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Commentary

Rethinking retention in treatment of opioid dependence—The eye of the beholder

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ABSTRACT

Opioid dependence often is a chronic relapsing disorder. The evidence for medication-assisted treatment (MAT) being the treatment of first choice is unequivocal. Yet, health systems, professionals and patients often fail to offer or, respectively, to enter long-term and low-threshold MAT and instead treat opioid dependence as a semi-acute disorder. We claim that the typical perspective on treatment retention, one of the pivotal outcomes used for evaluation of MAT, contributes to this phenomenon by obscuring the chronic nature of opioid dependence. To support this hypothesis, we use data of 11,819 patients obtained from the MAT register of the canton of Zurich 1991–2015 and illustrate three different perspectives on treatment retention: the prospective "trial" perspective looking at the duration of single treatment episodes; the retrospective "provider" perspective looking at the duration of treatment episodes of patients still in treatment; and the "public health" perspective looking at the proportion of days spent in treatment regardless of single treatment episodes. Integrating these perspectives will lead to a more realistic perception of the chronic nature of opioid dependence. This will allow determining more appropriate aims and time frames for MAT in practice and research.

Introduction

Substance dependence is generally a chronic, relapsing disorder associated with alterations in brain structure and function (Hser, Evans, Grella, Ling, & Anglin, 2015; Leshner, 1997; Lüscher, 2013). Like in other chronic conditions, its treatment should be open-ended and should comprise long-term care strategies and regular monitoring; medication should be accessible, with dosing and duration based on scientific evidence (McLellan, Lewis, O'Brien, & Kleber, 2000). These principles are well-accepted for other chronic conditions, such as asthma, diabetes, or obesity. However, despite comparable relevance of genetic vulnerability, environmental factors and individual decisions for the development of the disorder, this is not the case for substance dependence (McLellan et al., 2000).

Providers, patients and policy makers alike often fail to adopt the perspective of a chronic disorder when dealing with substance dependence. The most striking examples pertain to the provision of agonist (or medication-assisted) treatment, which involves the use of a medication with similar pharmacological effects as the drug of dependence, but ideally longer duration of action and slower onset of effects (Darke & Farrell, 2015). Agonist treatment has successfully been used mainly for opioid and nicotine dependence, but has also been suggested for cannabis, benzodiazepine or cocaine dependence (Darke & Farrell, 2015; Dürsteler et al., 2015; Nuijten et al., 2016; Weizman, Gelkopf, Melamed, Adelson, & Bleich, 2003).

Based on a multitude of studies in various settings, medication-assisted treatment (MAT) has been recognized as the treatment of choice for opioid dependence (OD) (WHO, 2009). Many treatment guidelines and organizations including the World Health Organization (WHO) now advocate open-ended, if necessary lifelong, MAT with methadone, buprenorphine, slow-release morphine sulphate or diacetylmorphine (Swiss Society of Addiction Medicine (SSAM), 2013; WHO, 2009). Yet, despite undisputed scientific evidence, globally only an estimated 8% of opioid-dependent persons receive MAT (Mathers et al., 2010). Many health systems fail to offer low-threshold MAT or advocate detoxification as first-line treatment (Harm Reduction International, 2014; Jürgens, Csete, Amon, Baral, & Beyrer, 2010; Mathers et al., 2010). In other

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settings, MAT is provided, but long-term treatment is restricted by regulations, such as the imposed compulsory goal of coming off the substitute, abstinence from substance use as precondition to enroll or stay in treatment, or arbitrary limitations on treatment duration or dosing of opioid agonists (European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2007; Kourounis et al., 2015; Stöver, 2011). Despite of conclusive evidence on the superiority of treatment with injectable diacetylmorphine over oral MAT in treatment-resistant opioid-dependent patients (Strang et al., 2015), most countries have failed to establish this long-term treatment option. The shortcomings concerning the establishment of MAT become particularly obvious in prison settings, where MAT is often not provided (Harm Reduction International, 2014; Hedrich & Farrell, 2012). An underlying perception is that the alleged unavailability of substances in the prison setting, and resulting abstinence, will lead to remission or even recovery from dependence. However, relapse rates after discharge are high and the associated overdose risk and mortality are increased substantially (Merrall et al., 2010). Many patients also remain reluctant to seek or accept MAT (Besson et al., 2014; Peterson et al., 2010). Others repeatedly enter abstinence-oriented treatments despite an increased risk of relapse and death.

Obviously, the reluctance to provide low-threshold, long-term MAT is a complex topic and a range of factors, such as politics, ideology, stigma, fear of negative legal consequences for prescribing (illicit) opioids or lobbyism play a role. For example, the recent move towards 'recovery' in the drug strategies of the UK, while including many important topics such as a more individual and patient-centered focus, is criticized as it could result in an increase of drug related deaths when treatment durations are shortened due to this new drug policy (Hickman, Vickerman, Robertson, Macleod, & Strang, 2011). Following, we demonstrate how the focus on a certain perspective on treatment retention in the evaluation of MAT may help explain different perceptions of MAT encountered in OD. We are convinced that this is an important factor which has been largely neglected in the debate on the insufficient provision of MAT.

Retention in treatment of OD—a paradox?

Resulting from the concept of chronicity and the notion that a therapy can only be effective when patients are engaging in it, retention in treatment has been established as a major outcome criterion of randomized controlled trials and meta-analyses in the field of OD. Retention has been associated with improved treatment outcomes such as reductions in substance use and criminal behavior, and increases in psychosocial functioning and quality of life (Mitchell et al., 2015; Perreault et al., 2015; Simpson, Joe, & Rowan-Szal, 1997). All-cause mortality in opioid-dependent populations is elevated outside of treatment, particularly in the period after treatment cessation (Cornish, Macleod, Strang, Vickerman, & Hickman, 2010; Cousins et al., 2016; Degenhardt et al., 2011). Interventions are typically appraised by their capability of reducing the often substantial dropout rate of opioid-dependent patients. This paves the way for a seeming paradox: OD is a chronic disorder, but the treatment episodes are often short, usually lasting less than one year (Nordt, Vogel, Dürsteler, Stohler, & Herdener, 2015). This ostensible discrepancy may contribute to the poor acceptance of the chronic nature of OD in various settings, and subsequent failure to offer widespread and low-threshold MAT.

The characteristic periods of remission and relapse may partly explain this apparent paradox: Inpatient, outpatient or self-controlled detoxification is common and often followed by a time period spent outside treatment (Cornish et al., 2010; Nordt et al., 2015; Nosyk et al., 2009). The typical treatment "career" is of equal significance. It consists of several consecutive periods spent inside and outside of MAT, with the duration of the former being rather constant and of the latter decreasing over time (Nordt et al., 2015). The narrow focus on treatment retention in single episodes fails to account for this cycling in and out of treatment and falls short particularly from a public health policy perspective. But the way that individuals, either directly affected by OD or involved in its treatment, perceive retention in MAT, may have a major impact on the conceptualization of OD as a chronic disorder. Comprehending these perspectives is helpful for understanding the reasons underlying diverging concepts of disease. To illustrate this, we explore three different perspectives on retention in MAT, which may contribute to an understanding of how diverging perceptions of chronicity in OD may develop between patients, researchers, providers and policy makers.

To this end, we use data of the MAT case register in Zurich collected between 1991 and the end of April 2015 (34,455 treatment episodes of 11,819 patients). After a careful check for overlapping periods we excluded 200 episodes. Details on the register as well as the treatment setting have been described elsewhere (Nordt & Stohler, 2006; Nordt et al., 2015). Importantly, MAT is offered on a low-threshold basis, with sufficient treatment capacities to accommodate all opioid-dependent persons opting for it. Patients can freely choose their provider and obligatory health insurance fully reimburses costs.

The "trial" perspective

The first perspective pertains to the duration of a single treatment episode, which is often the outcome measure of effectivity trials for opioid substitutes. But also 'recovery' oriented drug policies and many patients adopt this perspective, hoping that with the end of treatment their OD will have remitted permanently. Retention then refers to the time continually spent in treatment from the beginning of the episode until cessation (e.g. due to drop out, mutual agreement, or death). To address retention from this perspective the question would be something like this: "How long will this treatment go on?" The statistical method of choice to assess this is survival analysis with censored cases. Fig. 1 displays the survival probability by duration of single treatment episodes for all 31,998 episodes in the canton of Zurich that started between 1992 and 2014. About 8% of episodes (N = 2584) had not terminated before the end of March 2015 and, therefore, were treated as censored cases.

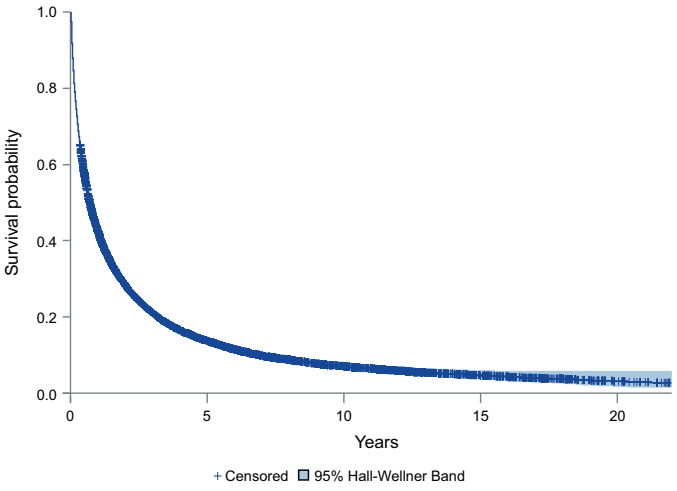

Fig. 1. Survival probability by duration of single treatment episodes for all 31,998 medication-assisted treatment episodes in the canton of Zurich initiated between 1992 and 2014.