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Evaluation of medication-assisted treatment of opioid dependence—The physicians' perspective

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ABSTRACT

Background: There is controversy about which outcome parameters should be employed to assess substance use treatment. Subjective measures of medication-assisted treatment (MAT) of opioid dependence are increasingly important. However, while patients' perspectives have been examined, the caregivers' views remain largely unknown. Here, we explore how physicians evaluate MAT, and which predictors are most relevant.
Methods: We conducted a retrospective cohort study of all MAT episodes with oral opioid agonists in the canton of Zurich between 1998 and 2013 using a case register. Termination forms of the register include a physician-completed assessment on the course of the treatment episode. Mixed model analysis was applied to determine relevant predictors.
Results: The analysis was based on 17,234 episodes from 7432 patients. Mean global assessment of the course of MAT was 'moderate'. The most important predictors for treatment evaluation by physicians were treatment break off as reason for termination ($p < 0.0001$), psychological improvement throughout treatment ($p < 0.0001$), wish for abstinence from the substitute ($p < 0.0001$), social integration index at termination ($p < 0.0001$), and social ($p < 0.0001$) as well as medical ($p < 0.0001$) improvement. The negative association of treatment break off with MAT assessment was more pronounced in semi-rural than urban areas ($p < 0.0001$).
Conclusion: Predictors relating to the well-being and functioning of the patient as well as the reasons underlying treatment termination appear to be more important for the treating physician's evaluation of medication-assisted treatment episodes than on-going substance use. Coming off the opioid medication plays a central role, independent of ongoing illicit substance use.

1. Introduction

Opioid dependence is a chronic disorder characterized by relapse and rare long-term cessation (Genberg et al., 2011; Termorshuizen, 2005). It often entails negative sequelae for the affected individuals and their families, and substantial public health consequences for society as a whole (Whiteford et al., 2013). In 2014, the prevalence of opioid dependence was estimated at 0.4% for the European Union (European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2014). Medication-assisted treatment (MAT) with methadone, L-polamidone, buprenorphine or slow-release oral morphine sulphate is considered to be the treatment of first choice (Dole and Nyswander, 1965; Mattick et al., 2014, 2009; Ward et al., 1999; WHO, 2009). Due to the chronicity of opioid dependence, current treatment guidelines favor the open-end nature of MAT, sometimes required to continue lifelong (APA, 2006; Swiss Society of Addiction Medicine (SSAM), 2013). In some countries, legal regulations still call for complete abstinence (including opioid substitutes) as mandatory treatment goal, but abstinence-oriented therapy is often unsuccessful due to high relapse rates

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with the risk of deteriorating psychosocial conditions or even death due to overdose after lost tolerance to opioids (Caplehorn et al., 1994; Merrall et al., 2010; Strang, 2003). The rate of spontaneous or professionally assisted remission remains controversial. A recent review found a rate of 9% annually (Calabria et al., 2010). Typically, however, when access to MAT is low-threshold, many opioid-dependent patients enter and leave treatment repeatedly in the course of their disorder (Bell et al., 2006), which, among other reasons (such as changing the responsible physician), may reflect patients' desire for more independence and 'getting clean', i.e., complete abstinence including the substitute (Gutwinski et al., 2014; Winstock et al., 2011).

There has been intensive debate on suitable outcome parameters in the evaluation of substance use treatment in general, and MAT in particular (Bühringer, 2012; Donovan et al., 2012; Tiffany et al., 2012; Uchtenhagen, 2012). MAT is associated with a reduction in substance use, mortality, treatment dropouts, HIV infections, psychosocial symptom load and delinquency, and an overall increase in quality of life (Brugal et al., 2005; Cacciola, 2001; Deck et al., 2009; Feelemyer et al., 2014; MacArthur et al., 2012; Mattick et al., 2009). Most treatment studies focused on putative objective parameters, while the subjective outcomes of MAT have received less attention. However, there is an increasing recognition that these constitute essential measures of MAT quality (Tiffany et al., 2012; Trujols et al., 2011; Uchtenhagen, 2015). Few studies have investigated subjective views of MAT episodes (Montagne, 2002; Stancliff, 2002), and, if so, mostly addressed patient satisfaction (Kelly et al., 2010; Marchand et al., 2011; Trujols et al., 2012). Fewer studies still have investigated the views of treatment providers (Becker and Fiellin, 2006). These mostly concentrated on *meta*-aspects, such as the provision of MAT and harm reduction (Deren et al., 2011; Forman et al., 2001; Notley et al., 2014), barriers to care (Schulte et al., 2013), the diversion and misuse of the medical replacement (Larance et al., 2011), reasons for dropout and treatment retention (Gutwinski et al., 2014) or combinations of the above (Besson et al., 2014). To our knowledge, Trujols et al. (2011) conducted the only study investigating both provider and patient views of single MAT episodes (Trujols et al., 2011). Using patient and clinician versions of the Global Impression of Improvement Scale in a sample of 110 MAT patients, they demonstrated that patients and providers often have discordant perceptions of improvement in treatment (Trujols et al., 2011). It remains unclear, however, which predictors determine physicians' assessments of MAT course and whether these are similar to the outcomes used in MAT evaluation. They reflect on providers' implicit treatment goals and conceptualisation of MAT, which may differ from those of patients, public health policy makers or researchers investigating MAT. Relevant predictors may be based on personal biases as well as scientific evidence and legal regulations. They may influence attitude towards the patient, and physician as well as patient behavior, such as the decision to enter, stay in or leave treatment, or shared-decision making during treatment.

The aim of this study was to determine the predictors of physicians' assessment of MAT using data from Zurich, Switzerland.

2. Methods

Zurich is both the most populous Swiss canton and the largest Swiss city. Following the development of open drug scenes, harm reduction measures were scaled up massively in the 1990s. MAT has since been offered on a low-threshold basis with opioid dependence as single entry criterion and wide accessibility. It is reimbursed by mandatory health insurance, and patients can freely choose their provider. Since 1991, the canton monitors MAT with methadone, buprenorphine, and recently slow-release oral morphine sulphate, with an anonymized treatment case register (Nordt and Stohler, 2006). Heroin-assisted treatment is excluded and evaluated separately. Physicians are required to complete a questionnaire at initiation and termination of treatment, as well as twice yearly or when changing the substitute. Collection and evaluation of data are in accordance with the data protection law of the canton of Zürich and the local ethics committee approved the analysis.

For analysis of clinicians' evaluation of treatment episodes, we used the question on "global assessment of treatment course", which physicians answered on a five-point Likert scale (1 "very unfavorable", 2 "rather unfavorable", 3 "moderate", 4 "rather favorable", 5 "very favorable") at termination of treatment.

The question on reasons for treatment termination in the evaluation questionnaire could originally be answered in seven ways: 1 "regular, abstinent (from substitute)", 2 "regular, in mutual consent", 3 "formal break off by patient", 4 'formal break off by physician', 5 "loss of contact", 6 "patient deceased" and 7 "other (to be specified)". For the multivariate analysis, we grouped those answers as follows: abstinent (option 1), regular (including option 2, 6 and 7), and treatment break off (option 3–5). Physicians were also asked to report *changes* in psychological, medical and social conditions of the patient throughout treatment and could answer on a three-point scale 1 "worsened", 2 "unaltered", 3 "improved". Moreover, we used data from the entry questionnaire on these conditions, coded 1 "(rather) bad", 2 "moderate", 3 "(rather) good". Using the mean of at least four of six items (having a full or part time job, earning one's living; living in a flat; having a partnership; good family relations; having friends outside the drug scene) we calculated a social integration index, ranging between 0 and 1 (Cronbach's Alpha = 0.58).

Furthermore, the questionnaire comprised items on the use of heroin, cocaine, illicit benzodiazepines and alcohol in the past 30 days before treatment termination, each answered on a four-point scale coded 1 "none", 2 "occasionally", 3 "(almost) daily", 4 "several times a day". We also used data on age of onset of heroin use (dichotomized as 18 years or earlier versus 19 years or later), duration of opioid use (in decades) and lifetime intravenous use. Moreover, we included age (in decades and centered at 30 years), number of MAT episodes and duration of current episode (in months, logarithmized) as predictors. Finally, treatment providers were characterized by type (private practice versus specialized institution) and by area. The latter was operationalized as "urban", corresponding to the city of Zurich, or "semi-rural", corresponding to the surrounding canton.

Between 1991 and the end of October 2014, 34,082 treatment episodes of 11,749 patients were collected. A careful check for overlapping treatment episodes led to the exclusion of 201 episodes. Although we used information of all entry forms for each patient, gender (6%), ever injecting status (8%), and nationality (13%) remained unknown for some patients. For about 28% of patients we could not obtain a plausible year of first regular heroin use (not before their 12th year of age, not after their first MAT according to our case register, difference in cases of multiple entry forms three years or less; Nordt and Stohler, 2006). As there were also missing data in time-dependent predictors that are most likely correlated within individuals (e.g., frequency of drug use, social integration), we applied the multiple imputation procedure of SPSS 22 in addition to a complete case analysis that could only use about 26% of the available data. We did not impute reasons of cessation, as some may occur repeatedly in a patient except in the case of death.

As our case register is far from being a balanced repeated-measure dataset – where all patients provide the same number of follow-up datasets within the similar time period – we applied a two-stage approach. The first stage included invariant personal

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