Predictors of the Successful Treatment of Addiction to Heroin and Other Illicit Opioids. Systematic review

ORLÍKOVÁ, B.[1,2]

1 | National Institute of Mental Health, Klecany, Czech Republic
2 | Department of Psychology, Faculty of Arts, Palacky University, Olomouc, Czech Republic

BACKGROUND: Dependence on heroin (and other illicit opioids) is a serious health and social problem. In the Czech Republic, there are an estimated 4,500 problem heroin users and 7,100 users of diverted buprenorphine (especially Subutex®). Users of heroin and other opioids are the second largest group of drug users in treatment. The treatment of opioid dependence involves psychosocial (abstinence-based) and/or pharmacological (substitution treatment) interventions. **METHODS:** Systematic review. Specialised databases (ScienceDirect, Scopus, Cochrane Database) and other sources (Medvik) were searched for both international and Czech scientific literature on the treatment of addiction to heroin (or other illegal opiates) and factors influencing its outcomes (published between 2000 and 2017). **CONCLUSIONS:** The basic positive predictors are the length of treatment and specific sociodemographic (such as age at entry to treatment) and psychological characteristics. Psychiatric comorbidity is generally a risk factor. The pressure of the client's conflicts with the law also improves retention in treatment and its overall outcome. Another positive predictor is a family situation with no major conflicts and the absence of addiction issues among client's family members. Substitution treatment was found to show higher treatment retention rates than abstinence-based psychosocial therapy. The success of substitution treatment is associated with higher doses of substitution medicines, psychosocial support during treatment and good relationships with the service staff. Taking other drugs during treatment was found to cause a deterioration of the outcomes. Users of opioids other than heroin and non-injecting users seem to achieve better treatment outcomes.

Corresponding author | Barbora Orlíková, Topolová 748, 250 67 Klecany, Czech Republic

barbora.orlikova@nudz.cz

● 1 INTRODUCTION

The aim of drug treatment is to bring about a change which improves health and quality of life to the greatest extent possible. These objectives are achievable and measurable but may not be achieved at all times and with each client under the same circumstances and conditions (Kalina, 2015). Retention in treatment, its successful completion, and its positive outcomes being sustained depend on a range of circumstances. In addition to factors on the part on the individual entering treatment, there are factors related to service provision (Mounteney & Baker, 1999), i.e. those which can be shaped by professionals to improve the effectiveness of the change processes (Kalina, 2015). Understanding of these factors (predictors) enhances the potential of the services to engage "difficult" clients in treatment and help them overcome barriers to entering and being retained in treatment (Kalina, 2015).

The text below summarises both international and Czech evidence concerning predictors of successful treatment outcomes in users of heroin and other illicit opioids. Given that opioid dependence treatment may involve both abstinence-oriented psychosocail approaches and pharmacological substitution treatment, the paper discusses evidence pertaining to both of these types of treatment interventions. Despite some enduring controversies, in Czech conditions substitution treatment is considered to be a key and fully-fledged way of treating addiction (Pavlovská & Minařík, 2015).
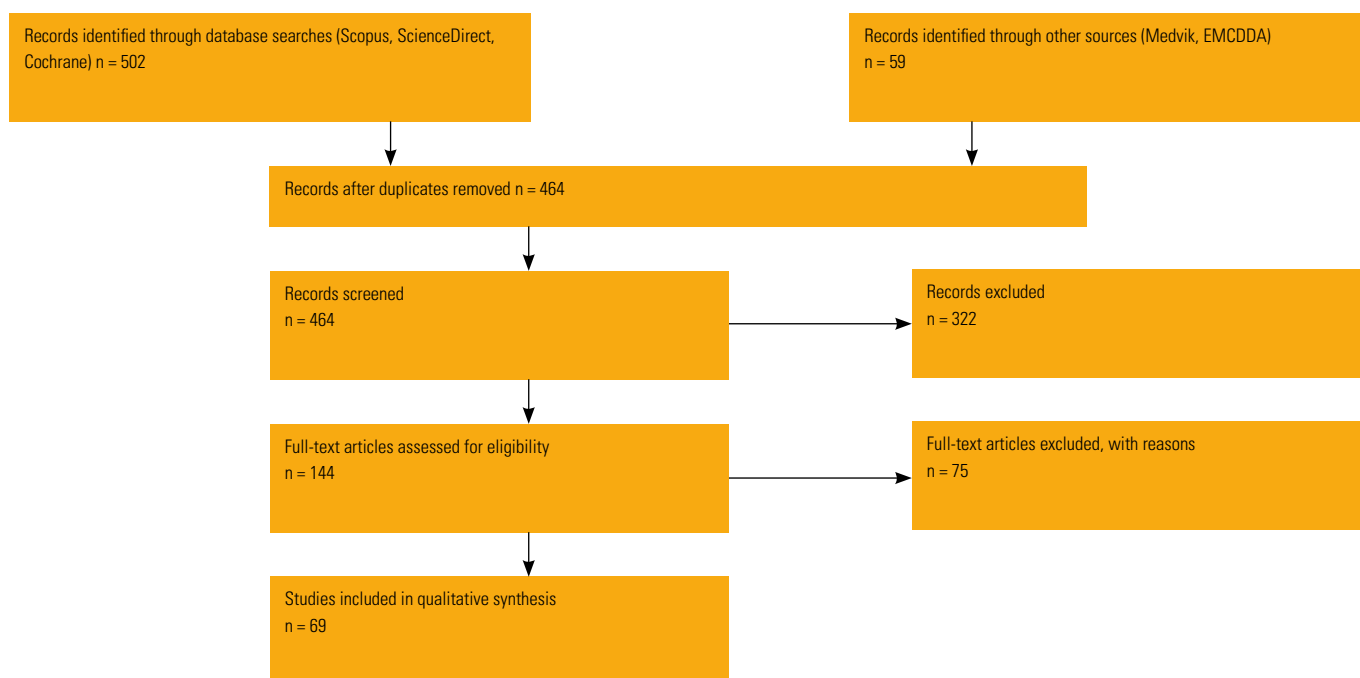
1.1 Use of heroin and other illicit opioids in the Czech Republic and internationally

Conducted by the National Monitoring Centre for Drugs and Addictions (the National Focal Point) and MindBridge Consulting, the 2016 National Survey on Substance Abuse found that one or more of the illicit drugs under study had been used at some point in their lifetime by a total of 30.5% of the general population aged 15-64, with men and women accounting for 38.8% and 22.7% respectively. Lifetime heroin use was reported by 0.7% of the respondents (1.2% of the men and 0.3% of the women), with 0.2% of the respondents having used the drug in the last year. The survey also looked into the use of opioid analgesics. Data on their use in the last 12 months and last 30 days is available. Within the last-year time frame, opioid-based medication had been used to relieve pain by 8.1% of the respondents (6.1% of the men and 10.1% of the women), with 53.4% of them obtaining these medicines without a prescription. According to a 2016 survey of the prevalence of drug use among the population of the Czech Republic, 1.1% of those in the 15-64 age category had used heroin at least once in their lifetime, while the figure was 1.3% among the group of young adults (aged 15-34) (Mravčík et al., 2017). The European School Survey on Alcohol and Other Drugs (ESPAD), carried out in the Czech Republic in 2015 among 16-year-old students, identified a 0.7% lifetime prevalence of the use of heroin and other opiates (Chomynová et al., 2016).

In 2016 there were estimated to be 46,800 problem (high-risk) users of methamphetamine (pervitin) and opioids, specifically 34,300 methamphetamine users, 3,400 heroin users, and 7,300 buprenorphine users. While still limited, the misuse of opioid analgesics appears to be on the rise among problem drug users. The number of problem users of other opioids was estimated at 1,700. Overall, the estimated number of opioid users was thus 12,500 (Mravčík et al., 2017).

In early 2015 the National Drug Demand Register (NRLUD) was put into operation, integrating two previously independent information systems: the Treatment Demand Register managed by the Public Health Service and the National Register of Users of Medically Indicated Substitution Substances (the Substitution Treatment Register). Because of changes in the reporting system and also some technical difficulties, the register probably lacks data from a significant segment of the treatment network for both 2015 and 2016. Until (and including) 2014 approximately 10,000 cases were reported to the Treatment Demand Register. In the long term, users of methamphetamine as the primary drug accounted for about 70% of all treatment demands and their number grew continuously, while the number of users of opioids (particularly heroin) was declining in the long term. In 2015 and 2016, the NRLUD register contained over 7,000 clients, including the newly reported users of alcohol and tobacco as the primary drugs and pathological gamblers, none of whome were subject to reporting until 2014. Alcohol users account for about a quarter of all the reported clients, while illicit drug users almost 70% (opioid users and methamphetamine users represent approximately one-third and one-fifth of all the clients respectively). The difference in the proportions of opioid and methamphetamine users in comparison to the former register administered by the Public Health Service and the NRLUD is mainly due to the fact that the NRLUD covers substitution treatment much more than it does low-threshold and counselling services. In 2016 the NRLUD registered a total of 2,266 patients in substitution treatment. Nevertheless, not all the patients are entered into the NRLUD register; the actual number of patients in substitution treatment is estimated at some 3,800 (Mravčík et al., 2016). In 2016 five preparations intended for substitution treatment were available in the Czech Republic, namely methadone, Subutex®, Buprenorphine Alkaloid®, Ravata® (the last three featuring buprenorphine as the active ingredient), and Suboxone® (a composite agent with buprenorphine and naloxone as the active substances) (Mravčík et al., 2017).

As regards opioid use in Europe and the rest of the world, the European Drug Report (EMCDDA, 2017) provides an expert estimate of 1.3 million problem (high-risk) opioid users. Opioids are reported as the primary drug by 38% of all the individuals demanding treatment in the EU. In 2015 substitution treatment was received by 630,000 opioid users. The World Drug Report (UNODC, 2017) indicates an estimate of 35.1 million opioid users, of whom 17.7 million are opiate users.

Records identified through database searches (Scopus, ScienceDirect, Cochrane) n = 502

Records identified through other sources (Medvik, EMCDDA) n = 59

Records after duplicates removed n = 464

Records screened n = 464

Records excluded n = 322

Full-text articles assessed for eligibility n = 144

Full-text articles excluded, with reasons n = 75

Studies included in qualitative synthesis n = 69

Figure 1 | 69 publications were included in the systematic review.

● 2 METHODOLOGY

Using the words "heroin"/"illicit (illegal) opiates" AND "treatment" AND "predictor"/"outcome", the ScienceDirect and Scopus databases were searched for relevant international scientific articles containing such words in their title, abstract, or key words. The search was limited to papers published in English from 2000 to 2017. The main criterion was the focus of the article on the treatment of addiction to heroin or other illicit opiates. A total of 502 scientific papers were identified, 351 in the Scopus database and 151 in ScienceDirect. Other sources included Czech professional papers contained in the Medvik database, which was searched using the key words "heroin" OR "opiáty"/"opiates". This search was limited to papers written in Czech, Slovak, or English and published in scientific journals between 2000 and 2017. The above sources were extended to include a few other texts dealing with dependence on heroin and other illicit opioids produced by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). A total of 59 publications were retrieved from other sources than international databases of scholarly papers.

After the removal of duplicates, 464 publications were selected for further screening. 322 of these records were excluded on the basis of the information provided in their abstracts – these were articles which concerned (a) the treatment of other conditions of drug users rather than addiction treatment, (b) individuals prior to their entering treatment and treatment entry predictors, (c) pre-clinical and neurobiological research, (d) in-treatment or post-treatment mortality, (e) the effects of the substitution treatment of pregnant women on unborn children, (f) dependence on prescription opioids, (g) diversion of substitution treatment preparations, and (h) only epidemiological data and characteristics of people in treatment without exploring the effects of such factors on treatment. After these texts had been excluded, 144 publications remained for further consideration.

After the full texts of the 144 publications had been assessed, 75 of them were excluded on the following grounds: a) the publication meets any of the aforementioned exclusion criteria, b) although the publication describes a study including individuals in treatment, no specific distinction is made between the category of users of heroin and other illicit opioids on the one hand and users of other substances on the other hand (e.g. general inpatient treatment outcomes are reported where both heroin and cocaine users are included), c) the publication describes a treatment strategy but little information is provided about predictors of successful treatment and other factors influencing its outcome, d) the publication reflects a significantly different sociocultural setting (this particularly refers to the exclusion of studies performed in Asia and a preference for the inclusion of those conducted in Europe, Australia, and North America), and e) studies which investigate treatment outcomes in the prison setting or among a narrowly defined group (e.g. the Native American community).

● 3 TREATMENT OUTCOME PREDICTORS

3.1 Length of treatment

One of the most important factors in the prediction of successful treatment is the time spent in treatment. The longer a client/patient can remain in treatment, the better the overall results (Corsi et al., 2009). Naturally, this factor is interconnected with other influences – some patients/clients

tend to drop out of treatment more often than others, and the examination of the underlying factors and their mitigation should then help in ensuring their better retention in treatment and improving their general outcome.

The length of treatment as a predictive factor was also pointed out by an Italian study of heroin-addicted patients (Salamina et al., 2010) and other studies concerned with the effectiveness of opiate dependence treatment (Bell et al., 2006; Eastwood et al., 2017; Peles et al., 2008). This factor was also ascertained in young people undergoing treatment for heroin dependence, irrespective of the type of therapy, i.e. maintenance or abstinence-oriented. The metaanalysis showed that adolescents in methadone-based substitution treatment displayed higher retention rates. However, those juvenile patients who stayed in drug-free treatment for at least six months showed better results than patients on methadone maintenance (Hopfer et al., 2002).

3.2 Client/patient characteristics

3.2.1 Psychological characteristics and psychiatric comorbidity

One of the factors which is generally assumed to predict a poor treatment outcome for clients/patients is psychiatric comorbidity. Some of the studies provide more detailed evidence on this topic. The Australian Treatment Outcome Study (ATOS), involving an 11-year follow-up, found major depression to be one of the strongest predictors of the participants' continuing to use heroin (Teesson et al., 2015). However, another research study, focusing on a substitution treatment modality, did not find differences in treatment outcomes in relation to baseline depressive symptoms or the length and severity of drug use. Surprisingly, it found tobacco use to be associated with poorer treatment outcomes. It was also reported that severe baseline anxiety symptoms had doubled the success of treatment (Ziedonis et al., 2009).

The prevalence of psychiatric dual diagnoses in heroin users and the effect of psychiatric comorbidity on repeated entry to treatment following methadone maintenance or naltrexone implant treatment were also investigated. It was found that 32% of the heroin-addicted patients had a dual psychiatric diagnosis. These had undergone significantly more treatment episodes than non-psychiatric comorbidity patients. However, the authors of the study recommended that this should be subjected to further research, as a psychiatric dual diagnosis may not predict poor treatment outcomes at all times (Ngo et al., 2011). Another research study focused on clients with a long history of heroin who were assigned to a buprenorphine maintenance programme. 68.4% of them were found to be affected by psychiatric comorbidity (major depression 29.6%, generalised anxiety disorder 11.2%, personality disorders 21.8%, and schizophrenia 6.3%). The major depression group showed a significantly higher treatment retention rate and were less likely to use illicit drugs while in treatment (and had better treatment outcomes than the non-comorbidity group). The

lowest treatment retention rate was found among patients with schizophrenia and personality disorders. It was concluded that better treatment outcomes in major depression patients may be attributed to the effect of buprenorphine, which seems to be more effective, particularly in this type of psychiatric comorbidity (Gerra et al., 2004; Gerra et al., 2006). According to Maremmani et al. (2008), clients with psychiatric comorbidity in methadone maintenance therapy whose psychiatric problems preceded the onset of their heroin use were more likely to remain in treatment.

A Czech study of retention in buprenorphine maintenance treatment suggested that psychosocial factors which may predict successful outcomes include the absence of any severe psychiatric disorder, a low score on the neuroticism scale (i.e. psychological stability), and a low level of craving (Večeřová-Procházková et al., 2007). There are other studies which mention psychiatric comorbidity as a risk factor in terms of the early termination of treatment (Clark et al., 2015; Michelazzi et al., 2008; Salamina et al., 2010). Subjects diagnosed with a concurrent addiction to alcohol or other substances in addition to their opioid dependence were also found to be dramatically more prone to relapse (Clark et al., 2015).

Marissen et al. (2006) examined the effect of attentional bias (AB) on patients in treatment for heroin dependence. Nešpor (2013) defines AB as a preferential perception of cues associated with addictive behaviour to the exclusion of other cues (or as distraction) which impairs effective decision making and the use of one's own experience or relevant ambient information. A higher level of AB at follow-up measurements was found to be associated with relapsing into heroin use. Abramsohn et al. (2009) studied the stability of a sense of coherence (SOC) on a sample of former heroin addicts in an Israeli methadone programme. The construct of the sense of coherence refers to a global orientation that expresses the extent to which the world is perceived as comprehensible, manageable, and meaningful and is associated with psychological resilience and the ability to make use of one's inner survival resources. The methadone programme patients were contacted at the beginning of the treatment and after one year. The SOC scores obtained at baseline and the one-year follow-up were similar, although they were generally lower among those patients who continued using drugs. Patients with higher SOC scores showed longer retention in treatment. It was concluded that SOC was a stable parameter and a predictor of successful methadone maintenance, in terms of both treatment retention and abstinence.

A U.S. study explored the influence of novelty-seeking on treatment retention among heroin-dependent cocaine users, who were treated with buprenorphine and contingency management. The Novelty Seeking scale from the TPQ personality questionnaire was used to conduct this research. The results showed that the users scoring high on the Novelty Seeking scale were more likely to drop out by the end of treatment but had higher retention rates in its early stages in comparison to those with lower scores. The authors of the study suggested that the high-novelty seek-

ers had viewed contingency management as a novel treatment modality. The inclusion of new treatment methods and approaches should thus be considered a factor which may foster treatment retention among this group of clients/patients (Helmus et al., 2001). The level of confidence and self-efficacy also appears to predict the outcome of treatment: it was found that clients with higher pre-treatment confidence scores were more likely to abstain from heroin after being discharged (Murphy et al., 2003). According to a British study, neuropsychological characteristics, particularly those linked to decision-making processes, predict treatment outcomes. It was found that the respondents from a community treatment programme with poorer performance on decision-making tests (*the Cambridge Gamble Task and the Iowa Gambling Task*) were much less likely to abstain from illicit drugs after three months into their treatment (Passetti et al., 2008). The results only applied to community-based (outpatient) treatment rather than residential settings, as was demonstrated by subsequent research (Passetti et al., 2011).

3.2.2 Sociodemographic characteristics

The studies generally look into respondents' sociodemographic characteristics, such as gender, age, level of education, socioeconomic level, marital status, and legal situation. Some of them draw conclusions about any of these characteristics having effects (whether positive or negative) on treatment outcomes.

A Slovak prospective study with 351 participants entering opiate dependence treatment pointed out that significantly better outcomes at the three-year follow-up were observed among those who had been employed or at school at the time of their admission to treatment (Okruhlica et al., 2002). Unemployment as a predictor of dropping out of treatment was also reported by an Irish study focusing on heroin users in a three-week buprenorphine-based detoxification programme (Williams et al., 2002). While the effect of employment status on retention in treatment and abstinence was brought up by a number of other studies (Eastwood et al., 2017; Kenne et al., 2010; Nosyk et al., 2013; Stein et al., 2005), there are some which failed to demonstrate such a relationship (Ziedonis et al., 2009).

An Australian study looked into factors predicting retention in treatment on the basis of data from health databases concerning patients in methadone treatment (sociodemographic characteristics, dropping out of treatment, re-entry to treatment). At the six-month follow-up, 51% of the patients remained in treatment, which corresponds to the results of other (not only) Australian studies. Two-thirds of those who had dropped out subsequently re-entered treatment, with multiple episodes of being in and out of treatment. The significant predictors of re-entry to treatment were age and the length of the first treatment episode. Those who were older and had undergone longer continuous treatment were less likely to re-enter. It was noted that the common phenomenon of client's cycling in and out of treatment may well be linked to methadone maintenance

becoming more available and accessible (Bell et al., 2006). A recent UK study also reported that older patients were more likely to complete treatment and less likely to re-enter after dropping out (Eastwood et al., 2017). Older age was a predictor of better treatment outcomes in other studies, too (Anderson & Warren, 2004; Backmund et al., 2001; Weinstein et al., 2017). Some studies, on the other hand, did not support the predictive value of age (Nosyk et al., 2013).

Research has yielded inconsistent results concerning the effect of education on treatment outcomes. Some studies did not find education to be a predictor of success, e.g. Ziedonis et al. (2009), while others concluded that the level of education may predict treatment outcomes (Avants et al., 2000; Backmund et al., 2001; Večeřová-Procházková et al., 2007).

Equally, there is inconsistent evidence about the effects of a history of offending and previous convictions. Some research suggests that previous imprisonment and current probation supervision may predict better retention in treatment (Backmund et al., 2001), while other studies demonstrated better outcomes for respondents who had not engaged in criminal activities prior to treatment (Darke et al., 2007; Hellemann et al., 2009). There are studies which found neither a positive nor a negative relationship between legal issues and the success of treatment (Ziedonis et al., 2009).

Evidence about the predictive value of gender in terms of treatment outcomes is also inconclusive. Ziedonis et al. (2009), for example, did not find that gender predicted the success of treatment. Data from a Prague-based methadone programme showed, however, that women sought methadone maintenance to the same extent as men, but displayed better abilities to adhere to treatment and perceived the rules as not being so strict. They were also more likely to progress towards complete abstinence by having their doses tapered and subsequently predominated among those who positively remained abstinent, according to the information available to the programme staff (Bečka, 2007).

As part of a national research project that investigated treatment outcomes (ATOS), an Australian study followed up heroin users for 36 months. No significant gender differences were found in terms of reporting sustained abstinence from heroin over 36 months. Women, however, were more likely to have abstained over the last 12 months. Nevertheless, only 8% of the respondents had sustained continuous abstinence for the whole of three years since baseline. While the vast majority of the respondents failed to maintain abstinence throughout the study period, 40% of them reported abstinence over the 12 months preceding the end of the study. The results suggest a long-term effect of treatment on a drug-free lifestyle (Darke et al., 2007). This "cumulative treatment effect" (including episodes of non-treatment-induced abstinence) has been confirmed by other authors (e.g. Nosyk et al., 2013).

In general, young adults (aged 18-25) show poorer treatment outcomes. A study which evaluated the outcomes of buprenorphine treatment for young adults and older pa-

tients demonstrated that, in comparison to older patients, younger patients showed a significantly lower rate of remaining in treatment and were more likely to test positive for illicit opioids (Schuman-Olivier et al., 2014). Similar findings were produced by other studies concerned with the treatment of adolescents and young adults (Warden et al., 2012), as well as other research (Burns et al., 2009; Hellemann et al., 2009; Kenne et al., 2010).

A number of studies refer to factors related to the respondents' race, but their results are also inconclusive. There are studies which do not prove any association between treatment outcomes and sociodemographic characteristics, including race (Ziedonis et al., 2009). Some American studies suggest lower success rates among respondents of Afro-American and Hispanic descent (Weinstein et al., 2017).

3.2.3 Family and social environment

An important factor which determines the success of treatment is the client's/patient's social environment, especially their family. The Drug Abuse Treatment Outcome Studies (DATOS), a U.S. research project, also included heroin-addicted respondents entering a methadone maintenance programme. Five years into the programme 27% of them had maintained abstinence. These respondents reported fewer family conflicts, had friends who did not use drugs or alcohol, and were supported by their family in their effort to achieve abstinence (Flynn et al., 2003). Having two or more friends who are drug-dependent people is regarded as a predictor of dropping out of treatment (Hellemann et al., 2009).

A person living with his/her family is more likely to retain in treatment. Salamina et al. (2010) reported a higher risk of dropping out of treatment for respondents who had lived alone prior to treatment. Similarly, this factor is upheld by a study focusing on marriage and a close relationship with one's spouse as a predictor of refraining from using non-prescription psychoactive substances during methadone maintenance (Heinz et al., 2009).

Exploring the influence of family factors on the outcome of methadone maintenance therapy, Pickens et al. (2001) found that patients whose parents were dependent on alcohol or other substances were more likely to show a greater level of severity of opiate dependence. Although they reduced their illicit opiate use while in treatment (receiving identical doses of methadone to patients with a negative family history of dependence), they used cocaine more while on substitution medication. It was concluded that genetic factors may play a role in both susceptibility to heroin dependence and response to methadone treatment. In addition to no family history of addiction, Poirier et al. (2004) also identified a negative family history of mood disorder as a predictor of success. It is hardly surprising that a study examining the use of other opioids among individuals in methadone maintenance therapy identified living with a heroin-using partner as one of the predictors of the continued use of non-prescribed substances (Lions et

al., 2014). The same finding was reported by other authors (Hser, 2007; Michelazzi et al., 2008).

One of the objectives of an Irish national study of treatment outcomes was to assess the effects of having children in the client's custodial care on their opiate dependence treatment. The respondents with children in their care were found to have reduced their heroin use significantly, but the frequency of their use of other opiates and alcohol increased. The respondents with no children in their care were more likely to use heroin, marijuana, and benzodiazepines. While those who had children in their care tended to reduce their use of illicit substances, they also showed a tendency towards the use of heroin substitutes associated with less social stigma (Comiskey, 2013).

A unique research project exploring the role of external factors and social context was undertaken in Australia. Its objective was to study the relationship between a sudden dramatic decrease in the availability of heroin and a major increase in its price (accompanied by the deterioration of its quality) on the Australian market on the one hand and entry and adherence to treatment for heroin dependence on the other hand. A drop in the number of young people entering substitution treatment and a dramatic decline in the number of treatment episodes involving detoxification only were observed. Some improvements in adherence to treatment and retention were found among heroin-dependent individuals during the period when the heroin supply was reduced. However, this complementary effect requires a balanced drug policy and good availability of treatment services (Degenhardt et al., 2005).

3.2.4 Substance use before and during treatment

Treatment retention and outcomes appear to be influenced by patterns of substance use before entering treatment (such as injecting use, polydrug use, and concurrent drug and alcohol dependence) and during treatment (such as illicit drug use while in substitution therapy). While this applies to both substitution and abstinence-oriented approaches, a larger body of evidence is available with respect to the former.

Patients' continued illicit drug use while in substitution treatment is a serious problem which undermines the goal of methadone maintenance and increases the risk of HIV infection for injecting drug users (Avants et al., 2000). Studies examining predictors of success and risk factors in relation to substitution treatment identify continued illicit drug use during treatment as a major risk factor.

Avants et al. (2000) examined drug use during the first three months of methadone maintenance treatment and the effects of cognitive, affective, and behavioural predictors of treatment outcomes. Continued heroin use was found to be associated with the severity of the pre-treatment addiction and strong self-identity as an addict ("addicted self-schema"). In addition to the severity of the pre-treatment addiction and addicted self-schema, co-

caine use during methadone maintenance treatment was predicted by low self-efficacy and the absence of negative cocaine-related experiences.

A study of heroin users entering treatment (as part of the ATOS project) looked into the effects of baseline cocaine use on treatment outcomes over a two-year period. Baseline interviews revealed that in addition to their primary drug two-fifths of 615 heroin-dependent participants had also used cocaine. Subsequent follow-ups (at three, 12, and 24 months) showed a decrease in cocaine use among the respondents. However, baseline cocaine use proved to be a significant predictor of poorer treatment outcomes after 24 months. Those who reported cocaine use at the baseline assessment showed higher levels of heroin use, unemployment, needle sharing, criminal activity, and incarceration over the two-year study period (Williamson et al., 2007). Franklyn et al. (2017) arrived at similar conclusions: patients who were found cocaine-positive on admission to substitution treatment were more likely to drop out of treatment and showed a generally lower treatment retention rate than patients who had tested negative for cocaine. The more intensive the cocaine use during treatment, the higher the risk of dropping out of treatment. Cocaine use during substitution treatment was also found to be a major risk factor for dropping out of treatment by Salamina et al. (2010). Such conclusions were supported by a German study involving patients maintained on buprenorphine/naloxone, which extended the predictors of early termination of treatment to include positive tests for benzodiazepines and opiates other than buprenorphine (Apelt et al., 2014). Similarly, Peles et al. (2008) reported a negative effect of cocaine and amphetamine use on retention in methadone maintenance among respondents in a U.S. clinic and of benzodiazepines and continued opiate use among patients at an Israeli methadone maintenance treatment clinic.

The authors of a U.S. study investigating marijuana use during methadone maintenance (Ghitza et al., 2007) focused on the relationship between the non-reporting of marijuana use during methadone treatment and treatment outcomes (with cannabis use not being the reason for exclusion from treatment). The respondents who failed to admit THC use were more likely also to use cocaine and heroin while in treatment. It was concluded, however, that the treatment outcome was affected by the non-reporting phenomenon rather than the actual use of cannabis. Looking for a possible association between opiate treatment outcomes and marijuana use among participants aged 15-21, Hill et al. (2013) identified no relationship between poorer treatment outcomes and cannabis use. Half of the clients in buprenorphine-based substitution treatment reported occasional marijuana use and one-sixth of the sample had smoked marijuana on a daily basis. The authors concluded that while cannabis use may be harmful, their study did not demonstrate its effect on the outcome of buprenorphine treatment in the age category under study.

Lions et al. (2014) examined the use of other opioids among subjects on methadone maintenance. 12 months into treat-

ment, 32% of the patients were found to have used non-prescribed opioids in the last month. Major risk factors included cocaine use during methadone maintenance and hazardous alcohol consumption. The role of the severity of alcohol use was supported by Abrahamsson et al. (2016). The AUDIT test result proved to be the key predictor of retention in treatment: the lower the score, the higher the chance of the client remaining in the substitution programme and advancing to the next (higher-threshold) treatment phase. Studying a sample of opiate-dependent adolescents and young adults (aged 15-21), Warden et al. (2012) found those respondents testing positive for opiates in the first two weeks of treatment to be at risk of dropping out.

A Canadian study of substitution treatment based on the administration of heroin and methadone investigated predictors of non-use of illicit heroin among patients on maintenance (the baseline assessment was performed on admission to treatment, with subsequent follow-ups after three, six, nine, and 12 months). The subjects who had not used illicit heroin in the last month also showed fewer days of cocaine use and criminal activities in the last month. In addition, lower levels of illicit heroin use were predicted by regular treatment attendance (fewer days of not showing up) and the total quantity of the substitution agent used in the previous month (Oviedo-Joekes et al., 2015). Patients who had had experience with diverted buprenorphine were found to show higher levels of retention in buprenorphine maintenance treatment than those without previous experience with buprenorphine (Monico et al., 2015).

Predictors of buprenorphine-based treatment outcomes for heroin-dependent individuals were examined by Woodcock et al. (2015). Predictors of better success in maintaining abstinence from heroin that were identified included older age at the onset of heroin use, fewer days of heroin use in the last month preceding entry to treatment (lower levels of heroin use prior to treatment), and a history of multiple attempts to abstain from heroin. Those who stayed heroin-free early in their treatment were more likely to remain abstinent towards the end of treatment and following the withdrawal of buprenorphine. Soyka et al. (2008), too, found age at the onset of regular opiate use to be one of the predictive factors: the younger the age at the onset of a drug career, the lower the retention in substitution treatment. Another major factor was the severity of withdrawal symptoms experienced at the beginning of treatment (the higher the Opiate Withdrawal Scale score, the higher the risk of dropping out). Finally, injecting drug use in the last month before entry to treatment appears to be a significant predictor of its early termination (Dayal & Balhara, 2017).

3.3 Service provision factors

These factors involve the configuration of the treatment strategy, type of treatment and treatment facility, the staff's attitude to clients, and, last but not least, the type of medication used (especially the type of substitution agent under maintenance therapy) and the offer of psychosocial/

psychotherapeutic support. They have an impact on client's satisfaction and engagement with treatment and determine treatment retention and outcomes.

3.3.1 Maintenance substances and their dosage

A number of studies compared the efficacy of different agents used for the substitution treatment of opiate dependence and the outcomes of maintenance treatment with respect to the level of doses of substitution preparations.

Systematic reviews suggest that methadone maintenance therapy is the most effective in retaining patients in treatment and suppressing heroin use, with higher doses of methadone being associated with better treatment outcomes (Amato et al., 2005). A recent systematic survey compared the effectiveness of methadone, buprenorphine, and a placebo (Mattick et al., 2014). Buprenorphine was found to be more effective than the placebo as regards retention in treatment. It appears to suppress illicit opioid use during treatment at higher doses only, while at lower doses its effect was similar to that of the placebo. Buprenorphine was further found to be less effective than methadone in terms of retaining patients in treatment. No differences were found between buprenorphine and methadone when administered in medium and high doses (Mattick et al., 2014). Other studies comparing the effectiveness of different substitution agents suggested that heroin may be a useful maintenance option for those clients who do not seem to profit from standard substitution therapies and have a history of multiple unsuccessful treatment episodes. In comparison to standard substitution treatment, heroin-assisted therapy can lead to better adherence, particularly among those who are less motivated to seek help (Bascaran et al., 2014; Nosyk et al., 2010; Oviedo-Joekes et al., 2009).

A German retrospective study, for example, compared patients undergoing substitution treatment with codeine and methadone and illicit heroin users in terms of their completion of residential abstinence-oriented detoxification. Patients who had undergone methadone substitution treatment were more successful in completing detoxification than codeine-substituted patients and both groups on substitution drugs were significantly more likely to complete detoxification than heroin users (Backmund et al., 2001). Another study which also looked into the type of medication used during the 14-day detoxification confirmed better outcomes for patients treated with buprenorphine and naloxone than for those patients receiving clonidine (Ziedonis et al., 2009). These conclusions were supported by research into the differences between treatment outcomes among patients treated with buprenorphine or clonidine (Marsch et al., 2005).

A study comparing the efficacy of buprenorphine and methadone for opioid maintenance treatment found that higher doses of substitution agents, both methadone and buprenorphine, were predictive of better outcomes (fewer positive urine tests for illicit drugs). The efficacy of both substances was demonstrated to a comparable degree, with buprenorphine showing higher efficacy in patients

with depressive symptoms (Gerra et al., 2004). Higher doses of a substitution agent as a predictor of better treatment outcomes are reported by other authors (Michelazzi et al., 2008; Peles et al., 2008; Villafranca et al., 2006), although such conclusions were not supported by Soyka et al. (2008), whose study did not demonstrate any relationship between retention in substitution treatment and the size of the dose. In their retrospective cohort study, Dayal and Balhara (2017) assessed the level of retention in buprenorphine maintenance treatment among young adults and looked for retention-relevant factors. The daily doses of buprenorphine were found to be an important predictor. Lower doses were likely to result in the termination of treatment. A 1-mg increase in the dose reduced the probability of dropping out by 14%.

Studying the effectiveness of substitution treatment, Clark et al. (2015) noted that patients treated with buprenorphine or methadone showed a lower risk of relapsing into illicit drug use than patients who had undergone abstinence-based therapy. They also found an association between the length of treatment and the risk of relapse.

3.3.2 Other treatment characteristics

Conducted as part of the NTORS, a substudy with opiate-dependent patients in methadone maintenance treatment assessed pre-treatment motivation, the frequency and content of counselling services, perceptions of the programme, and the level of methadone doses in terms of the association of such parameters with treatment outcomes at one- and six-month follow-ups. Several relationships were identified: perceptions of the programme and methadone doses were associated with reduced heroin use after one month. The use of counselling services was related to reduced heroin use at the six-month follow-up. Heroin use one month into treatment predicted heroin use at six months. Although treatment factors appear to have important effects, especially in the early stages of treatment, they can also have an impact on long-term outcomes and successful treatment (Gossop et al., 2003). Satisfaction with treatment was also pointed out as one of the strongest predictors of retention in methadone maintenance therapy in a study involving opioid-dependent veterans (Villafranca et al., 2006).

The importance of the psychosocial components of substitution treatment and their effects on treatment outcomes were also noted in a Czech study by Kostínková (2008). In line with her findings, Salamina et al. (2010) found that psychotherapeutic support during treatment reduced the risk of dropout by half. The use of social and psychological services during substitution therapy as a factor which improves treatment outcomes was supported by other studies (Amato et al., 2008; Avants et al., 2000; Oviedo-Joekes et al., 2015; Stein et al., 2005). The quality of the contact with counsellors (Backmund et al., 2001) and regular attendance (Oviedo-Joekes et al., 2015) were also reported as predictors of success.

In a study that looked into the characteristics of treatment facilities and their effect on treatment outcomes, other fac-

tors that may affect retention in methadone treatment were identified. The retention of patients in the methadone programme was higher if the focus of the programme placed less emphasis on changing the lifestyle of the patient and less pressure on learning new skills. Additionally, the programmes were more successful if there was a low proportion of former drug users among the staff members (Hser et al., 2001).

The provision of buprenorphine maintenance treatment in the Czech Republic was examined by Večeřová-Procházková et al. (2007). Their study, with the respondents being recruited from three types of substitution settings (a specialised centre, a specialised centre in combination with a general practitioner, and a general practitioner), indicated that the form in which treatment was provided did not have an influence on patients' retention in the programme (at a three-month follow-up). Similarly, Comiskey and Cox (2010) reported no association between the outcomes of methadone treatment and the type of setting where it was provided.

Ziedonis et al. (2009) studied predictors of successful withdrawal management among opiate-dependent patients in a 14-day detoxification programme. They noted that the type of therapy was predictive of successful completion of detoxification and abstinence from drugs during the programme. Inpatient treatment was found to be more successful than outpatient detoxification (Ziedonis et al., 2009).

Salamina et al. (2010) studied heroin-dependent clients/patients receiving treatment in different settings (methadone maintenance therapy, a therapeutic community, and other residential abstinence-oriented treatment facilities). The type of therapy was found to be the strongest predictor of retention in treatment. Inpatient abstinence-oriented settings other than therapeutic communities showed the lowest retention rate, while with methadone treatment, the retention depended on the dose. In an Australian study of heroin users (ATOS), respondents from four types of facilities were assessed in terms of their success in abstaining over a period of 36 months. Respondents from residential abstinence-oriented treatment showed the highest rates of abstinence from heroin over the entire 36 months. Those in substitution treatment also showed relatively high abstinence rates during the study period. Respondents who completed detox only were less likely to abstain, and none of the respondents contacted in low-threshold facilities succeeded in abstaining from heroin over the 36 months (Darke et al., 2007).

Lions et al. (2014) noted a good patient-physician relationship as a predictor of non-use of non-prescribed opioids during methadone maintenance. They suggested that more attention should be paid to patients' relationships with service staff and issues related to the former's partner relationships and social network as a way of improving the outcomes of methadone treatment. In an abstinence-oriented treatment setting, too, predictors of successful treatment outcomes included a good relationship with service staff,

a sense of security, and a non-discriminating attitude to clients (Brener et al., 2010).

Parmenter et al. (2013) assessed patients in primary care substitution treatment one, five, and eleven years after their entry to treatment. Continuous treatment was found to be the strongest predictor of positive outcomes.

● 4 SUMMARY

Although the studies vary in their definition of "treatment success" and the indicators under scrutiny, it is possible to summarise the key factors that seem to determine positive outcomes. The following are the key client/patient predictors which appear to have a positive effect on treatment outcomes and which are consistently identified as such by the authors of the studies addressing the treatment of addiction to heroin and illicit opiates:

– duration of treatment (the longer the treatment, the better the outcome),
– certain sociodemographic characteristics (especially older age on entry to treatment),
– certain psychological characteristics (e.g. higher levels of sense of coherence and self-efficacy) and psychiatric comorbidity; while some studies suggest that clients/patients with psychiatric diagnoses (particularly depressive disorders) may, surprisingly, show higher retention in treatment, a psychiatric dual diagnosis is generally considered a risk factor,
– a family situation involving no major conflicts and addiction issues among family members and partners and a social network providing support for recovery efforts,
– the use of illicit/non-prescribed substances during treatment results in poorer outcomes, especially when relapse occurs at the beginning of the treatment process.

As regards treatment-related factors, there are differences between abstinence-based (psychosocial) treatment and substitution therapy, with the substitution modality showing higher retention rates. Successful outcomes of substitution treatment are associated with higher doses (whether with methadone or buprenorphine as the most common substitution agents), psychosocial support during treatment, and good relationships with service staff. On the other hand, unreasonable pressure on clients to change their lifestyle should be avoided.

● 5 CONCLUSION

The outcomes of the treatment of addiction to heroin and other illicit opioids are influenced by a number of factors. Studies are not always consistent in their findings, however, particularly as regards the effects of individual sociodemographic and psychological factors. Generally, it can be concluded that predictors of positive treatment outcomes include the client's being of a higher age, stable family and social support, and a social network. On the other hand, the

use of non-prescribed substances during treatment, severe psychiatric comorbidity, and unstable family circumstances usually predict poorer outcomes. It should be noted that clients/patients in treatment should be dealt with individually and that treatment provision factors (such as good relationships with service staff, appropriate configuration of treatment, including dosage, and psychosocial and psychotherapeutic support) should be given particular attention as a way of providing effective assistance to clients/patients who may experience adverse baseline conditions.

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