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Barriers to access to opioid medicines for patients with opioid dependence: a review of legislation and regulations in eleven central and eastern European countries

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ABSTRACT

Background and aims Barriers linked to drug control systems are considered to contribute to inequitable access to controlled medicines, leaving millions of people in pain and suffering. Most studies focus on access to opioids for the treatment of severe (cancer) pain. This study aims to identify specific access barriers for patients with opioid dependence in legislation and regulations of 11 central and eastern European countries. **Methods** This study builds on a previous analysis of legislation and regulations as part of the EU 7th Framework Access To Opioid Medication in Europe (ATOME) project. An in-depth analysis was undertaken to determine specific barriers for patients with opioid dependence in need of opioid analgesics or opioid agonist therapy (OAT). For each country, the number and nature of specific potential barriers for these patients were assessed according to eight categories: prescribing; dispensing; manufacturing; usage; trade and distribution; affordability; penalties; and other. An additional keyword search was conducted to minimize the omission of barriers. Barriers in an additional category, language, were recorded qualitatively. Countries included Bulgaria, Cyprus, Estonia, Greece, Hungary, Latvia, Lithuania, Serbia, Slovakia, Slovenia and Turkey. **Results** Ten of the 11 countries (all except Estonia) showed specific potential barriers in their legislation and regulations. The total number of barriers varied from two (Slovenia) to 46 (Lithuania); the number of categories varied from one (Slovenia) to five (Lithuania). Most specific potential barriers were shown in the categories 'prescribing', 'usage' and 'other'. The total number in a single category varied from one to 18 (Lithuania, prescribing). Individual differences between countries in the same specific potential barrier were shown; for example, variation in minimum age criteria for admission to OAT ranging from 15 (Lithuania, in special cases) to 20 years (Greece). All countries had stigmatizing language in their legislation. **Conclusions** Patients with opioid dependence are likely to experience specific barriers to accessing opioids in addition to those experienced by other non-dependent patients.

Keywords Access, addiction, barriers, buprenorphine, legal, methadone, OAT, opioid dependence, OST, regulatory.

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INTRODUCTION

The urgent need to establish equitable access to controlled medicines was called attention recently to by the Global Commission on Drug Policy [1,2]. Each year tens of millions of people suffer from unrelieved pain due to lack of access to controlled medicines [3]. It is estimated that 92% of the global supply of morphine is consumed by only 17% of the world's population [4]. In its report, the Global Commission on Drug Policy addresses the crucial role played by barriers linked to the international drug control system in limiting access to controlled medicines. From a historical perspective, as international drug control policies aimed at preventing illicit use and diversion using punitive approaches, public health and human rights are not prioritized. This imbalance in drug control policies has

resulted in inequitable access to controlled medicines. A particularly disadvantaged group are people with opioid dependence. Despite strong lobbying efforts from international harm reduction organizations, access to controlled medicines for the treatment of opioid dependence remains a relatively neglected area. When discussing patients in need of controlled medicines, patients with cancer pain tend to be prioritized over patients with opioid dependence [2].

The existing literature recognizes the major role of drug control policies in limiting access to opioid medicines in addition to other factors such as economic aspects, lack of knowledge and societal attitudes [3–5]. Available data indicate that when drafting legislation and regulations, the need to prevent non-medical use and diversion is prioritized over the need to ensure access to and availability of opioid medicines [2,3]. As a consequence, national governments and policymakers frequently implement unduly strict control measures that impede access to opioid medicines in a way that is disproportional to their impact on the prevention of abuse and diversion [6]. A previous analysis of legislation and regulations as a part of the EU 7th Framework Access To Opioid Medication in Europe (ATOME) project revealed a total of 778 potential barriers to access to opioid medicines in 11 central and eastern European countries with statistical evidence of low morphine consumption per capita (Bulgaria, Cyprus, Estonia, Greece, Hungary, Latvia, Lithuania, Serbia, Slovakia, Slovenia and Turkey) [7]. Frequently reported legal and regulatory restrictions to access included limitations on the treatment period or dosage that can be provided in a prescription, restrictions regarding prescribing or dispensing privileges (for example, limited to a certain medical speciality), the use of special prescription forms in multiple copies and burdensome administrative requirements for record-keeping and storage [6–13].

While the frequently reported barriers—when encountered—apply to all or the majority of patients, specific patient groups may experience specific barriers in accessing opioid medicines. In particular, this is the case for patients with opioid dependence. For example, access to opioid agonist treatment (OAT) is often hindered due to strict admission criteria such as minimum age restrictions that deny access to young people who use drugs [14]. Specific barriers to access for patients with opioid dependence that may be linked to drug control systems include high costs for OAT, limited coverage of harm reduction services, lack of access to OAT through primary care or in prison, long waiting-lists, strict supervision requirements upon administration of medicines, lack of confidentiality and privacy and difficulties in accessing adequate pain relief [2,3,14,15]. The clinical consequences, both at an individual and a global level, can be immense [2,17]. Observational studies, for example, show that access to methadone used for OAT is associated with an average 54% reduction in the risk of HIV transmission among people who inject drugs (PWID) [18]. In addition, implementation of OAT is associated with reductions in the risk of hepatitis C infection, opioid overdose, drug-related deaths and crimes [17,19]. Moreover, OAT has been shown to increase adherence to tuberculosis treatment and antiretroviral therapy [17,19]. It is estimated that OAT has a benefit return of four times its treatment costs, with OAT with methadone being among the most cost-effective treatments [2,19–21].

Despite solid evidence supporting the effectiveness and cost-effectiveness of OAT, coverage of OAT is considered to be very low [2,4,22]. The International Narcotics Control Board (INCB) reported that narcotic drugs were used in OAT in drug dependence in 68% of the 100 surveyed countries in 2014 [4]. In countries where OAT is available, the quality and coverage of OAT are frequently below international standards [2]. A systematic review of the literature showed that national and regional coverage of OAT in PWID varied from one to 61 recipients per 100 PWID per year [22]. Other data from the INCB show a major imbalance between the consumption of methadone and the prevalence of people who inject drugs in eastern Europe [4]. In eastern Europe, the level of methadone consumption seems to be very low despite a high prevalence of people who inject drugs, which may be related to the fact that several countries in eastern Europe do not recognize the use of methadone [4].

To date, several studies demonstrated potential barriers to access to opioids that can be linked to the international drug control system. However, the majority of these studies focus on the treatment of moderate to severe (cancer) pain, and little is known on these types of barriers affecting patients with opioid dependence. The aim of this study was to identify specific potential barriers to access to opioid medicines for patients with opioid dependence through an in-depth analysis of national legislation and regulations in these countries.

METHODS

The methods used to review national legislation and regulations systematically have been described in detail in a previous study [7]. An additional in-depth analysis was undertaken within the results of the previous study (all provisions that were considered to contain at least one potential barrier to access to opioid medicines) to identify all specific potential barriers to access to opioid medicines for patients with opioid dependence. No analytical software was used for the retrieval and coding of data in the previous study or in the additional in-depth analysis.

General review: selection of potential barriers to access to opioid medicines (all patient groups) [7]

In short, legislation and regulations concerning opioid medicines were selected by key experts in each country in the period March 2011 until February 2013. Legislation and regulations were translated into English by a professional translation agency specialized in the field of health and law (NOVA Language Services, Barcelona, Spain) if it was available only in the national language. In order to review selected legislation and regulations, a method was developed using a template with potential barriers to access to opioid medicines focusing on eight different categories (prescribing; dispensing; manufacturing; usage; trade and distribution; affordability; penalties; and other) and language issues. The template was developed based on World Health Organization (WHO) policy guidelines and additional literature regarding barriers to access [3,9,11,23,24].

A total of 93 relevant legal and regulatory documents were (partly) analysed by one reviewer (M.J.M.V.) ranging from three (Greece) to 15 (Latvia) documents per country (see Supporting information, Table S2). Legal or regulatory provisions related to controlled substances and opioid medicines were selected and were subsequently reviewed further independently using the template by three reviewers (J.A.L., M.D.B.S. and M.J.M.V.). Potential barriers to access to opioid medicines were identified and differences in views between the reviewers regarding the identification of potential barriers were discussed until consensus was reached. Newly identified barriers were added to the template and the reviewed legislation and regulations were checked retrospectively to complete the process.

The reliability of the selection of provisions for further review by one reviewer (M.J.M.V.) was validated by assessing the inter-rater reliability of the selection of provisions between two reviewers (M.D.B.S. and M.J.M.V.) for a selected number of countries. The controlled substances law of three randomly selected countries (Hungary, Serbia and Slovakia) was reviewed by the two reviewers and provisions were selected independently for further review. The selection by the two reviewers was compared using Cohen's kappa statistics and was rated to be very good (kappa = 0·87). Following validation of the selection of provisions, the assessment instrument was piloted by all three reviewers to align the review process: selected provisions of one country (Greece) were analysed based on the assessment instrument and the three reviewers met to discuss differences of views which concerned general interpretation of the assessment instrument.

Current analysis: identification of specific potential barriers for patients with opioid dependence

For the purpose of this paper, an in-depth analysis was made by reviewing all previously identified 778 potential barriers to access (ranging from 22 in Cyprus to 128 in Lithuania; see Fig. 1) that were identified in eight categories (all except language) to identify potential barriers that are applicable exclusively for patients with opioid dependence. For each provision, the patient group that could be affected was determined (M.J.M.V), and provisions were selected if this patient group was limited to patients with opioid dependence. The selected provisions were checked by one reviewer (M.D.B.S.) and were recorded as potential barriers to access to opioid medicines exclusively for patients with opioid dependence. An additional search was made within all 778 potential barriers that were identified in the previous study using a set of keywords

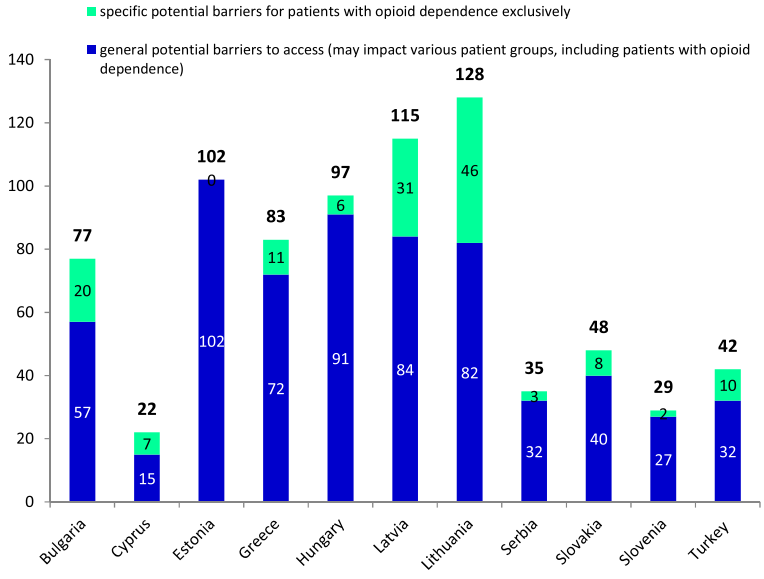

Figure 1 Number of specific potential barriers for patients with opioid dependence exclusively in relation to the number of general potential barriers identified per country (except category language). [Colour figure can be viewed at wileyonlinelibrary.com]

('substitution', 'substitute', 'OAT', 'OST', 'methadone, 'buprenorphine', 'prison', 'detention', 'harm reduction' and 'substance abuse') to reduce the omission of potential barriers for patients with opioid dependence. Additionally, all potential barriers in the category language identified in the previous study were reviewed and potential barriers that contribute to the stigmatization of patients with opioid dependence were recorded qualitatively. Validation of the methods and results have been described in detail in the previous study [7]. No changes were made to the results of the additional analysis based on the keyword search.

Data analysis

The total number of specific potential barriers for patients with opioid dependence was calculated by country and by category (all categories except 'language'). The total number of specific barriers was also calculated in relation to the total number of barriers identified in the previous analysis. The presence of potential barriers in the category language was recorded qualitatively per country. Examples of potential barriers were highlighted for the categories prescribing, usage, affordability, other and language.

RESULTS

Specific potential barriers for patients with opioid dependence

In total, 778 potential barriers to access to opioids were reviewed in 11 countries varying from 22 (Cyprus) to 128 (Lithuania). Of these 778 potential barriers, a total of 144 barriers (19%) in 10 countries (all except Estonia) were considered potential barriers exclusively for patients with opioid dependence, with the smallest number in Slovenia (n = 2, 7%) and the largest number in Lithuania (n = 46, 36%) (Fig. 1). The number of categories where dependence-related items were found varied between one (Slovenia) and five (Lithuania) of the eight categories (Fig. 2). Nine countries showed potential barriers in the category 'prescribing', while the total number of barriers in each category varied from one (several countries, several categories) to 18 (Lithuania, prescribing) (Fig. 2). Most barriers were identified in the categories prescribing, usage and other. All 11 countries use language in their legislation that contributes to the stigmatization of patients with opioid dependence (see Supporting information, Table S1).

Examples of provisions identified (categories prescribing, usage, affordability, other and language)

Examples of potential barriers concerning the usage of opioid medicines included strict admission and exclusion criteria for accessing OAT, such as minimum age criteria varying from 15 to 20 years (Bulgaria, Greece, Latvia and Lithuania), the requirement of evidence of repeated failure to successfully complete a therapeutic treatment programme aiming at abstinence (Bulgaria and Latvia) or the requirement of being opioid-dependent for a minimum period of time (Latvia) (see Supporting information, Table S1). Examples of potential barriers concerning the prescribing of opioid medicines included limitations regarding authorization to prescribe opioid medicines or assign OAT (Bulgaria, Latvia, Lithuania, Serbia, Slovakia), administrative requirements for prescribing opioid medicines or assigning OAT (Cyprus, Greece, Hungary, Latvia, Lithuania and Serbia) and limitations regarding the dosage or amount to be prescribed (Latvia, Serbia, Slovenia and Turkey) (see Supporting information, Table S1). Examples of other potential barriers included the availability and affordability of OAT (Bulgaria, Latvia, Lithuania, Serbia and Turkey) and requirements that may interfere with the privacy of patients (Bulgaria, Cyprus, Lithuania, Slovakia and Turkey) (see Supporting information, Table S1). Examples of language used in legislation and regulations that

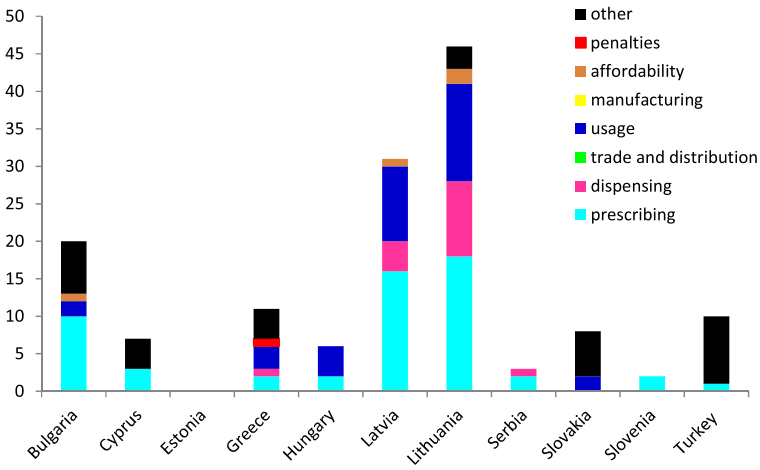

Figure 2 Total number of specific potential barriers for patients with opioid dependence identified per country according to category (except category language). [Colour figure can be viewed at wileyonlinelibrary.com]

contributes to the stigmatization of patients with opioid dependence include referring to patients with opioid dependence as 'addicts' (all except Hungary and Lithuania), referring to dependence as 'addiction' (all countries) or referring to medicines used in OAT as substances to be used as a substitute for addictive narcotics (see Supporting information, Table S1).

DISCUSSION

The results of this study showed that patients with opioid dependence may experience specific barriers to access to opioid medicines that can be linked to drug control systems. The majority of these potential barriers concerned the prescribing and usage of opioid medicines, such as minimum age criteria for admission to harm reduction treatment services and other admission criteria for accessing OAT. Additionally, all countries use language in their legislation and regulations that contributes to the stigmatization of opioid dependence.

This is the first in-depth analysis of national legislation and regulations focusing upon potential barriers to access to opioid medicines for patients with opioid dependence. Barriers to access to harm reduction services have been reported previously by other studies that used different methods, such as survey research, a review of literature and descriptive studies [14–16,20,25]. The majority of these studies addressed several types of barriers, including barriers that may be linked to drug control systems. For example, a survey by Schulte *et al.* revealed that physicians in Germany considered strict legislation and regulations in combination with complex documentation requirements the main obstacles for the provision of OAT [16]. Other reported barriers by Schulte *et al.* included financial remuneration, insufficient medical qualification of professionals providing OAT and inadequate interdisciplinary cooperation [16]. Results of previous studies that were similar to the results of the current study included age restrictions for accessing harm reduction services, strict admission criteria, treatment costs and strict exclusion criteria [14–16,20,25]. Different results were described, for example, for fear of legal sanctions for violating controlled substances legislation or regulations. Although overly strict legal sanctions were identified in the previous analysis [7], these sanctions were considered to be aimed at preventing non-medical use of opioids and diversion in general and were therefore not identified as potential barriers for patients with opioid dependence.

A considerable proportion of the potential barriers to opioid medicines that can be linked to the drug control system affects primarily patients with opioid dependence. As a result of these legal and regulatory barriers, health-care professionals may be unable or reluctant to prescribe or dispense opioid medicines. Fear for sanctions for unintended violations and (high costs associated with) strict requirements may deter health-care providers from initiating or continuing treatment. Similarly, patients with opioid dependence may be unable or unwilling to use opioid medicines due to the stigma associated with opioids and opioid dependence, the high treatment costs and access restrictions. Government representatives, policymakers and other stakeholders should recognize this vulnerable patient group while drafting new legislation and regulations. This is even more important considering that international lobbying efforts for this patient group due to the stigma related to opioid dependence fall short compared to other patient groups in need of opioid medicines. Misconceptions and even prejudices about opioid dependence being a wilful choice or a moral weakness often prevail, and opioid dependence is rarely acknowledged as a medical condition [26]. The language used in legislation and regulations revealed in this in-depth analysis confirms an attitude towards people with opioid dependence characterized by stigmatization and criminalization (see examples in Supporting information, Table S1). Additionally, given that a chain is only as strong as its weakest link, other factors that limit access should be taken into account while developing strategies to improve access to opioid medicines. These factors may be interlinked: the fear that non-medical use and diversion of opioid substances may result in overly strict drug control measures, and overly strict control measures may cause fear among patients, health-care professionals and policymakers for using opioid medicines. This may, in particular, be the case for patients with (a history of) dependence in need of treatment with opioid analgesics; due to the fear that they are more susceptible to developing opioid dependence, they may face more difficulties in accessing adequate pain relief [2]. More scientific data are needed to assess the different types of barriers that limit access to opioid medicines and the impact of lifting these potential barriers in clinical practice for individual patients with opioid dependence and for public health. To increase insight into the impact of potential barriers in clinical practice, a survey could be undertaken among patients with opioid dependence and their health-care providers in the European countries that participated in the ATOME project. This survey could focus upon the quality of the treatment provided, both from a patient and health-care provider perspective and on barriers that were encountered that hampered adequate treatment. In addition to the current study, which comprises a static analysis of legislation and regulations, future studies could also look into the dynamic process of development of legislation and regulations while taking into account evolving evidence-based medical treatment insights and changes in concerns that existed within society regarding opioid

dependence. Further studies could also generate an overview of best practice examples from countries that successfully revised their outdated legislation while providing information on the characteristics of their legal system; this information may be beneficial to other countries with a similar legal system.

Several limitations of this in-depth analysis should be mentioned, which concern primarily limitations that were reported in the previous study [7]. The results of this study showed a variation between countries in the total number of potential barriers for patients with opioid dependence. This variation may be the result of differences in the level of impediment of national drug control systems. The differences may also be associated with the level at which certain requirements are set out. For example, admission criteria for accessing OAT may be set out in national laws, regulations, ministerial decrees and guidelines, or may be left at the discretion of individual treatment centres. The variation in potential barriers between countries could (partly) be the result of incomplete selection of legislation and regulations in the 11 countries, which is a limitation of this study. Legislation regulating opioid substances and medicines was provided by key experts in 11 countries (see Supporting information, Table S2). Under-reporting of potential barriers due to incomplete selection of legislation and regulations cannot be precluded. A second limitation of this study is the translation of legal and regulatory data, which may have caused incomplete or incorrect reporting of potential barriers. Actions were undertaken to minimize incomplete selection of documents and incorrect translation such as training and support of the key experts and dissemination of the results among the national counterparts with the explicit request to provide feedback [7]. A third limitation of this study concerns the analysis; as the methods of this study comprise an analysis of legal text, inevitably variation of interpretation may occur. By involving multiple reviewers, the chances of divergent interpretations have been minimized.

In conclusion, the results of this in-depth analysis of national legislation and regulations of central and eastern European countries showed that patients with opioid dependence may experience particular challenges in accessing treatment with opioid medicines in addition to those experienced by other patients. As most other analysis of legal and regulatory texts have focused upon access to opioid medicines used in (cancer) pain management, access to opioid medicines for the treatment of opioid dependence remains a neglected area of study. More research is therefore needed to assess the relation between barriers linked to drug control systems and access to treatment with opioid medicines for patients with opioid dependence. As these findings suggest that a considerable proportion of the drug control provisions may interfere primarily with the adequate treatment of patients with opioid dependence, government representatives and policymakers should keep this vulnerable patient group in mind, and possibly reconsider existing legislation from this angle.

Declaration of interests

The Division of Pharmacoepidemiology and Clinical Pharmacology of Utrecht University is designated as a WHO Collaborating Centre for Pharmaceutical and Regulation. The WHO Collaborating Centre for Pharmaceutical Policy and Regulation receives no direct funding or donations from private parties, including the pharma industry. Research funding from public–private partnerships, e.g. IMI, TI Pharma (www.tipharma.nl), is accepted under the condition that no company-specific product or company related study is conducted. The Centre has received unrestricted research funding from public sources, e.g. Netherlands Organization for Health Research and Development (ZonMW), the Dutch Health Care Insurance Board (ZIN), EU 7th Framework Program (FP7), the Dutch Medicines Evaluation Board (MEB), and the Dutch Ministry of Health, Welfare and Sport.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1 examples of potential barriers for patients with dependence (categories prescribing, usage, affordability and other).
Table S2 legal and regulatory documents (partly) translated (printed in bold type) and (partly) analysed per country.