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Effectiveness of treatment for opioid use disorder: A national, five-year, prospective, observational study in England

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ABSTRACT

BACKGROUND: This the first 5-year effectiveness study of publicly funded treatment for opioid use disorder (OUD) in England.

METHODS: All adults initiating treatment in 2008/09 in all 149 local treatment systems reporting to the National Drug Treatment Monitoring System (n=54,347). Admission polydrug use sub-populations were identified by Latent Class Analysis. The treatment outcome measure was 'successful completion and no re-presentation within six months' (SCNR) analysed by multilevel, multivariable logistic regression and funnel plots to contrast outcome by treatment system.

RESULTS: SCNR was achieved by 21.9%. Heroin and crack cocaine users were significantly less likely to achieve this outcome than patients who used heroin only (adjusted odds ratio [AOR] 0.90; 95% confidence interval [CI] 0.85-0.95). Older patients (AOR 1.09; CI 1.07-1.11), those employed (AOR 1.27; CI 1.18-1.37) and those enrolled for longer treatment were more likely to achieve the outcome measure. After risk adjustment, the local treatment systems that achieved substantially better outcome performance (14/149) had a lower rate of opiate prevalence in the local population at time of study initiation (incidence rate difference [IRD] 4.1; CI 4.0-4.2), fewer criminal offences per thousand (IRD 28.5; CI 28.1-28.8) and lower drug-related deaths per million (IRD 5.9; CI 5.9-5.9).

CONCLUSIONS: In an English national study, one fifth of patients successful completed treatment for OUD and did not present for further treatment within six months. Longer time in treatment increases the probability of achieving and maintaining clinical benefit from treatment. After risk-adjustment, an important minority of treatment systems achieve substantially better outcome performance.

Keywords: Treatment effectiveness; opioid use disorder; national; prospective

1. Introduction

Heroin and non-medical opioids are associated with a substantial global burden of disease (Degenhardt et al., 2013). In the United States (US), it is estimated that 2.6 people per 1,000 aged 12 and above used heroin in the past year (Jones et al., 2015). In Europe, the estimated annual heroin use prevalence is 4 per 1,000 aged 15-64 (EMCDDA, 2015) and 7.3 per 1,000 among people aged 16-64 in England (Hay et al., 2014).

Opioid use disorder (OUD), and the conceptually identical 'opioid dependence', is a debilitating and often chronic bio-behavioural disorder (DSM-5; American Psychiatric Association, 2013; ICD-10; WHO, 2016). People with OUD typically use illicit heroin and/or non-medical opioid pharmaceutical products, developing physiologically dependence and strong motivational urges. Around one quarter of opioid users develop OUD (Gable, 1993; Anthony et al., 1994). Left untreated, OUD typically follows a chronic course causing substantial health, social and economic problems (Hser et al., 2001; Grella and Lovinger, 2011; Hser et al., 2015). In the classic Grella and Lovinger study, half of the sample died and a quarter did not experience any sustained improvement in their drug use (Grella and Lovinger, 2011).

The OUD population is far from homogenous. Several behaviours are associated with increasing severity of the disorder (Marsden et al., 2014) and treatment effectiveness may vary between sub-populations. For example, drop-out is more likely among patients with comorbid psychiatric conditions and more criminal justice involvement in the year before treatment, and less likely among those living with dependent children (Evans et al., 2009). Ethnic minority populations have been reported to have a lower rate of treatment episode completion (Mennis and Stahler, 2016). An important sub-population are polydrug users, typically involving concurrent use of one or more of the following: alcohol, cocaine powder, smokeable (*crack*) cocaine and benzodiazepines (Darke and Hall, 1995; Monga et al., 2007; Harrell et al., 2012; Kuramoto et al., 2011). Heroin smokers who use crack cocaine are substantially less likely to be infected with Hepatitis C virus that those who inject heroin (Harrell et al., 2012). Opioid-polydrug users have been observed to have greater

health and social problems (Leri et al., 2003) and a relatively poorer response to OUD treatment (Williamson et al., 2006; Marsden et al., 2011, 2009).

The majority of countries with a high prevalence of OUD have an array of well-developed treatment services. The opioid medications methadone and buprenorphine are front-line, randomised-controlled trial supported pharmacotherapies (Mattick et al., 2014, 2009). Some OUD patients may receive psychosocial interventions without opioid psychotherapy. Interventions are typically provided by specialist community, primary care and hospital providers. Inpatient withdrawal management and drug-free residential rehabilitation services are also available. In addition to case management, national clinical guidelines recommend psychosocial interventions to address cognitive and behavioural symptoms of OUD (e.g. National Institute for Clinical Excellence, 2007).

Internationally, there have been several longitudinal cohort studies of the effectiveness of these interventions as delivered under routine conditions by public treatment systems (e.g. Simpson and Sells, 1990; Stewart et al., 2002; Darke et al., 2007; Marsden et al., 2009; White et al., 2015). Taken together, these studies conclude that treatment is associated with reduced opioid use, drug injecting, and offending behaviour, and improvements in health (including a substantially reduced risk of fatal overdose), social functioning and employment.

Longitudinal cohort studies are time consuming and expensive. Public accountability means that the commissioners of publicly funded services need information on the effectiveness of treatment as it is delivered. Various proxy measures of outcome have been used in treatment systems research, including unsanctioned discharge (drop-out) from treatment and retention (Brorson et al., 2013; Stark, 1992; Faggiano et al., 2003). A commonly used measure is the proportion of patients treated who complete treatment successfully (Alterman et al., 2001). This indicator is associated with reduced drug use (Evans et al., 2009; Kornør and Waal, 2005), increased employment (Lang and Belenko, 2000; Zarkin et al., 2002; Evans et al., 2009; Sung and Chu, 2011), lower arrests and incarceration (Campbell et al., 2007; Evans et al., 2009; Gifford et al., 2014), and a reduced likelihood of readmission to treatment services (Luchansky et al., 2000). In the US, substantial inter-state (Arndt et al., 2013) and regional variation in completion rates have been reported

(Hawkins et al., 2014), and this is now monitored at the federal/government level (Stahler et al., 2016).

The ‘successful completion’ indicator has a key limitation – it does not capture the extent to which treatment benefit is enduring. This is important because relapse is common, affecting 50-60% of people within six months after leaving treatment (McLellan et al., 2005). The process of achieving stable recovery from OUD may involve several cycles of treatment over a decade or more (Dennis et al., 2005; Hser et al., 1997).

To fully assess the effectiveness of treatment systems, national administrative databases need to be able to capture this process, yet the requirements of such systems are difficult to implement. In the US, the absence of a patient consent prevents linkage across consecutive treatment episodes. At the national level, the impact of this is twofold: it is not possible to objectively assess whether an individual has previously engaged in treatment (an indicator of patient-level complexity (Marsden et al., 2012; Siguel and Spillane, 1978). It is also not possible to determine whether a patient’s successful completion status is enduring.

England has a well-developed public treatment system for drug use disorders with service delivery involving specialist clinics in the National Health Service (NHS) and non-governmental sector. Services are commissioned by 149 local treatment systems across the country aligned to local government geographical boundaries. All public providers report clinical and effectiveness data to the National Drug Treatment Monitoring System (NDTMS). NDTMS is operated by Public Health England and provides outcome monitoring and performance benchmarking for each local system (see Marsden et al., 2009 for an operational description). The latest national report shows that 28% of people treated for OUD complete treatment successfully (Public Health England, 2016a).

With temporal linkage of episodes, NDTMS can record re-presentation to treatment as a proxy remission indicator. To our knowledge, a ‘successful completion and no re-representation’ outcome measure has not been used in previous OUD treatment systems research. Accordingly, the aim of this study was to estimate the effectiveness of OUD treatment in England for OUD using this indicator and contrast the effectiveness of local treatment systems.

2. Methods

2.1 Design

This was an English national, five-year, prospective, observational cohort study of publicly-funded, specialist treatment services for OUD reporting to the NDTMS, and reported following the STROBE guideline for observational research (Elm et al., 2007). The population for the study was all adults (≥18 years) diagnosed with OUD who presented for treatment in England between 1 April 2008 and 31 March 2009.

The study included all local treatment systems and all operational specialist community agencies in the NHS and third-sector providing pharmacotherapies, psychosocial interventions and adjunctive support services for OUD in community, inpatient (short-term medically supervised withdrawal), and residential (drug-free rehabilitation) settings.

2.2 NDTMS database

NDTMS captures a core dataset of all clients entering the treatment system, and is designed to record key information at each stage of the treatment process. An initial triage assessment is conducted by clinical staff at each treatment service during the first face-to-face meeting following referral to treatment which can, in the case of self-referrals for example, take place on the same day. Where a treatment need is clinically indicated, the substance(s) and patient demographics are recorded on NDTMS and an appointment for a treatment intervention is arranged. The mean waiting time to initiate this intervention is 2.2 days for OUD patients, and 98% start treatment within three weeks (Public Health England, 2016a). Each treatment intervention received is recorded on NDTMS (section 2.2.1). Treatment is not time-limited: patients are maintained in treatment for as long as clinically indicated (section 2.2.2).

2.2.1 OUD treatments

The opioid pharmacotherapies included methadone, buprenorphine and also naltrexone. Psychosocial interventions such as contingency management and motivational interviewing

complement pharmacotherapy and target underlying psychological aspects of dependence. In addition to opioid pharmacotherapy and/or psychosocial interventions, a patent's treatment programme could include adjunctive 'recovery support' services, including: facilitated access to mutual aid; complementary therapies; and family, housing, employment, education and training supports.

2.2.2 Treatment episodes and journeys

Following the NDTMS reporting protocol, each patient-level 'treatment journey' comprised: a single episode of pharmacotherapy or psychosocial intervention provided by a clinic; enrolment in concurrently delivered medication and psychosocial interventions (from one or more clinics); or a continuing care package in which an intervention was followed by one or more further interventions. Episodes commencing after 21 days are classified as a new treatment journey (Public Health England, 2015). Recovery support services are offered concurrently or following a treatment episode. Patients are regularly reviewed, treatment provision changes, and at the end of the 'treatment journey', patients who overcome their dependence are successfully discharged from the treatment system.

When a patient was discharged from treatment, one of the following exit reasons was recorded: successful completion; drop-out (patient left treatment without discussion or before completing their care plan); unsuccessful transfer (patient was referred to another treatment service but does not enter treatment within 21 days); incarceration (treatment is prematurely terminated due to criminal justice action); or patient died. After this point, further treatment was classified as a new treatment journey.

2.3 Outcome measure

The outcome measure for the study combined two components: successful completion and no re-presentation. Successful completion was assigned to each patient that was reported by the clinic as meeting the following criteria within five years (ending 31 March 2014):

- in remission from OUD;

- abstinent from all opioids and crack cocaine;
- completed all opioid pharmacotherapy and psychosocial interventions;
- met all care plan goals, with mutual agreement to exit treatment.

For the 'no re-presentation' element of the outcome measure, we judged that a six-month period was reasonable (ending 30 September 2014). Therefore, the effectiveness measure was assigned to those patients who met the above criteria at exit from treatment and did not re-present for any treatment within six months ('successful completion, no re-representation', SCNR for economy herein).

2.4 Covariates

We followed an integrated variable-centred and person-centred approach to evaluate treatment effectiveness for OUD using the following patient demographic, clinical information and previous treatment exposure (all recorded at initial assessment):

Demographic. Sex; age (centred at 18 years and grouped in five-year increments); Black and Minority Ethnicities (BME: a legal monitoring requirement (*Race Relations (Amendment) Act*, 2000)); employed; housing problems (defined primarily as having no fixed abode, but can also include squatting, short-term hostel/B&B, staying with friends/relatives; [(homeless, herein]).

Social deprivation. Local area deprivation was measured by the Indices of Multiple Deprivation (IMD; (Department for Communities and Local Government, 2007)). IMD data were linked to NDTMS based on the patient's residential postcode district or the location of their first treatment provider in instances of missing postcode information.

Injecting status. Three levels of injecting status are recorded at the start of treatment: never injected; lifetime history of injecting, and current injector.

Career length. The number of years between first initiating opioid use and enrolment in the index treatment journey (length of the substance-using career). This measure was mean centred and coded in five-year increments.

Treatment history. Referral route into treatment was categorised into whether the patient was self-referred, referred via the criminal-justice system or other (e.g., referral from health service or substance abuse service). Whether an individual had previously accessed treatment was also included.

2.5 Statistical analysis

All analyses were done in Mplus (version 7.11) and Stata (version 13.1).

2.5.1 Drug use sub-populations

Given anticipated heterogeneity in drug use profile of the OUD population at presentation to treatment (Monga et al., 2007; Public Health England, 2016a), we used latent class analysis (LCA) in Mplus to identify discrete sub-populations of OUD patients who presented for treatment with concurrent disorder with one or more of the following 6 substances: crack cocaine; cannabis; alcohol; non-medical opioids; stimulants (powder cocaine and *d*-amphetamine) and benzodiazepines.

The LCA was iterative with an unconditional 1-class model initially fit to the data and sequentially increased to a 6-class model. Each model used 5,000 random sets of starting values to guard against convergence on local maxima (McLachlan and Peel, 2000) and a minimum class size of 5% of the cohort was set for utility (Willey et al., 2016; Borders and Booth, 2012). Class identification was informed by posterior fit statistics, including the Bayesian and Akaike information criteria and entropy. A multinomial logistic regression was then used to characterise the latent classes on the patient-level characteristics. Given the hierarchical structure of the study, with patients clustered in treatment services and services clustered in local treatment systems, confidence intervals (CI) were calculated using robust standard errors.

2.5.2 Outcome analysis

A three-level, multivariable logistic regression was used for the analysis of the outcome measure (Stata command: *meqrlogit*). The complete-case model contained the following random intercepts:

patients (level one); treatment services (level two); and local treatment system (level three). Model discrimination and variation (at level two and three) was estimated by c-index (Hanley and McNeil, 1982), and intra-cluster correlation (ICC), respectively.

Reflecting the hierarchical design of the study (Hofmann, 1997; Heo and Leon, 2008) and with alpha, statistical power and a medium effect size on the outcome measure pre-set (0.05, 0.90 and $f^2 = 0.15$, respectively [Cohen, 1988]), we ensured that that there were at least 15 cases per covariate in the regression analysis to minimise overfitting (Green, 1991; Babyak, 2004).

With no contrary evidence that data loss was missing-at-random (Little and Little, 2002), a multiply imputed dataset was computed by chained equations (Stata command: *mi: impute chained*). An all-case multivariate logistic model was run to check on potential bias and loss of precision (Sterne et al., 2009). To achieve a relative efficiency above 98% (Rubin, 1987), and to ensure that reduction in power was less than 1% (Graham et al., 2007), 20 datasets of probabilistic values were created, each analysed separately, and then combined using Rubin's rules.

2.5.3 Analysis of local treatment systems

A fixed-effects approach was used to determine the relative effectiveness of each local treatment system because random intercepts could mask real variation in achieving the outcome (Marsden et al., 2012). For each treatment system, predicted outcome probabilities were summed across patients and divided by the number of patients treated in the area. A risk-adjusted outcome rate was then calculated by dividing the expected rate by the observed rate and multiplying this by the national average.

A funnel plot with 95% control limits (Spiegelhalter, 2005) then identified areas where outcome performance was better or worse than expected (where the area was located above or the control limit, respectively). Local treatment systems rates of opiate prevalence, offending and drug-related deaths were contrasted by incidence-rate ratio.

Outcome performance was contrasted using pooled estimates of the rate of opiate users per thousand inhabitants (Hay et al., 2010), incidence of drug related deaths per million inhabitants

(Public Health England, 2016b) and the criminal offence rate per thousand inhabitants (Office for National Statistics, 2016) The offending rate was based on the local area population estimates used in the development of the opiate prevalence estimates (Hay et al., 2010).

3. Results

3.1 Study cohort and follow-up

The population for the study was all adults (≥18 years) diagnosed with OUD who presented for treatment in England between 1 April 2008 and 31 March 2009 (N=56,156). As 1,799 (3.2%) people did not commence treatment by 31 March 2014, they were removed from further analyses.

Patients in the cohort (n = 54,357) commenced treatment for OUD in 1,421 specialist clinics and primary care teams in the National Health Service (NHS) and the non-governmental sector (median of 12 patients per service; IQR 3-45), and in all 149 local treatment systems in England (median 302 patients per area; interquartile range [IQR] 184-470]).

At the end of the five-year period, 7,890 people (14.5%) were continuously enrolled in treatment for OUD. Given the aims of the present study, this group was removed. Among the final all-case cohort (n = 46,467), 9,007 patients (19.4%) had missing observations on one or more covariates, yielding a complete-case cohort of 37,460. The covariate with the highest level of missing data was length of heroin use career (11.4%), followed by employment status (9.1%), housing status (3.4%) and injecting (3.4%).

3.2 Drug use sub-populations

At clinical assessment, 67% of patients had a concurrent substance use disorder, as follows: crack cocaine (44.1%), cannabis (14.1%), alcohol (13.3%), other illicit opioids (11.4%), benzodiazepines (9.4%) and other stimulants (8.8%).

Table 1 displays the results of the LCA models. The value of each information criterion (Akaike, Bayesian and adjusted Bayesian) reduced as the number of classes increased, indicating successively better fitting models. The bootstrapped likelihood ratio test confirmed that each model

was a statistically better fit than the preceding one. Entropy was high (>0.8) for all except the 3-class solution, which reflected relative uncertainty in the assignment of individuals to the third class. The 5-class and 6-class solutions resulted, however, in at least one class with less 5% of the cohort. Accordingly, we judged that a 4-class solution best identified the heroin and other drug use sub-populations at treatment admission, and labelled these as follows:

- **Class 1** (n=30,339, 56%: *heroin low level concurrent drug use disorders)*;
- **Class 2** (n=2,794, 5%: *heroin, crack, alcohol*);
- **Class 3** (n=17,907, 33%: *heroin, crack*);
- **Class 4** (n=3,257, 6%: *heroin, crack, cannabis*).

3.3 Characteristics of the cohort

Table 2 shows the demographic and clinical characteristics of the cohort and the results of the multinomial logistic regression analysis of the profile of the drug problem classes on socio-demographic, injecting, heroin career and treatment referral characteristics (with the heroin and low concurrent drug use disorders [class 1] as the referent).

There were relatively less employment and more homelessness among the members of classes 2, 3 and 4. Class 4 was also relatively more likely to be referred to treatment from the criminal justice system (35.3%) and have previous OUD treatment (50.4%).

3.4 Treatment exposure and status at exit

Patients in the cohort received a median of 31.0 weeks of treatment (IQR 12.6-80.3) and 13,360 (28.8%) successfully completed their treatment journey (**Table 3**). One-third (32.1%) of discharged patients were readmitted for further treatment for substance use disorders within six months.

Readmission was more likely for those who were incarcerated (re-admission rate 45.2%; odds ratio [OR] 2.67; 95% CI 2.50-2.82), dropped out (re-admission rate 34.8%; OR 1.72; 95% CI 1.63-1.81), or transferred unsuccessfully to another SUD treatment service (re-admission rate 28.3%; OR

1.27; 95% CI 1.20-1.35) compared with those who completed treatment successfully (re-admission rate 23.7%).

Relative to Class 1, patients assigned to Class 2 and Class 4 were less likely to have received opioid pharmacotherapy, Class 4 was more likely to have received psychosocial interventions, and Class 2 received more in-patient services. Class 1 received the least amount of residential services and was retained in treatment longer than any other class. Class 3 reported more incarceration, unsuccessful transfers and dropouts, but less deaths, while Class 2 had fewer incarcerations but more drop outs. There were relatively fewer deaths in Class 4.

3.5 Successful completion of treatment and no re-presentation within six months

Overall, 21.9% of the cohort (10,194) attained the SCNR outcome (**Table 3**). Class 3 were less likely to achieve the outcome. After negative multi-collinearity screening for all covariates, the results of the unadjusted, covariate adjusted complete-case (n=37,460) and multiply-imputed, all-case (n=46,467) analyses are shown in **Table 4**.

The complete- and all-case models yielded very similar covariate estimates. In the all-case model, with statistically significant adjustment for clustering effects associated with treatment agency and local treatment system (ICC 0.13 and 0.17, respectively) there was satisfactory discrimination between patients who achieved the SCNR outcome (c-index 0.74; 95% CI 0.74-0.75).

There was an increased likelihood of positive outcome among older patients, those with pre-treatment employment, and those who with longer time enrolled in treatment (particularly for more than 2 years; adjusted odds ratio [AOR] 2.60; 95% CI 2.43-2.78).

A negative outcome was associated with men, patients who were homeless before admission and in areas of greater social deprivation (gradient with likelihood lowest at highest quintile; AOR 0.77; 95% CI 0.70-0.85); drug injectors; those referred from the criminal justice system; those with previous treatment for OUD; those with shorter heroin using career; and members of class 3.

3.6 Comparison of local treatment systems

Following risk-adjustment, 14 of 149 local treatment systems were classified as achieving performance that was better than expected on the SCNR outcome, and 38 local treatment systems achieved performance that was worse than expected (**Figure 1**). In comparison to the better performing areas, these 38 areas were characterised with a higher estimated level of opiate use in the local population (an extra 4.1 (95% CI 4.0-4.2) opiate users per thousand population), a higher level of drug-related offences (an extra 28.5 (95% CI 28.1-28.8) offences per thousand population), and more drug-related deaths (an extra 5.9 (95% CI 5.9-5.9) deaths per thousand population) (**Table 5**).

4. Discussion

Over the five-year observation period, we observed that nearly one in three patients successfully completed treatment for OUD. Reinforcing previous research (Luchansky et al., 2000), patients who successfully completed treatment were least likely to be re-admitted to treatment within a subsequent six month period. In our national population of patients accessing publicly-funded treatment, one in five achieved a sustained benefit from treatment.

Other studies have noted two (Shand et al., 2011), three (Harrell et al., 2012; Monga et al., 2007), five (Kuramoto et al., 2011), or eight (Patra et al., 2009) latent class structures. Our analysis of polydrug dependence in patients seeking treatment for OUD in England revealed a four class structure. Crack cocaine was a defining characteristic in three of these classes, with one class being further classified with alcohol dependence and another classified with cannabis dependence. It is interesting to note that the only crack cocaine class without alcohol or cannabis dependence had worse outcomes than the heroin with low polydrug class.

4.1. Integration with the literature

Unlike other large-scale studies on treatment completion (Arndt et al., 2013; Mennis and Stahler, 2016), in our unadjusted models patients from Black and Minority Ethnicities (BME) were more likely to recover. After controlling for other socio-economic factors, however, this disparity no longer held, highlighting the importance controlling for employment and stable housing (Saloner

and Lê Cook, 2013; Hawkins et al., 2014). Our findings provide general support for the construct of 'physical capital' (Cloud and Granfield, 2008) playing a major role in recovery from heroin use disorder, as employment and stable housing were found to significantly affect the likelihood of recovery. The finding that increased time spent engaged in treatment increases the likelihood of successful completion aligns with previous research (Hubbard et al., 2003; Simpson and Sells, 1990) and provides evidence that OUD treatment should not be time-limited (Advisory Council on the Misuse of Drugs, 2014).

After controlling for patient-level and area-level deprivation predictors of outcome, local treatment systems that were performing significantly below the expected rate also appeared to have a much larger opiate using population and, presumably as a result of this, a higher rate of both offending and drug-related deaths. We are not able to determine a mechanism for this association. There may be social network influences in operation. For example, social networks can influence both a transition to injecting heroin (Neaigus et al., 2006) and the decision to share injecting equipment (De et al., 2007). Heroin users who have achieved abstinence often cite moving away from drug-using social networks and receiving support from non-using friends as a contributory factor to their success (Best et al., 2008).

4.2. Strengths and limitations

The main study strength is the national, large scale, long-term follow-up of all individuals accessing treatment for heroin use disorder in England and the utilisation of the national administrative database to monitor relapse. Unlike other comprehensive administrative datasets (Sahker et al., 2015; Alterman et al., 2001; Stahler et al., 2016), NDTMS has patient-level identifiers that enable cross-referencing with subsequent treatment admissions. This utility provides not only an objective summative measure of the sustainability of recovery in this population, it also enables national administrative systems to objectively capture whether patients had previously accessed treatment services, which is an important negative predictor of treatment outcome (Siguel and Spillane, 1978; Marsden et al., 2012).

Several study limitations are also acknowledged: firstly, our analysis of OUD sub-populations is based on clients entering the treatment system in 2008/09. It is possible that since this period, with the rise of novel psychoactive substances for example, a different class structure would emerge for clients currently accessing treatment. Second, we were not able to access data from the national deaths registry or the national prisons system, and there remains a concern that at least some of our patients who did not re-present to treatment were simply unable to. Third, while all available covariates in NDTMS were screened in the present analysis, other covariates could further elucidate the likelihood of sustaining recovery, including treatment motivation (Simpson and Joe, 1993), engagement (Simpson et al., 1995) and other recovery strengths (Gossop et al., 2002). Fourth, it is possible that other interventions were experienced by the patients in this cohort, such as privately-funded residential treatment or attending Alcoholics Anonymous, but these interventions are not captured by NDTMS and it is not possible to assess the potential impact these may have had.

4.3. Conclusions

Relapse requiring treatment is relatively common in the six months following treatment completion. This study highlights the importance of including re-presentation to treatment as a summative measure of the effectiveness of local treatment systems. We note a sizeable proportion of individuals, nearly one in seven, who have been continuously engaged in treatment throughout the five-year observation period. The next questions for our research group are whether, and to what degree, heroin and other drug use changes throughout this time period; how change in heroin use relates to change in other drugs; whether five-year in-treatment change predicts subsequent successful completion of treatment, and to examine the longitudinal inter-relationship between substance use, employment and housing.

Table 1. Unconditional latent class analysis of drug use at presentation to treatment (n=54,347)

	Model [a]					
Parameter	**Class 1**	**Class 2**	**Class 3**	**Class 4**	**Class 5**	**Class 6**
No. of parameters	6	13	20	27	34	41
AIC	266,371.29	264,740.91	262,525.26	261,201.63	260,527.17	260,033.40
BIC	266,424.71	264,856.65	262,703.32	261,442.02	260,829.88	260,398.43
aBIC	266,405.65	264,815.33	262,639.76	261,356.22	260,721.83	260,268.13
aBIC change (%)	-	-0.60	-0.82	-0.49	-0.24	-0.17
Entropy	-	0.999	0.718	0.830	0.861	0.857
BLRT	-	-133,179.65	-132,357.45	-131,242.63	-130,573.82	-130,229.58
BLRT reduction (%)	-	-	0.62	0.84	0.51	0.26
Class (probability)						
1	1.00 (1.00)	0.44 (1.00)	0.06 (0.99)	0.56 (0.83)	0.29 (0.99)	0.01 (0.71)
2	-	0.56 (1.00)	0.38 (1.00)	0.05 (0.99)	0.04 (0.97)	0.55 (0.79)
3	-	-	0.56 (0.69)	0.33 (0.99)	0.05 (0.99)	0.04 (0.99)
4	-	-	-	0.06 (0.99)	0.06 (0.99)	0.06 (0.99)
5	-	-	-	-	0.56 (0.84)	0.29 (0.99)
6	-	-	-	-	-	0.05 (0.98)

AIC, Akaike Information Criterion; BIC, Bayesian Information Criterion;
aBIC, sample-size adjusted BIC; BLRT, bootstrapped likelihood ratio test (all $P < 0.00005$).

[a] For the following drugs: crack cocaine, cannabis, alcohol, other opioids, benzodiazepines and other stimulants.

Classification based on most likely latent class membership.

Table 2. Characteristics of the cohort and drug use sub-populations

	Total					
	n	(%)	**Class 1**	**Class 2**	**Class 3**	**Class 4**
Covariate			n=30,339	n=2,794	n=17,907	n=3,257
Socio-demographic						
Male	41,099	(75.6)	(76.5)	**(74.9)**	**(73.0)**	**(82.0)**
Age [a]	32.9	(7.8)	32.9 (7.9)	34.2 (7.9)	33.0 (7.5)	**31.9 (7.9)**
Black/Minority Ethnic	7,342	(13.5)	(10.9)	**(15.8)**	**(15.9)**	**(22.4)**
Employed	6,222	(12.5)	(14.7)	**(8.1)**	**(9.7)**	**(11.4)**
Homeless	17,343	(32.9)	(29.5)	**(43.1)**	**(36.8)**	**(35.1)**
Social deprivation:						
Quintile 1 (lowest)	10,857	(20.0)	(21.6)	(19.9)	(17.1)	(20.4)
2	10,922	(20.1)	(19.9)	(21.9)	(20.1)	(20.3)
3	10,823	(19.9)	(19.9)	(23.3)	(19.3)	(20.2)
4	10,859	(20.0)	(19.8)	(18.9)	(20.3)	(20.6)
Quintile 5 (highest)	10,896	(20.0)	(18.7)	**(16.0)**	**(23.2)**	(18.5)
Clinical						
Heroin career [a]	11.4	(7.5)	(7.6)	(8.3)	(7.2)	(7.4)
Drug injecting:						
Never	17,715	(33.6)	(32.8)	(32.5)	(33.1)	(44.5)
Lifetime	18,004	(34.2)	(34.9)	(35.4)	(33.5)	**(30.4)**
Current	16,996	(32.2)	(32.3)	(32.1)	(33.4)	**(25.0)**
Referral source:						
Other	17,453	(32.1)	(35.0)	(35.1)	(27.6)	(27.2)
Self	20,570	(37.8)	(39.4)	(37.6)	(35.2)	(**37.5)**
Criminal justice	16,334	(30.0)	(25.6)	(27.3)	**(37.1)**	**(35.3)**
Previous OUD treatment:	30,212	(55.6)	(55.6)	**(52.4)**	(57.0)	**(50.4)**
< 6 months	20,835	(38.3)	(35.3)	(45.1)	(41.4)	(44.1)
6 months to < 1 year	8,917	(16.4)	(16.1)	**(16.4)**	**(16.9)**	(17.0)
1 year to < 2 years	8,014	(14.7)	(15.4)	**(14.3)**	**(13.6)**	**(14.9)**
2 years to 5 years	16,591	(30.5)	(33.2)	**(24.3)**	**(28.1)**	**(24.0)**

Class 1: Heroin and low likelihood of problem substance use;
Class 2: Heroin, problem crack cocaine and alcohol use;
Class 3: Heroin and crack cocaine use;
Class 4: Heroin and crack and cannabis use.

Figures in parentheses in table are percentages unless otherwise stated.

[a] Year (SD)

Emboldened percentages and means are statistically significant ($P < 0.05$) from multivariable, multinomial logistic regression (Class 1: referent).

Table 3. Treatment interventions received, by treatment leavers, SCNR outcome and latent class

Treatment characteristics	**Total** (n=46,467)	**Class 1**: *Heroin, low poly-substance* (n=25,469)	**Class 2**: *Heroin, crack, alcohol* (n=2,496)	**Class 3**: *Heroin, crack* (n=15,566)	**Class 4**: *Heroin, crack, cannabis* (n=2,936)
Exposure – interventions received					
Opioid pharmacotherapy, n (%)	36,122 (77.7)	20,377 (80.0)	**1,602 (64.2)**	12,082 (77.6)	**2,061 (70.2)**
Psychosocial interventions, n (%)	25,742 (55.4)	13,682 (53.7)	1,537 (61.6)	8,694 (55.9)	**1,829 (62.3)**
In-patient withdrawal management, n (%)	3,010 (6.5)	1,546 (6.1)	**275 (11.0)**	1,021 (6.6)	168 (5.7)
Residential rehabilitation, n (%)	1,620 (3.5)	711 (2.8)	**167 (6.7)**	**617 (4.0)**	**125 (4.3)**
Median weeks to discharge					
Successful completion (IQR)*	39.5 (15.3-109.9)	46.0 (16.6-119.7)	**30.9 (14.9-79.1)**	**34.1 (14.0-99.3)**	**31.9 (14.6-90.4)**
Died, (IQR)	81.0 (32.0-147.9)	83.4 (35.7-150.0)	51.4 (16.4-177.2)	81.1 (32.0-140.3)	65.3 (11.0-142.1)
Incarcerated, (IQR)	35.4 (14.7-82.6)	38.4 (16.0-85.9)	33.9 (13.3-87.0)	**32.3 (13.3-79.0)**	**34.4 (13.0-73.9)**
Unsuccessful transfer, (IQR)	32.4 (12.9-79.3)	35.0 (13.3-84.3)	**27.1 (10.3-74.9)**	**30.7 (12.3-75.6)**	**27.6 (11.1-66.3)**
Dropped out, (IQR)	22.9 (9.9-57.7)	25.1 (10.7-61.9)	**19.1 (9.1-46.7)**	**20.9 (8.9-52.7)**	**20.3 (9.7-55.9)**
Total, (IQR)	31.0 (12.6-80.3)	34.3 (13.3-87.0)	**25.6 (11.8-67.9)**	**28.0 (11.6-73.4)**	**27.0 (11.9-69.9)**
Treatment exit status					
Successful completion, n (%)	13,360 (28.8)	7,675 (30.1)	718 (28.8)	4,066 (26.1)	901 (30.7)
Died, n (%)	684 (1.5)	435 (1.7)	52 (2.1)	**182 (1.2)**	**15 (0.5)**
Incarcerated, n (%)	7,425 (16.0)	3,820 (15.0)	**299 (12.0)**	**2,845 (18.3)**	461 (15.7)
Unsuccessful transfer, n (%)	8,385 (18.1)	4,498 (17.7)	449 (18.0)	**2,922 (18.8)**	516 (17.6)
Dropped out, n (%)	16,613 (35.8)	9,041 (35.5)	**978 (39.2)**	**5,551 (35.7)**	1,043 (35.5)
Treatment outcome					
Successful completion and no re-presentation within six months, n (%)	10,194 (21.9)	5,882 (23.1)	566 (22.7)	**3,063 (19.7)**	683 (23.3)

Emboldened percentages and means are statistically significant (P < 0.05) from multinomial logistic regression (Class 1: referent).

* IQR = interquartile range

Table 4. Unadjusted and multi-level, complete-case and all-case multivariable logistic regression of SCNR outcome

Covariates	**Unadjusted** **OR** (95% CI) (n=37,460)	**Complete-case** **AOR** (95% CI) (n=37,460)	**All-cases** **AOR** (95% CI) (n=46,467)
Socio-demographic			
Male	**0.87 (0.82, 0.92)**	**0.88 (0.83, 0.94)**	**0.88 (0.83, 0.93)**
Age	**1.07 (1.06, 1.09)**	**1.09 (1.07, 1.11)**	**1.09 (1.07, 1.11)**
BME	**1.11 (1.03, 1.20)**	1.05 (0.97, 1.14)	1.02 (0.94, 1.09)
Employed	**1.46 (1.36, 1.58)**	**1.24 (1.15, 1.34)**	**1.27 (1.18, 1.37)**
No fixed abode	**0.74 (0.70, 0.79)**	**0.85 (0.80, 0.91)**	**0.86 (0.81, 0.91)**
Deprivation:			
Quintile 2	**0.88 (0.80, 0.96)**	0.93 (0.84, 1.02)	0.94 (0.86, 1.02)
Quintile 3	**0.82 (0.74, 0.90)**	0.91 (0.82, 1.00)	**0.91 (0.83, 1.00)**
Quintile 4	**0.79 (0.71, 0.87)**	**0.84 (0.76, 0.93)**	**0.86 (0.78, 0.94)**
Quintile 5 (highest)	**0.63 (0.57, 0.70)**	**0.74 (0.67, 0.83)**	**0.77 (0.70, 0.85)**
Clinical			
Injecting:			
Previously injected	**0.81 (0.76, 0.86)**	**0.87 (0.81, 0.93)**	**0.86 (0.81, 0.91)**
Currently injector	**0.59 (0.55, 0.63)**	**0.64 (0.60, 0.69)**	**0.64 (0.60, 0.69)**
Referral route:			
Self	0.95 (0.88, 1.01)	0.96 (0.90, 1.03)	0.97 (0.92, 1.04)
Criminal justice	**0.58 (0.54, 0.63)**	**0.68 (0.63, 0.74)**	**0.68 (0.63, 0.73)**
Drug use class:			
Class 2: Heroin, crack & alcohol	0.92 (0.81, 1.03)	1.02 (0.90, 1.15)	0.97 (0.87, 1.08)
Class 3: Heroin & crack	**0.82 (0.77, 0.87)**	**0.92 (0.86, 0.98)**	**0.90 (0.85, 0.95)**
Class 4: Heroin, crack & cannabis	0.99 (0.89, 1.11)	1.08 (0.97, 1.20)	1.02 (0.92, 1.12)
Previously treated	**0.64 (0.61, 0.67)**	**0.66 (0.62, 0.69)**	**0.66 (0.63, 0.70)**
Heroin career	**0.99 (0.97, 1.00)**	**0.97 (0.95, 0.99)**	**0.97 (0.95, 0.99)**
Time in index treatment journey:			
6 months to < 1 year	**1.28 (1.19, 1.39)**	**1.28 (1.19, 1.38)**	**1.32 (1.23, 1.41)**
1 year to < 2 years	**1.43 (1.33, 1.55)**	**1.40 (1.29, 1.51)**	**1.39 (1.30, 1.49)**
2 years to 5 years	**2.70 (2.51, 2.90)**	**2.59 (2.41, 2.79)**	**2.60 (2.43, 2.78)**
Model statistics			
Constant	-	0.38 (0.33, 0.43)	0.39 (0.34, 0.44)
Wald X^2 (d.f. = 21)	-	1,538	1,834-1,854
LR test X^2 (d.f. = 2)	-	938	1,342-1.349
Random effects parameters (ICC):			
Treatment system (Level 3)	-	0.01 (0.00, 0.02)	0.17 (0.11, 0.27)
Treatment agency (Level 2)	-	0.13 (0.11, 0.15)	0.13 (0.11, 0.15)

SCNR, 'successful completion of treatment journey and no representation to treatment within six months'; OR, odds ratio; AOR, adjusted odds ratio; CI, confidence interval; d.f., degrees of freedom; ICC, intra-class correlation coefficient.

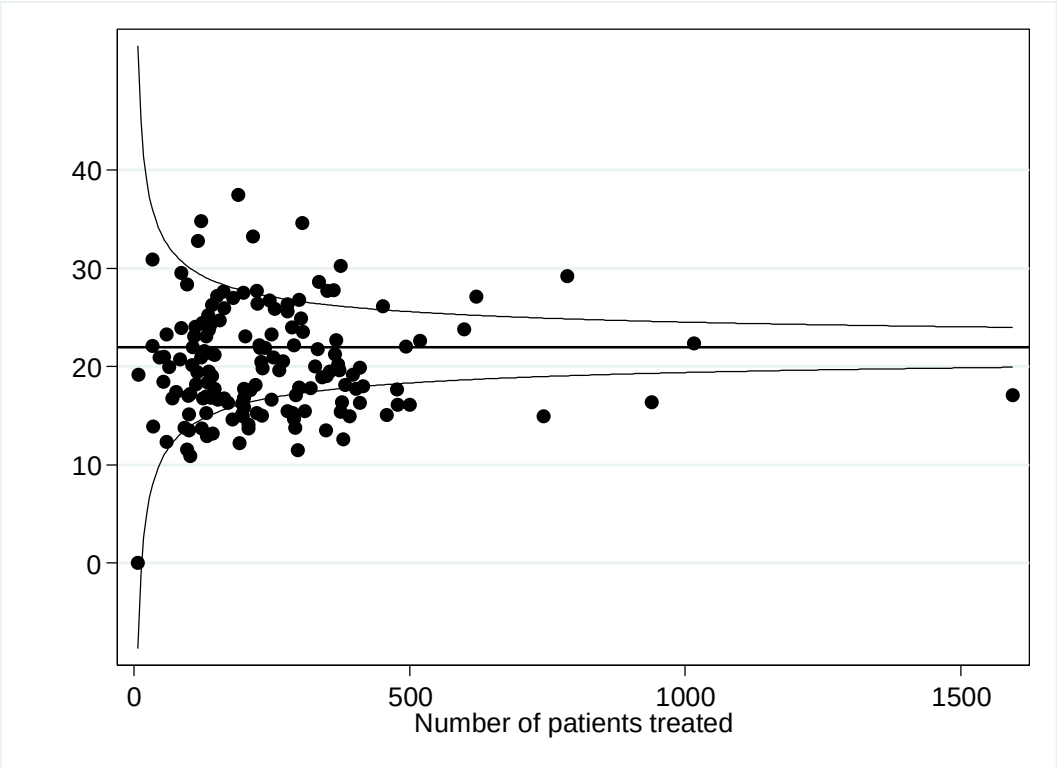
Emboldened percentages and means are statistically significant (P < 0.05)

Table 5. Population estimates by local treatment system outcome performance, England

Estimates	All local systems (n=149)	Performance better than expected (n=14)	Performance worse than expected (n=38)	Incidence rate difference
Median of population aged 16-64 (interquartile range) [a]	172,000 (127,100-272,700)	210,550 (171,250-433,725)	170,100 (140,625-219,725)	-
Number of opiate users per 1,000 (95% CI) [a]	7.7 (6.5-9.0)	6.3 (5.0-7.6)	10.4 (9.1-11.9)	4.1 (4.0-4.2)
Offence rate per 1,000 (95% CI) [b]	106.3 (106.2-106.4)	97.5 (97.2-97.8)	126 (125.7-126.2)	28.5 (28.1-28.8)
Drug-related deaths per million (95% CI) [c]	33.5 (32.7-34.4)	32.9 (30.2-35.8)	38.8 (36.9-40.8)	5.9 (5.9-5.9)

[a] (Hay et al., 2010)
[b] (Office for National Statistics, 2016)
[c] (Public Health England, 2016b)

Figure 1. Funnel plot of outcome performance (SCNR rate) by local treatment system



NB: The horizontal line is the national average for the SCNR outcome. The curved lines are the upper and lower 95% confidence interval. Each black dot represents a local treatment system. Local systems lying above the upper CI have an SCNR outcome performance that is better than average after risk-adjustment. Local systems lying below the lower CI have an SCNR outcome performance that is worse than average after risk-adjustment.

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