# Modelling Long-Term Joint Trajectories of Heroin Use and Treatment Utilisation: Findings from the Australian Treatment Outcome Study

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## ARTICLE INFO

## ABSTRACT

*Background:* Heroin is currently contributing to the worst drug addiction epidemic in United States history; recent rates of use, dependence and death have also increased dramatically in parts of Europe. An improved understanding of the long-term relationship between heroin use and treatment utilisation is essential to inform both clinical and public health responses. We aimed to identify i) joint trajectories of heroin use and treatment utilisation, ii) predictors of joint group membership, and iii) outcomes associated with joint group membership; over 10−11 years among a cohort of Australians with heroin dependence.

*Methods:* A total of 615 people with heroin dependence were recruited as part of a prospective longitudinal cohort study between 2001 and 02. This analysis focuses on 428 participants (70.1% of the original cohort) for whom complete data were available over 10−11 years.

*Findings:* Five joint trajectory groups were identified: i) 'long-term stable' (17%: decrease in probability of heroin use alongside high treatment utilisation); ii) 'long-term success' (13%: decrease in heroin use alongside decreased treatment utilisation, until there was maintained abstinence from heroin with no treatment utilisation); iii) 'treatment failure' (12%: no decrease in heroin use alongside high treatment utilisation); iv) 'late success' (9%: gradual decrease in heroin use alongside increased treatment utilisation); and v) 'relapsed' (9%: relapse in heroin use alongside an increase and decrease in treatment utilisation). Few variables were found to predict joint group membership, but group membership was predictive of demographic, substance use and physical and mental health outcomes at 10−11 years.

*Interpretation:* The role of treatment in recovery from heroin dependence is undeniable; however, a considerable proportion of people are able achieve and maintain abstinence without the need for ongoing treatment. An equally significant proportion will continue to use heroin despite being in long-term treatment.

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## 1. Introduction

Heroin use is currently contributing to the worst drug addiction epidemic in United States history [1−3], with use, dependence and death dramatically increasing over the past few years [1−5]. Between 2001 and 02 and 2012−13, the prevalence of lifetime heroin use and dependence increased five-fold and three-fold, and overdose deaths related to heroin increased by more than 420% between 2010 and 2015 [4,5]. Heroin-related deaths have substantially increased in the United Kingdom, rising by 57% between 2013 and 14, and 26% between 2014 and 15 [6]. Given the high mortality rate associated

with heroin and other opiate dependence [7−10], it is unsurprising that the burden of disease associated with these disorders is greater than any other illicit drug class [11]. The burden associated with these conditions reflects the chronicity of heroin dependence; a condition that often persists over the life-course [12].

Research has consistently demonstrated a positive association between treatment duration and favourable outcomes [13−19]; however, treatment for drug use is rarely a 'one-off' event with multiple attempts sometimes needed to achieve reduction or abstinence [16,20−23]. There are several treatment options available for opioid dependence, and no single treatment will suit or be effective for all users [24]. Treatment options include: detoxification/withdrawal management; pharmacotherapy (opioid agonist treatment: methadone, buprenorphine or partial agonist Suboxone; antagonist treatment: naltrexone); residential rehabilitation; and outpatient counselling [25,26]. Recent evidence from economic studies illustrates that costs associated

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with opioid treatment are only a small proportion of costs to society in terms of morbidity and mortality, and represent substantial cost-effectiveness [27,28].

Longitudinal research has identified that trajectories of heroin use, and recovery are heterogenous, but there is a critical need to better understand how these patterns relate to treatment utilisation. Such knowledge may provide insights as to how, and when, effective treatments may be used to target potential pivotal periods for relapse. This insight would not only provide information relevant for individual trajectories, but broader implications for informing clinical and public health responses to heroin use.

Building on our examination of trajectories of heroin use [29] the current study uses a group-based trajectory approach to examine the relationship between patterns of heroin use and patterns of treatment utilisation. More specifically, the study aimed to identify i) joint trajectories of heroin use and treatment utilisation, ii) predictors of joint trajectory group membership, and iii) outcomes associated with joint trajectory group membership; over 10−11 years among a cohort of Australians with heroin dependence.

## 2. Method

### 2.1. Design

Data were collected as part of the Australian Treatment Outcome Study (ATOS) - a naturalistic prospective longitudinal cohort study of 615 people with heroin dependence [30]. Participants were recruited from Sydney, Australia (2001−2002). Participants comprised 535 entering agencies treating heroin dependence, randomly selected within each modality and stratified by regional health area (201 methadone/buprenorphine pharmacotherapy, 201 detoxification, 133 residential rehabilitation). In addition, a group of 80 people with heroin dependence not entering treatment were recruited from needle and syringe programs within the same regional health areas. Ethical approval was obtained from the Human Research Ethics Committees of the University of New South Wales and participating area health districts.

Seventy percent (n = 431) of the cohort were reinterviewed 10−11-years following study entry [17]. Of the original cohort, 63 (10·2%) had died, 42 (6·8%) refused to participate, 7 (1·1%) were incarcerated and could not be interviewed, and a further 71 (11·5%) could not be contacted. One participant was excluded due to safety concerns. The current paper focuses on the 428 (69·6%) participants who had complete heroin use and treatment data over 10−11 years. Participants were recompensed A\$40 for completing the 10−11 yr interview. The sample reinterviewed at 10−11-years was broadly representative of the initial cohort. The only independent predictors of loss to follow-up were male sex, and a baseline diagnosis of major depression [17].

### 2.2. Measures

#### 2.2.1. Baseline

A structured interview utilising measures with established psychometric properties was administered to participants at baseline and are described in detail elsewhere [17,30]. Briefly, baseline interviews addressed demographic characteristics (including age, sex, main source of income in the past month), past month drug use (including use of heroin and other opiates, alcohol, cannabis, benzodiazepines, amphetamines, hallucinogens, cocaine, inhalants and tobacco), treatment history (number of episodes, treatment modality, duration), criminal involvement, major depression, post-traumatic stress disorder (PTSD), borderline personality disorder (BPD), and antisocial personality disorder (ASPD).

Past month drug use and criminal involvement were assessed using the Opiate Treatment Index (OTI) [31]. General physical and mental health were measured using the Short-Form-12 (SF-12) [32]. The Composite International Diagnostic Interview version 2·1 (CIDI) [33] was used to establish DSM-IV diagnoses of past-month heroin dependence, major depression, lifetime trauma exposure and lifetime PTSD. ASPD was assessed using a modified version of the Diagnostic Interview Schedule [34], and participants were screened for ICD-10 BPD using the International Personality Disorders Examination Questionnaire [35].

### 2.3. 10−11-year follow-up interview

The sections relating to demographics, drug use, criminal involvement, general physical and mental health, and major depression were readministered at 10−11 years. In addition, participants were asked the number of times they had commenced treatment for heroin dependence in each modality (opioid pharmacotherapy, inpatient and outpatient detoxification, residential rehabilitation), the recency, and duration of each episode [17]. In order to maximise participant recall, the 10−11-year interviews were administered using the life chart approach, based on the timeline follow-back (TLFB) method, which anchors interview questions to significant events in participants' lives (e.g., relationships, divorces, birth of children, time in prison) [36]. The life event chart was completed at the beginning of the interview, and participants were referred to the chart when subsequent questions required the participant to recall dates (e.g., periods of abstinence, time in treatment).

Patterns of heroin use were identified by asking about periods of one or more months of abstinence for each year of the study [29]. If a person reported < 12 months of abstinence within a calendar year, they were coded as having used heroin in that year. Similarly, for each

year, a person was coded as being in treatment if they reported having spent any time in any treatment modality within that calendar year.

## 2.4. Statistical analysis

A four stage group-based trajectory modelling approach was used to identify joint trajectories of heroin use and treatment utilisation [37,38] using procedures outlined by Jones and Nagin [39]. Analysis of missing data revealed 17·3% missing data across the follow-up period. According to the results of the Little missing completely at random test, the data could be considered to be missing completely at random ($\chi^2_7 = 3\cdot38$, $p = \cdot848$).

## 2.5. Stage 1: Identification of trajectory groups of heroin use and treatment utilisation

The first stage involved modelling separate trajectories of heroin use and treatment utilisation and calculating the probability of group membership for each. The process used to identify heroin use trajectories has been described elsewhere [29]. The same two-step process was used to identify treatment trajectories: i) selecting the number of trajectory groups, and ii) determining the order of the polynomial defining each group's trajectory (i.e., zero-order, linear, quadratic, cubic), using backwards selection at $p < \cdot05$ [38]. A series of 2−8 trajectory models were fit and the final models selected by comparing the goodness of fit using the following diagnostic criteria: i) Bayesian Information Criteria (BIC; lower scores indicate better model fit); ii) average posterior probabilities of group assignment ($> 0\cdot7$ acceptability threshold); iii) odds of correct classification ($> 5$ acceptability threshold); close correspondence between the estimated probability of group membership and the proportion of the sample assigned to each group based on posterior probability of group membership [38]. Fit statistics of treatment utilisation are provided in supplementary tables (Tables 5 and 6); fit statistics for heroin use have been previously reported [29].

## 2.6. Stage 2: Modelling joint trajectories of heroin use and treatment utilisation

The second stage involved modelling joint heroin use and treatment utilisation trajectories. Three sets of probabilities from the joint trajectories were examined: i) heroin use conditional on treatment utilisation; ii) treatment utilisation conditional on heroin use; and iii) the probabilities of joint membership across each of the unique combinations of heroin use/treatment utilisation groups [38,40]. Analyses for stages 1 and 2 were conducted using the SAS PROC TRAJ procedure [37]. Comparisons of treatment exposure between selected groups was conducted using ANOVA and Kruskal Wallis tests for normally and non-normally continuous data (using PASW statistics 24).

## 2.7. Stage 3: Predictors of joint trajectory group membership

The third stage involved conducting a series of bivariate multinomial logistic regressions to determine associations between baseline covariates and joint trajectory group membership, using PASW statistics 24. The analysis was exploratory and included an examination of all variables listed in Table 2. To account for multiple comparisons, the significance level was set at $p < 0\cdot005$.

## 2.8. Stage 4: Associations between joint trajectory group membership and 10−11-year outcomes

The final stage involved examining whether joint trajectory groups were related to subsequent 10−11-year outcomes. As with stage 3, the significance level was set at $p < 0\cdot005$ to account for multiple comparisons (0·05/10 comparisons).

# 3. Results

## 3.1. Heroin use trajectory groups

As previously reported [29], a six-group model was derived for heroin use, with the final model consisting of two cubic, two quadratic, one linear, and one zero order trajectories (BIC -1927·44 (N = 4708); − 1901·07 (N = 428); Fig. 1). The groups were characterised as: 1) 'rapid decrease to maintained abstinence' (16·1%); 2) 'rapid decrease with rapid relapse' (7·5%); 3) 'rapid decrease with late relapse' (15·8%); 4) 'gradual decrease to near abstinence' (17·1%); 5) 'gradual decrease' (21·5%) and; 6) 'no decrease' (22·1%).

## 3.2. Treatment Trajectory Groups

A four-group model for treatment utilisation provided the best fit for the data with two cubic and two quadratic trajectories (BIC -2258·86 (N = 4673); − 2238·54 (N = 428); Fig. 1). Model diagnostics are provided in the supplementary materials (Tables 5 and 6). The four groups were characterised as: 1) 'late increase in treatment' (21·7%); 2) 'reduced treatment' (30·1%); 3) 'rapid increase with gradual decrease in treatment' (13·7%), and; 4) 'long-term treatment' (34·5%).

## 3.3. Modelling Joint Trajectories

Table 1A illustrates the probability of treatment trajectory group membership contingent on heroin use group membership. Seventy-one percent of those in the rapid decrease to maintained abstinence group were in the reduced treatment trajectory; 54% of those in the rapid decrease with rapid relapse group were in the late increase in treatment trajectory; 34% and 36% of those in the rapid decrease with late relapse in heroin use were in the reduced treatment and long-term treatment groups, respectively; 47% of those in the gradual decrease to near abstinence group were in the rapid increase with gradual decrease in treatment group; 44% of those in the gradual decrease group were in the late increase in treatment group; and 54% of those in the no decrease group were in the long term treatment group.

From the alternative perspective, Table 1B illustrates the probability of membership in the heroin use groups conditional on treatment group membership. Thirty-six and 31% of those in the late increase in treatment utilisation group were in the gradual decrease or no decrease in heroin use groups, respectively; 53% of those in the reduced treatment group were in the rapid decrease to maintained abstinence group; 59% of those in the rapid increase with gradual decrease in treatment group were in the gradual decrease to near abstinence in heroin use group; and 34% of those in the long-term treatment utilisation group were in the no decrease in heroin use group.

Table 1C illustrates the probability of membership in each of the 24-joint heroin use and treatment trajectory groups. Thirteen percent were in the joint 'rapid decrease to maintained abstinence' heroin use and 'reduced treatment' groups; 12% were in the 'no decrease' heroin use and 'long-term treatment' groups; 9% were jointly in the 'gradual decrease' heroin use and 'late increase' treatment groups; and 8% were in the 'gradual decrease to near abstinence' heroin use and 'rapid increase with gradual decrease in treatment' groups.

## 3.4. Comparison of Selected Joint Groups

For further comparison of joint trajectory groups, we focused on five combinations of trajectory groups based on probability of joint group membership and potential clinical relevance (Table 1). The three groups with the highest joint memberships were characterised as a 'long-term success' group, comprising those who achieved maintained abstinence from heroin use, alongside a reduction in treatment utilisation (13% of the cohort); a 'treatment failure' group (12% of the cohort), who demonstrated no decrease in heroin use,
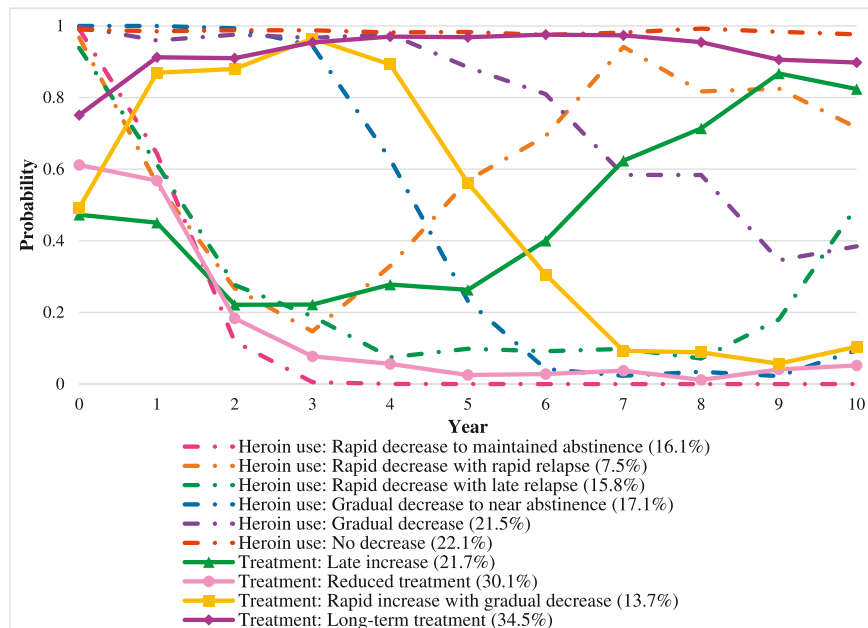
**Fig. 1.** Joint trajectories of heroin use and treatment utilisation.

alongside high treatment utilisation; and a 'late success' group (9% of the cohort), who gradually reduced heroin use alongside a late increase in treatment utilisation. In addition, a 'relapsed' group was formed by combining trajectories of those who experienced rapid decrease with rapid relapse from heroin use alongside late increase in treatment, and rapid decrease with late relapse from heroin use alongside reduced treatment utilisation (9%; sum of percentages 5 and 4 from Table 1C); as was a 'long-term stable' group, which comprised those who reduced heroin use over time, whilst in long-term treatment (17%; sum of percentages 4, 6 and 8 from Table 1C).

### 3.5. Predictors of Joint Trajectory Group Membership

Characteristics of individuals assigned to each of the selected joint trajectory groups are shown in Table 2. Joint trajectory group membership was associated with baseline treatment modality. Those in the 'long-term success' group were significantly less likely to have entered

methadone/buprenorphine pharmacotherapy at baseline compared to the 'long-term stable' ($p < \cdot 0001$) and 'treatment failure' groups ($p = \cdot 002$); and significantly more likely to have entered 'residential rehabilitation' than the 'long-term stable' group ($p < \cdot 0001$)(Table 3).

### 3.6. Characteristics of Joint Treatment Groups

Several treatment characteristics measured over 10−11-years were associated with joint group membership, including: total days in treatment ($p < 0.001$), total number of treatment episodes ($p < 0.001$), total number of detoxification episodes ($p < 0.001$), total number of maintenance episodes ($p < 0.001$), total days spent in detoxification ($p < 0.001$), and total number of days spent in maintenance ($p < 0.001$) (Table 3).

Those in the 'long-term success' joint trajectory group spent fewer days in treatment than the 'long-term stable' ($p < \cdot 0001$), 'late success' ($p < \cdot 0001$) and 'treatment failure' ($p < \cdot 0001$) groups; had fewer

**Table 1**
Conditional and joint probabilities of heroin use and treatment trajectories.

| Treatment utilisation trajectory group | Heroin use group | | | | | |
|---|---|---|---|---|---|---|
| | Rapid decrease to maintained abstinence | Rapid decrease with rapid relapse | Rapid decrease with late relapse | Gradual decrease to near abstinence | Gradual decrease | No decrease |
| A: Probability of treatment group membership conditional on heroin use group[†] | | | | | | |
| Late increase in treatment | 3·0 | 54·0 | 18·0 | 10·0 | 44·0 | 36·0 |
| Reduced treatment | 71·0 | 15·0 | 34·0 | 11·0 | 7·0 | 8·0 |
| Rapid increase with gradual decrease in treatment | 5·0 | 7·0 | 12·0 | 47·0 | 11·0 | 2·0 |
| Long-term treatment | 20·0 | 24·0 | 36·0 | 31·0 | 37·0 | 54·0 |
| | | | | | | |
| B: Probability of heroin use group membership conditional on treatment group[‡] | | | | | | |
| Late increase in treatment | 2·0 | 15·0 | 10·0 | 7·0 | 36·0 | 31·0 |
| Reduced treatment | 53·0 | 5·0 | 21·0 | 8·0 | 7·0 | 8·0 |
| Rapid increase with gradual decrease in treatment | 6·0 | 3·0 | 13·0 | 59·0 | 16·0 | 3·0 |
| Long-term treatment | 10·0 | 5·0 | 15·0 | 16·0 | 21·0 | 34·0 |
| | | | | | | |
| C: Joint probability of membership in heroin use and treatment groups[§] | | | | | | |
| Late increase in treatment | 0·6 | 3·8 | 2·6 | 1·8 | 9·2 | 8·0 |
| Reduced treatment | 12·5 | 1·1 | 4·9 | 1·9 | 1·5 | 1·8 |
| Rapid increase with gradual decrease in treatment | 0·9 | 0·5 | 1·8 | 8·4 | 2·3 | 0·4 |
| Long-term treatment | 3·6 | 1·7 | 5·3 | 5·6 | 7·7 | 12·1 |

[†] Columns add to 100%.
[‡] Rows add to 100%.
[§] All cells add to 100%.

**Table 2**
Treatment characteristics of joint trajectory groups.

| | Long-term success group (n = 57) | Treatment failure group (n = 50) | Relapsed group (n = 32) | Long-term stable group (n = 74) | Late success group (n = 31) | Total (n = 288) |
|---|---|---|---|---|---|---|
| Mean days in maintenance therapy over 10−11 years (SD)*** | 173·05 (340·00) | 2789·12 (1195·03) | 625·84 (762·56) | 3192·12 (843·21) | 1137·03 (763·59) | 1806·61 (1524·57) |
| Median days in residential rehabilitation over 10−11 years (range) | 28 (0−546) | 21 (0−1092) | 77 (0−518) | 0 (0−819) | 8 (0−1400) | 14 (0−1400) |
| Median days in detoxification over 10−11 years (range)*** | 0 (0−28) | 14 (0−231) | 0 (0−56) | 0 (0−406) | 14 (0−140) | 0 (0−406) |
| Mean days in treatment over 10−11 years (SD)*** | 287·57 (315·23) | 2938·08 (1123·64) | 770·13 (776·85) | 3297·03 (754·14) | 1346·60 (609·51) | 1941·25 (1484·12) |
| Median number treatment episodes over 10−11 years (range)*** | 2 (1−7) | 5 (1−44) | 4 (1−16) | 4 (1−85) | 4 (1−18) | 4 (1−85) |
| Median number maintenance therapy episodes over 10−11 years (range)*** | 0 (0−2) | 2 (0−15) | 1 (0−6) | 1·5 (1−10) | 1 (0−5) | 1 (0−10) |
| Median number detoxification episodes over 10−11 years (range) *** | 0 (0−3) | 1 (0−44) | 0.5 (0−5) | 0 (0−82) | 1 (0−12) | 0 (0−82) |
| Median number residential rehabilitation episodes over 10−11 years (range) | 1 (0−4) | 1 (0−8) | 1 (0−6) | 0 (0−10) | 0 (0−9) | 0 (0−10) |

treatment episodes than those in the 'treatment failure' group ($p < ·0001$); fewer detoxification episodes than those in the 'late-success' ($p = ·003$) and 'treatment failure' ($p = ·001$) groups; fewer maintenance episodes compared to those in the 'long-term stable' ($p < ·0001$), 'late success' ($p < ·0001$) and 'treatment failure' ($p < ·0001$) groups; fewer days in detoxification than those in the 'late success' ($p = ·001$) or 'treatment failure' groups ($p = ·003$), and fewer days in maintenance therapy than the 'long-term stable', 'late success' or 'treatment failure' groups ($p$'s $< ·0001$) (Table 3).

Those in the 'relapsed' group also spent significantly fewer days in maintenance therapy than those in the 'long-term stable' group ($p < ·0001$), and the 'long-term stable' group spent significantly more days in maintenance therapy than those in the 'late success' group. Those in the 'treatment failure' group spent significantly more days in maintenance therapy than those in the 'relapsed' and 'late-success' groups ($p$'s $< ·0001$)(Table 3).

### 3.7. Associations Between Joint Trajectory Group Membership and 10−11-Year Outcomes

Outcomes across each of the joint trajectory groups are illustrated in Table 4.

### 3.8. Demographic outcomes

Receiving a wage as a main source of income ($p < ·0001$) and criminal involvement ($p = 0.004$) were the only demographic outcomes associated with group membership. The 'long-term success' group were more likely than any other group to report wage as a main source of income (ORs 4·38−10·53).

The 'long-term success' group were significantly less likely than the 'relapsed' group to have been involved in past-month crime; compared to the 'late success' group (OR 0·13).

### 3.9. Drug use and treatment outcomes

Heroin use ($p < ·0001$) and dependence ($p < ·0001$), benzodiazepine use ($p < ·0001$), polydrug use ($p = 0.001$), injection-related health problems ($p < ·0001$) and being in current treatment ($p < ·0001$) were the only drug-related outcomes significantly associated with joint group membership.

The 'treatment failure' group were significantly more likely to be using heroin at 10−11 years than all other groups (ORs 3·91−99·56); the 'relapsed' group were also more likely to be using heroin at 10−11 years compared to the 'long-term success' group (OR 25·45).

The prevalence of heroin dependence among the 'long-term success' joint trajectory group at 10−11 years was zero. Those in the

'treatment failure' groups were more likely to be heroin dependent compared to those in the 'long-term stable' group (OR 12·67).

The 'long-term success' group were significantly less likely to have used benzodiazepines during the past month at 10−11 years compared to the 'treatment failure', 'long-term stable', and 'late success' groups (ORs 0·07, 0·22, 0·16 respectively). The 'treatment failure' group were more likely than the 'relapsed' and 'long-term stable' groups, to have used benzodiazepines in the past month at 10−11 years (ORs 5·83, 3·01 respectively). The 'treatment failure' group were also more likely to be polysubstance using at 10−11 years compared to those from the 'long-term success' group (OR 9·14). Those in the 'treatment failure' group were also significantly more likely to have experienced injection-related health problems in the past month at 10−11 years than those in the 'long-term success' (OR 19·5) or 'long-term stable' (OR 6·2) groups.

With regard to treatment, those in the 'long-term success' group were significantly less likely to be in current treatment at 10−11 years compared to all other groups (ORs 0·01−0·06). Compared to the 'treatment failure' (OR 0·17) and 'long-term stable' (OR 0·18) groups, those in the 'relapsed' group were significantly less likely to be in treatment.

There were no physical or mental health outcomes associated with joint group membership at 10−11 years.

### 3.10. Associations between Joint Trajectory Group Membership and Group Characteristics over 10−11-Years

Associations between joint group membership and group characteristics measured over 10−11 years are reported in Table 5 and Supplementary Table 9. The 'long-term success' group were less likely to have spent time in prison over the 10−11 years compared to the 'treatment failure' and 'late success' groups (ORs 0.21, 0.12 respectively). Compared to the 'relapsed' group, the 'late success' group were significantly more likely to have spent time in prison over the 10−11 years (OR 5.65). The 'long-term success' group were significantly less likely to have experienced trauma over the 10−11 years compared to the 'late success' group (OR 0.08).

## 4. Discussion

This study is the first to examine joint trajectories of heroin use and treatment utilisation and further emphasise the heterogeneity in patterns of drug use and recovery [41−44].

Research has consistently demonstrated that long-term stable retention in treatment is key to achieving positive outcomes [13−19]. Unique to the current study however, was the identification of a 'long-term success' joint trajectory group (with the highest joint membership; 13%) that demonstrated decreasing heroin use alongside reductions in

**Table 3**
Baseline characteristics of select joint trajectory groups[†].

| | Long-term success group (n = 57) | Treatment failure group (n = 50) | Relapsed group (n = 32) | Long-term stable group (n = 74) | Late success group (n = 31) | Total (n = 288) |
|---|---|---|---|---|---|---|
| *Demographics* | | | | | | |
| % Aged 30 or more | 49·1 | 44·0 | 43·8 | 36·5 | 32·2 | 41·4 |
| % Female | 33·3 | 38·0 | 40·6 | 40·5 | 22·6 | 36·1 |
| % Completed year 10 of schooling | 77·2 | 64·0 | 78·1 | 66·2 | 67·7 | 70·1 |
| % Australian born | 73·7 | 74·0 | 90·6 | 85·1 | 74·2 | 79·5 |
| % Wage main source of income | 17·5 | 16·0 | 25·0 | 12·2 | 25·8 | 17·6 |
| % Living in unstable accommodation[‡] | 19·3 | 6·0 | 6·3 | 6·8 | 16·1 | 10·7 |
| % Prison history | 31·6 | 44·0 | 34·4 | 43·2 | 32·3 | 38·1 |
| % Past month criminal activity | 49·1 | 56·0 | 50·0 | 55·4 | 51·6 | 52·9 |
| | | | | | | |
| *Drug use history* | | | | | | |
| % Age first got high > 13 | 61·4 | 48·0 | 43·8 | 48·6 | 41·9 | 50·0 |
| % Age first used heroin < 17 | 36·8 | 40·0 | 46·9 | 40·5 | 54·8 | 42·2 |
| % Used heroin for < 10 years | 61·4 | 60·0 | 62·5 | 64·9 | 67·7 | 63·1 |
| % Heroin dependent | 96·5 | 98·0 | 96·9 | 100 | 96·8 | 98·0 |
| | | | | | | |
| *Past month use of* | | | | | | |
| % Heroin | 100 | 100 | 93·8 | 97·3 | 100 | 98·4 |
| % Other opiates | 33·3 | 30·0 | 34·4 | 33·8 | 25·8 | 32·0 |
| % Cocaine | 35·1 | 44·0 | 37·5 | 43·2 | 45·2 | 41·0 |
| % Amphetamines | 24·6 | 32·0 | 43·8 | 35·1 | 12·9 | 30·3 |
| % Hallucinogens | 10·5 | 14·0 | 15·6 | 6·8 | 6·5 | 10·2 |
| % Benzodiazepines | 42·1 | 46·0 | 50·0 | 55·4 | 32·3 | 46·7 |
| % Antidepressants | 10·5 | 20·0 | 12·5 | 18·9 | 3·2 | 12·3 |
| % Alcohol | 49·1 | 52·0 | 62·5 | 48·6 | 45·2 | 50·8 |
| % Cannabis | 66·7 | 72·0 | 68·8 | 73·0 | 71·0 | 70·5 |
| % Tobacco | 100 | 90·0 | 100 | 94·6 | 100 | 96·3 |
| % Inhalants | 0 | 2·0 | 3·1 | 0 | 0 | 0·8 |
| % Polydrug use[§] | 91·2 | 86·0 | 93·8 | 89·2 | 90·3 | 89·8 |
| % Ever overdosed | 50·9 | 58·0 | 50·0 | 59·5 | 38·7 | 53·3 |
| % Ever injected | 91·2 | 98·0 | 100·0 | 97·3 | 90·3 | 95·5 |
| | | | | | | |
| *Treatment history* | | | | | | |
| % Previous treatment at baseline | 89·5 | 98·0 | 96·9 | 82·4 | 87·1 | 89·7 |
| % In maintenance therapy at baseline[***] | 12·3 | 40·0 | 12·5 | 52·7 | 25·8 | 32·0 |
| % In detoxification at baseline | 43·9 | 28·0 | 40·6 | 32·4 | 45·2 | 36·9 |
| % In residential rehabilitation at baseline[***] | 35·1 | 20·0 | 37·5 | 6·8 | 12·9 | 20·9 |
| % Not in treatment at baseline | 8·8 | 12·0 | 9·4 | 8·1 | 16·1 | 10·2 |
| | | | | | | |
| *Physical and mental health* | | | | | | |
| % Lifetime trauma exposure | 94·7 | 94·0 | 96·9 | 91·9 | 100 | 94·7 |
| % Past month severe physical health disability | 7·0 | 6·0 | 9·4 | 12·2 | 6·5 | 8·6 |
| % Past month severe mental health disability | 57·9 | 38·0 | 62·5 | 40·5 | 32·3 | 45·9 |
| % Past month major depression | 22·8 | 28·0 | 43·8 | 21·6 | 9·7 | 24·6 |
| % Lifetime PTSD | 43·9 | 38·0 | 46·9 | 36·5 | 32·3 | 39·3 |
| % Lifetime ASPD | 66·7 | 78·0 | 81·3 | 78·4 | 61·3 | 73·8 |
| % Lifetime BPD | 47·4 | 50·0 | 43·8 | 40·5 | 41·9 | 44·7 |
| % Ever attempted suicide | 29·8 | 44·0 | 21·9 | 31·1 | 35·5 | 32·8 |

[***] $p < ·0001$.
[†] Note that 140 participants were not included in this comparison because they were members of the joint groupings that did not conceptually fit into those compared.
[‡] Unstable accommodation defined as living in boarding house/hostel, shelter/refuge, no fixed address/homeless.
[§] Polydrug use defined as the use of more than one class of drug (excluding antidepressants and tobacco).

treatment utilisation, until there was maintained abstinence from heroin without the need for ongoing treatment. Contrary to the long-standing conceptualisation of heroin dependence as a chronic, relapsing condition [12] requiring long-term stable treatment, this finding indicates that a significant proportion of people will be able to achieve and

**Table 4**
Covariates associated with joint trajectory group membership.

| Joint trajectory group | p | OR | Lower 95%CI | Upper 95%CI |
|---|---|---|---|---|
| **In maintenance therapy at baseline** | | | | |
| Long-term success group | **Constant** | **Constant** | **Constant** | **Constant** |
| Long-term stable group | <·0001 | 7·96 | 3·19 | 19·84 |
| Treatment failure group | 0·002 | 4·76 | 1·80 | 12·59 |
| **In residential rehabilitation at baseline** | | | | |
| Long-term success group | **Constant** | **Constant** | **Constant** | **Constant** |
| Long-term stable group | <·0001 | 0·13 | 0·05 | 0·39 |

maintain abstinence without the need for further treatment. At the other end of the spectrum, an equally significant proportion of people continued using heroin despite being in long-term treatment and may be characterised as 'treatment resistant'. These findings conflict with recent research from the United States, which indicated that more months in treatment was significantly associated with a 'low use' opioid trajectory, and fewer months with a 'high use' opioid trajectory [45].

Although the bulk of research in this space has consistently demonstrated a positive association between treatment duration and favourable outcomes [13–19,45], the current study findings highlight the complexity of this relationship and the need for clinicians to recognise the early signs of non-response to treatment. Despite spending more days in treatment than all other trajectory groups excluding the 'long-term stable' group, those in the 'treatment failure' group demonstrated poorer clinical profile across a number of domains at 10−11 years than any other trajectory group, including significant

**Table 5**
Joint trajectory groups associated with 10−11-year outcomes[†].

| | Long-term success group (n = 57) | Treatment failure group (n = 50) | Relapsed group (n = 32) | Long-term stable group (n = 74) | Late success group (n = 31) | Total (n = 288) |
|---|---|---|---|---|---|---|
| *Demographics* | | | | | | |
| % Wage main source of income*** | 63·2 | 14·0 | 28·1 | 20·3 | 22·6 | 30·3 |
| % Living in unstable accommodation[‡] | 1·8 | 8·0 | 9·4 | 4·1 | 0 | 4·5 |
| % Past month criminal involvement*** | 7·0 | 26·0 | 37·5 | 16·2 | 25·8 | 20·1 |
| % Past month prison history | 0 | 4·3 | 28·6 | 8·3 | 5·3 | 7·3 |
| | | | | | | |
| *Drug use* | | | | | | |
| *Past month use of:* | | | | | | |
| % Heroin*** | 1·8 | 64·0 | 31·3 | 12·2 | 25·8 | 24·6 |
| % Other opiates | 22·8 | 26·0 | 21·9 | 20·3 | 22·6 | 22·5 |
| % Cocaine | 5·3 | 4·0 | 6·3 | 2·7 | 12·9 | 5·3 |
| % Amphetamines | 10·5 | 14·0 | 25·0 | 16·2 | 9·7 | 14·8 |
| % Hallucinogens | 3·5 | 0 | 0 | 0 | 0 | 0·8 |
| % Benzodiazepines*** | 10·5 | 62·0 | 21·9 | 35·1 | 41·9 | 34·0 |
| % Antidepressants | 21·1 | 40·0 | 34·4 | 21·6 | 22·6 | 27·0 |
| % Alcohol | 56·1 | 46·0 | 59·4 | 44·6 | 58·1 | 51·2 |
| % Cannabis | 22·8 | 52·0 | 40·6 | 36·5 | 32·3 | 36·5 |
| % Tobacco | 71·9 | 82·0 | 91·3 | 85·1 | 96·8 | 82·4 |
| % Inhalants | 0 | 0 | 0 | 0 | 6·5 | 0·8 |
| % Polydrug use[§]*** | 63·2 | 94·0 | 87·5 | 77·0 | 80·6 | 79·1 |
| % Heroin dependent*** | 0 | 42·0 | 21·9 | 5·4 | 12·9 | 14·8 |
| % Injection-related health problems*** | 5·3 | 52·0 | 21·9 | 14·9 | 22·6 | 22·1 |
| % Overdosed in past 12 months | 0 | 10·0 | 6·3 | 2·7 | 16·1 | 5·7 |
| | | | | | | |
| *Treatment* | | | | | | |
| % In current treatment*** | 3·5 | 78·0 | 37·5 | 77·0 | 61·3 | 52·9 |
| % In maintenance therapy | 1·8 | 76·0 | 34·4 | 77·0 | 54·8 | 50·8 |
| % In detoxification | 0 | 2·0 | 0 | 0 | 3·2 | 0·8 |
| % In residential rehabilitation | 0 | 0 | 0 | 0 | 3·2 | 0·4 |
| | | | | | | |
| *Physical and mental health* | | | | | | |
| % Past month severe physical health disability | 15·8 | 10·0 | 12·5 | 8·1 | 6·5 | 10·7 |
| % Past month severe mental health disability | 15·8 | 32·0 | 28·1 | 20·3 | 19·4 | 22·5 |
| % Past month major depression | 14·0 | 28·0 | 28·1 | 15·1 | 22·6 | 20·2 |
| % Past 12-month PTSD | 7·0 | 32·0 | 18·8 | 23·0 | 19·4 | 20·1 |
| % Attempted suicide in past 12 months | 10·5 | 14·0 | 12·5 | 13·5 | 6·5 | 11·9 |
| | | | | | | |
| *Characteristics of joint trajectory groups over 10−11-years* | | | | | | |
| % In prison since baseline | 15·8 | 46·9 | 21·9 | 32·4 | 61·3 | 33·7 |
| % Overdosed since baseline | 22·8 | 34·0 | 43·8 | 35·1 | 45·2 | 34·4 |
| % Trauma since baseline | 54·4 | 76·0 | 62·5 | 77·0 | 93·5 | 71·7 |
| % Attempted suicide since baseline | 8·8 | 20·0 | 18·8 | 18·9 | 12·9 | 16·0 |

*** $p < ·0001$.

[†] Note that 140 participants were not included in this comparison because they were members of the joint groupings that did not conceptually fit into those compared.

[‡] Unstable accommodation defined as living in boarding house/hostel, shelter/refuge, no fixed address/homeless.

[§] Polydrug use defined as the use of more than one class of drug (excluding antidepressants and tobacco).

increased likelihood of benzodiazepine, heroin and polysubstance use, injection-related health problems, and reliance on government benefits as main source of income at 10−11 years.

Those in the 'treatment failure' group, however, had a greater number of treatment episodes, which has consistently been associated with poorer treatment outcomes [17,19,46,47]. The patterns observed among the 'relapsed', 'late success' and 'long-term stable' groups highlight the need for treatment strategies to incorporate relapse prevention and long-term assertive follow-up to ensure that relapses can be addressed early, before a person returns to previous patterns of use [48]. Collectively, these associations also emphasise the importance of quality and quantity (duration rather than number of treatment episodes) as core tenets in the long-term treatment of heroin dependence.

Consistent with previous research [44,49] examination of predictors of group membership did not reveal any significant demographic, drug use history, physical or mental health factors that may help to identify those who are more likely to achieve 'long-term success', and who may fall into the 'treatment failure' group. The only factor that distinguished these two groups was entering methadone/buprenorphine therapy at baseline. Given the amount of movement between treatment modalities, however, these findings do not provide definitive evidence

regarding which treatments may be more efficacious. Further research examining the potential influence of other factors such as genetic variability may shed light on this issue.

Findings from the current study should be interpreted within the context of the study limitations. By necessity, the study relied almost exclusively on self-report measures. Although there is debate regarding the validity and reliability of self-report as a tool for measuring drug use, there is an extensive body of international literature on self-reported substance use among heroin users, demonstrating its consistent validity and reliability in research settings [31,50−52]. Participants were required to report on events that occurred over a 10−11-year period, however, and findings may therefore be subject to recall bias. To minimise the impact of recall bias, data collected were limited to periods of use, abstinence and treatment; however, more predictive capacity may have been possible had more detailed measures of quantity and frequency of use been collected. While recruitment involved the random selection of treatment agencies stratified by modality, and demographic characteristics and drug use histories of the ATOS cohort were consistent with previous Australian and international studies of heroin use [53−55], care should be taken in generalising findings to other treatment systems. Given the relatively small sizes of some

**Table 6**
10−11 year outcomes associated with joint trajectory group membership.

| Joint trajectory group | p | OR | Lower 95%CI | Upper 95%CI |
|---|---|---|---|---|
| **Receiving wage as main source of income** | | | | |
| Long-term success group | **Constant** | **Constant** | **Constant** | **Constant** |
| Treatment failure group | <·0001 | 0·09 | 0·04 | 0·25 |
| Relapsed group | 0·002 | 0·23 | 0·09 | 0·58 |
| Long-term stable group | <·0001 | 0·15 | 0·07 | 0·32 |
| Late success group | 0·001 | 0·17 | 0·06 | 0·46 |
| | | | | |
| **Past month criminal involvement** | | | | |
| Long-term success group | **Constant** | **Constant** | **Constant** | **Constant** |
| Relapsed group | 0·001 | 7·95 | 2·29 | 27·55 |
| | | | | |
| **Past month heroin use** | | | | |
| Treatment failure group | **Constant** | **Constant** | **Constant** | **Constant** |
| Long-term success group | <·0001 | 0·01 | 0·00 | 0·08 |
| Relapsed group | 0·005 | 0·26 | 0·10 | 0·66 |
| Long-term stable group | <·0001 | 0·08 | 0·03 | 0·19 |
| Late success group | 0·001 | 0·20 | 0·07 | 0·53 |
| | | | | |
| **Past month heroin use** | | | | |
| Relapsed group | **Constant** | **Constant** | **Constant** | **Constant** |
| Long-term success group | 0·003 | 0·04 | 0·00 | 0·33 |
| | | | | |
| **Past month heroin dependence** | | | | |
| Treatment failure group | **Constant** | **Constant** | **Constant** | **Constant** |
| Long-term stable group | <·0001 | 0·08 | 0·02 | 0·25 |
| | | | | |
| **Past month benzodiazepine use** | | | | |
| Long-term success group | **Constant** | **Constant** | **Constant** | **Constant** |
| Treatment failure group | <·0001 | 13·87 | 5·00 | 38·48 |
| Long-term stable group | 0·002 | 4·60 | 1·74 | 12·16 |
| Late success group | 0·001 | 6·14 | 2·03 | 18·56 |
| | | | | |
| **Past month benzodiazepine use** | | | | |
| Treatment failure group | **Constant** | **Constant** | **Constant** | **Constant** |
| Relapsed group | 0·001 | 0·17 | 0·06 | 0·47 |
| Long-term stable group | 0·004 | 0·33 | 0·16 | 0·70 |
| | | | | |
| **Past month polysubstance use** | | | | |
| Treatment failure group | **Constant** | **Constant** | **Constant** | **Constant** |
| Long-term success group | 0·001 | 0·11 | 0·03 | 0·40 |
| | | | | |
| **Past month injection-related health problems** | | | | |
| Treatment failure group | **Constant** | **Constant** | **Constant** | **Constant** |
| Long-term success group | <·0001 | 0·05 | 0·01 | 0·19 |
| Long-term stable group | <·0001 | 0·16 | 0·07 | 0·38 |
| | | | | |
| **In current treatment** | | | | |
| Long-term success group | **Constant** | **Constant** | **Constant** | **Constant** |
| Treatment failure group | <·0001 | 97·50 | 20·46 | 464·68 |
| Relapsed group | 0·001 | 16·50 | 3·39 | 80·27 |
| Long-term stable group | <·0001 | 92·21 | 20·34 | 417·92 |
| Late success group | <·0001 | 43·54 | 8·92 | 212·50 |
| | | | | |
| **In current treatment** | | | | |
| Relapsed group | **Constant** | **Constant** | **Constant** | **Constant** |
| Treatment failure group | <·0001 | 5·91 | 2·22 | 15·74 |
| Long-term stable group | <·0001 | 5·59 | 2·28 | 13·71 |

trajectory groups, caution should be used when interpreting non-significant results.

Despite these limitations, the current study provides clinically and internationally relevant information on trajectories of heroin use and treatment utilisation. It also emphasises the vital role of longitudinal research in examining the natural history of heroin dependence. While patterns of heroin use and treatment utilisation are diverse, it is clear that for some, heroin dependence is a chronic, debilitating condition, that recurs over the life-course and demands early intervention and a long-term response. For others, however, long term abstinence is possible, and these people may not need further treatment. Few characteristics differentiated between who will achieve maintained abstinence and who will continue to use in a chronic high use, high treatment utilisation pattern. Both paths however, have crucial implications in terms of long-term outcomes and the critical timing of interventions.

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### Declaration of Competing Interests

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### Contributors

CM conceptualised and designed the study, carried out the analyses, and drafted the manuscript. KLM conceptualised and designed the study, critically reviewed the results of analyses, and reviewed and revised the manuscript. TS, SD, JR and MT critically reviewed the results of analyses and reviewed and revised the manuscript. All authors approved the final manuscript as submitted.

### Transparency declaration

CM affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.eclinm.2019.07.013.

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