history was 47.0% (95%CI 42.5% to 51.5%), and for patients never injected before was 69.6% (95%CI 64.5% to 74.3%). Patients with no injection history were 48.1% more likely to success in completing initial treatment than patients who had injection history (risk ratio for success, 1.48, 95% CI 1.32 to 1.66, p< 0.0001). The probability of successfully completing the treatment programme for those who had an injection history was 22.6% (95%CI 16.1% to 29.1%) smaller than those who had never injected before (p< 0.0001).

Effectiveness of Peer Mentoring Program

Figure 2 demonstrates primary outcome regarding relapse-free survival. 174 (40.2%) patients in the study who received peer mentoring programme relapsed to opiate use within two years, while 224 (52.5%) patients in standard of care group relapsed. The overall median estimated relapse-free duration for patients in standard of care group was 452 days; this duration for peer mentoring group was failed to be computed due to small number of relapses occurred. The crude hazard ratio for relapse comparing peer mentoring group and standard care group was 0.72 (95% CI 0.59 to 0.88), and adjusted hazard ratio was similar at 0.72 (95%CI 0.59 to 0.87). The 12-month relapse-free survival rates were 63.6% and 53.7% for patients received peer mentoring programme and standard of care, respectively.

Table 2 shows the results of time-splitting analysis and subgroup analysis as prior specified. Among all 815 patients, 224 experienced relapses in first four months (hazard ratio 0.90, 95%CI 0.69 to 1.17), as compared with 174 relapses in 565 patients after four months post-rehab (hazard ratio 0.54, 95%CI 0.40 to 0.74). Female witnessed a hazard ratio of 0.66 (95%CI 0.44 to 0.97) and male witnessed a hazard ratio of 0.75 (95%CI 0.59 to 0.94), the effect of the peer mentoring group compared to standard group on survival did not differ in the two gender strata (p = 0.58). Similarly, the hazard ratio of relapse comparing the two trial groups did not differ between patients with injection history (hazard ratio 0.79, 95%CI 0.61 to 1.01) and with no injection history (hazard ratio 0.63, 95%CI 0.45 to 0.87; p = 0.32).

The average social wellbeing score for standard of care group was 45.20 (95%CI 43.9 to 46.5), and the average difference of social wellbeing score was 0.658 (95%CI -1.17 to 2.48) for patients in peer mentoring programme group compared with patients in standard of care group (p= 0.48). After controlling for gender, age, SES, injection history, duration use, and initial treatment success, the average difference was 0.270 (95%CI -1.26 to 1.80).

Sensitivity Analysis

Relapse-free survival were compared under the assumption that all censoring cases were considered to relapse at the time point when they were censored, the crude hazard ratio of relapse was 0.78 (95%CI 0.66 to 0.93, p = 0.006).

DISCUSSION

In this trial, we found that both duration of previous opiate use and injection history are associated with initial treatment success. Overall, the shorter the previous opiate use duration, the more likely the initial treatment would success, although the observed magnitude of the successful rate increase was not evident. Free of injection history is another positive indicator for treatment success; the average successful probability was one-and-one-half fold larger for patients with no injection history compared to patients with injection history (from 47% to 69.6%). The contributory factors detected in our study provide important guidance for medical personnel in England to optimize personalized patient-centred care, and improve medical resource allocation to help patients with previous injection history and has a longer history of drug abuse, enhancing recovery of OUD patients at initial treatment.

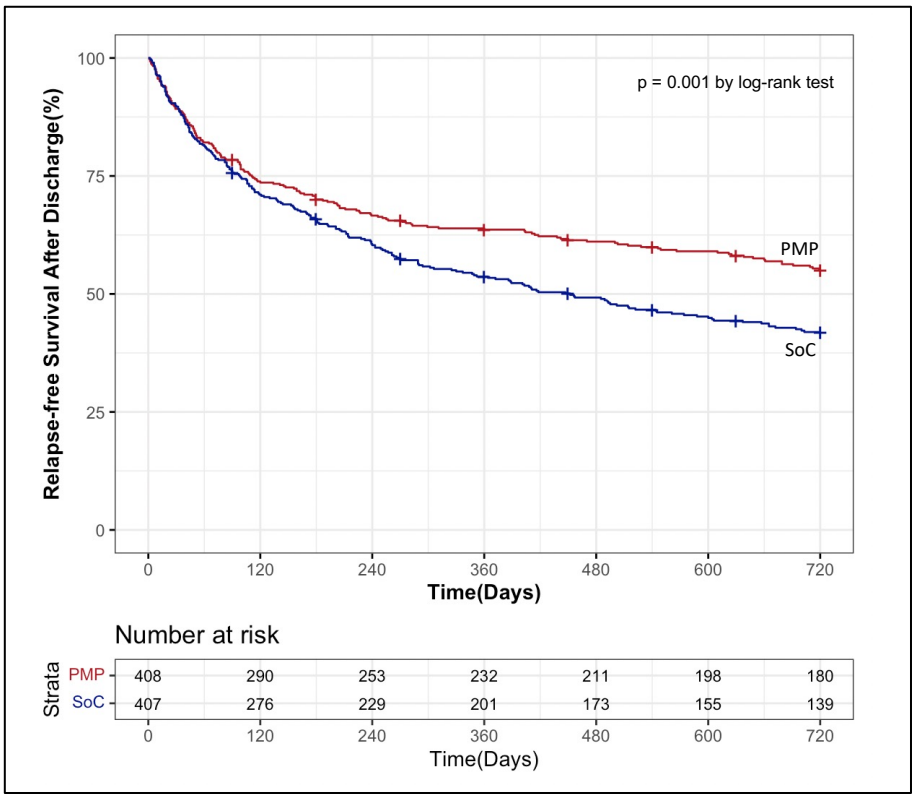

Figure 2. Kaplan-Meier Estimates for the Relapse-free Survival, according to Randomised Post Discharge Group. PMP: Peer mentoring programme; SoC: Standard of care.

Table 2. Adjusted Hazard Ratios, Time-Splitting Hazard Ratios and Subgroup Hazard Ratios for Peer Mentoring Programme Group, as Compared with Standard of Care Group

	No. of Patients	No. of Relapses	Hazard Ratio for Relapse (95% CI)	Median survival (months)	P value $
Overall	815	398	0.72 (0.59-0.88)	672	0.001 **
Multivariate #	815	398	0.72 (0.59-0.87)	672	0.0012 **
Time Group					0.014 *
First four months	815	224	0.90 (0.69-1.17)	-	
Four months after	565	174	0.54 (0.40-0.74)	-	
Gender					0.58
Female	213	102	0.66 (0.44-0.97)	712	
Male	602	296	0.75 (0.59-0.94)	660	
Injection history					0.32
With history	463	247	0.79 (0.61-1.01)	495	
No history	339	148	0.63 (0.45-0.87)	-	

$ Overall, multivariate, and subgroup p value is generated by log-rank test, adjusted Cox regression test and Cox regression interaction test. * $p < 0.05$, ** $p < 0.01$

Multivariate Cox regression adjusting gender, age, SES, injection history and duration use.

Furthermore, we found prominent beneficial effect of peer mentoring programme regarding relapse-free survival, which emits stronger positive affect after four months of peer mentor support intervention. The delayed therapeutic action indicates a threshold effect on peer supporting for OUD patients building stronger self-discipline. The early intervene of any form of peer supporter is necessary in clinical practice to achieve better efficacy. In addition, we also found that gender and previous injection history did not differ the protective effect of peer mentoring, thus there is no indication of differential treatment. There was no significant difference on one-year social wellbeing score for the peer mentor programme compared to standard of care, which suggests the peer mentoring programme did not mitigate the social and economic impacts of drug addiction within a year. Longer trial could be introduced to further evaluate the long-term impact of peer supporting regarding social function of patients.

Several limitations should be acknowledged. There was a considerable amount of loss of follow-up with incomplete ascertainment of outcomes (19.5%), which may bias the study result significantly[5, 6]. We found those who lost to follow up were more likely to be unsuccessful in initial treatment ($p < 0.001$), thus might be more prone to relapse or relapse earlier than those who complete the entire study. This may lead to us underestimating the relapse rates for the two groups. However, the loss of follow-up rate is equally distributed between the two groups in each stage of the study, and the adjusted multivariate model and sensitivity analysis conducted showed robust results; therefore, the effect of peer mentoring programmed is confirmed. Furthermore, although participants were from diverse socioeconomic background in England, ethnicity were not recorded in the study, which might compromise the generalizability to other areas outside England.

Overall, this randomized trial provides gold standard level evidence in England that the peer mentoring programme post-rehabilitation discharge expedite reduction on relapse for opiate addiction patients. There was no significant improvement for peer mentoring on general social well-being one year after discharge. Long-term peer mentoring could be considered to improve general recovery for OUD patients, albeit further exploratory on treatment is still on demand.

1. **Alenezi A, Yahyouche A, Paudyal V.** Current status of opioid epidemic in the United Kingdom and strategies for treatment optimisation in chronic pain. *Int J Clin Pharm*. Apr 2021;43(2):318-322. doi:10.1007/s11096-020-01205-y
2. **Volkow ND, Jones EB, Einstein EB, Wargo EM.** Prevention and Treatment of Opioid Misuse and Addiction: A Review. *JAMA Psychiatry*. Feb 1 2019;76(2):208-216. doi:10.1001/jamapsychiatry.2018.3126
3. **Kakko J, Alho H, Baldacchino A, Molina R, Nava FA, Shaya G.** Craving in Opioid Use Disorder: From Neurobiology to Clinical Practice. *Front Psychiatry*. 2019;10:592. doi:10.3389/fpsyt.2019.00592
4. **Naji L, Dennis BB, Bawor M, et al.** A Prospective Study to Investigate Predictors of Relapse among Patients with Opioid Use Disorder Treated with Methadone. *Subst Abuse*. 2016;10:9-18. doi:10.4137/SART.S37030
5. **Akl EA, Briel M, You JJ, et al.** LOST to follow-up Information in Trials (LOST-IT): a protocol on the potential impact. *Trials*. Jun 11 2009;10:40. doi:10.1186/1745-6215-10-40
6. **Akl EA, Briel M, You JJ, et al.** Potential impact on estimated treatment effects of information lost to follow-up in randomised controlled trials (LOST-IT): systematic review. *BMJ*. May 18 2012;344:e2809. doi:10.1136/bmj.e2809