Opioid agonist treatment
Guiding principles for legislation and regulations

Expert group on the regulatory framework for the treatment of opioid dependence syndrome and the prescription of opioid agonist medicines.

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The preparation and drafting of this report was undertaken by Lausanne University Hospital (Community Psychiatry Department, Addiction Centre) as part of a mandate from the Swiss Federal Office of Public Health.

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Foreword

In the United States, 12 prosecutors have been tasked with identifying doctors and pharmacists throughout the country who prescribe or dispense medicines containing opioids without any regard as to how they are to be used. At the same time, the uncontrolled use of opioids has caused a new spate of fatalities in North America, which is in the throes of a real public health crisis. Why is the United States undergoing such a crisis? What can Europe do to avoid it?

It is not within the remit of this report to find answers to the first question. However, the Guiding Principles and their explanatory report try to provide specific answers to the second question. Putting the principles into effect should ensure a safe treatment framework and thereby prevent a situation as in North America.

As psychoactive substances under the control of international conventions, opioid medicines have always been subject to special regulations. These regulations have developed in a particular manner in each country, and one can safely say, with hindsight and in the light of two comparative law studies carried out by the EMCDDA and the University of Louvain in 2003 and the Institute of Health Law of the University of Neuchâtel in 2012, that they are, at the very least, rather disparate and hardly suited to current challenges. A large number of studies carried out by experts working under the auspices of international organisations such as the WHO and the International Narcotics Control Board (INCB), have found that there are fundamental difficulties in access to opioid medicines and related care.

Further to a proposal from the Swiss Federal Office of Public Health, the Pompidou Group mandated an expert group to examine the impact of legislation and regulations developed over time on access to and the quality of the treatment of opioid dependence syndrome. The aim of the project was to draw up recommendations for legislative and administrative authorities, in the form of guiding principles which will enable them to amend their national regulations on the prescription of agonist medicines to persons suffering from this illness.

In their work, the experts drew upon two key sources, first, international recommendations stemming from the results of scientific research and best practices and, second, the latest developments in fundamental human rights relating to health.

When a wave of heroin use hit the West at the end of the 1960s, lawmakers were, of course, not aware of the results of this scientific research. They were obliged to proceed by trial and error and adopted an array of punitive measures to provide a framework for what was then called "substitution" medical treatment. As such, these measures were a continuation of the prohibition of the substances consumed. Today, in retrospect and with the development of clinical, epidemiological and social knowledge, this essentially punitive approach has proven to be ineffective. On the contrary, having easy access to care is the best way of ensuring that the quality of life of those affected and their family and friends will improve, that they will be fully integrated, both socially and professionally, leading to a reduction of infectious diseases and crime.

Based on these findings, the experts from the Pompidou Group analysed the legislative provisions which impede access to care. They went even further and also examined the necessary related measures covering fields as varied as certification and control of medicines, the training and supervision of healthcare professionals, research and epidemiology, as well as the monitoring of the care system at national level and the necessary coordination at international level. Thus these Guiding Principles and four essential recommendations were born. The aim of the project was to produce global and coherent recommendations and to build bridges between the different sectors involved in the treatment provided for opioid dependence syndrome.

The added value of the project also resides in the willingness to bring together current schools of thought in the field of public health and of human rights. This is reflected in the composition of the expert group brought together to carry out this project and in the two partners which initiated the project, i.e., a public health department and an international body committed to developing and promoting human rights, the Pompidou Group.

The Pompidou Group has very clearly expressed its commitment to the inclusion of human rights in drugs policies and has decided to place those rights at the heart of these policies. The member states of the Pompidou Group have responded to this objective with concrete examples and produced several documents: the Policy paper providing guidance to policy makers for developing coherent policies for licit and illicit drugs (2011), the 2013 Athens Declaration on protecting public health in drug policy under austerity budgets and the Policy paper on preventing risks and reducing harm linked to the use of psychoactive substances (2013). In the latter, the Pompidou Group stated that "risk and harm reduction measures impact different policy areas, in particular healthcare, social welfare, law enforcement, criminal justice, international relations and human rights". The policy paper stresses that "risk and harm reduction policies have significant human rights relevance to the extent that they affect the well-being and quality of individuals` lives. Risk and harm reduction measures can play an important role in overcoming prejudice and discrimination that may result from drug use and addiction." Opioid agonist treatment (so-called "substitution treatment") is one of the measures listed by the Pompidou Group.

Whilst there is no doubt that opioid use in a therapeutic setting must be properly controlled, it is crucial to redefine what is necessary and sufficient in order to strike a better balance between controlling risks linked to the specific nature of opioid medicines and easy access to care. This new approach must make it possible to bring this illness into the ordinary health care setting and to remove it from harmfull social marginality. It is only occasionally that these "extraordinary" measures, i.e., those outside the ordinary health care setting, remain justified. These considerations led the experts to setting four key recommendations (removal of prior authorisation schemes, abolishing financial barriers, establishing an ad hoc follow up and coordination body and close attention to terminology).

Throughout its work, the expert group was mindful of the fact that the ultimate goal was to find a middle ground between the control that is necessary to avoid health and public safety risks arising from inordinate prescriptions and defending the rights and interests of persons in treatment suffering from an illness, for whom treatment has evolved in the light of new medical and epidemiological knowledge.

The Pompidou Group and the Federal Office of Public Health are proud to present the results of the work of this interdisciplinary group and to contribute thereby to the debate on these very important issues.

Our warm thanks go to this expert group for the quality of its work and its unwavering commitment, and in particular to the drafting committee which steered the project and supervised the final drafting of the Guiding Principles and the explanatory report.

Jan Malinowski
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Executive Summary

Context, objective, mandate

According to data from the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), out of an estimated population of 1.3 million “high risk opioid users” in the European Union, less than 650,000 people receive opioid agonist treatment. This treatment is defined as a “treatment for opioid dependence syndrome, including the long-term prescription of opioid agonist medicines (OAMs)”, principally methadone and buprenorphine.

This average figure hides wide disparities. Whilst in certain European Union countries this rate approaches 80%, in others, it is below 20%. In other parts of the world, certain countries continue to exclude, in law or in fact, such prescriptions (figure 1). Differences between countries are explained by a number of factors such as limited access to opioid agonist treatment or overall limited availability of any kind of treatment services. However, regional differences exist also within countries, notably between urban and rural areas, as well as disparities amongst populations at risk of discrimination, such as women, minors, migrants, or detained persons (Map 1). Only a limited number of European countries provide wide access to opioid agonist treatment, through primary-care physicians and dispensing pharmacies (map 2), so as to facilitate treatment outside major urban areas.

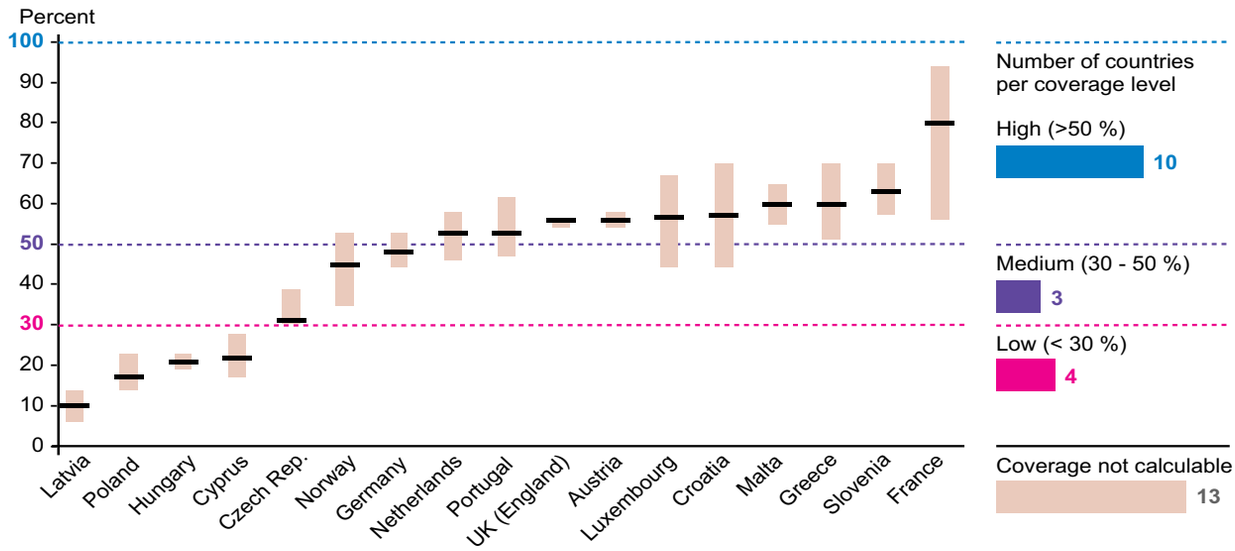
Prior authorisation schemes are a further barrier to accessing opioid agonist treatment. First implemented in the 1970s, these follow in the footsteps of the international system for the control of psychoactive substances. These schemes have in common that, in many countries, fully licenced physicians are not allowed to initiate a much-needed evidence-based therapy without first obtaining permission from the administration or from a medical government agency. An analysis of these schemes reveals that they stem from a historical, but scientifically and medically erroneous understanding, of “replacing an illicit drug by a legal drug”.

However, by their pharmacological action, opioid agonist medicines prescribed for the treatment of opioid dependence syndrome have very different effects from opioids used for hedonic purposes in a non-medical setting. Implemented according to appropriate arrangements, these medicines have positive effects on persons in treatment: they stabilise the emotional state, reduce or eliminate the subjective reinforcing effects causing dependence, and protect against opioid-induced death. They constitute therefore a central element of a treatment integrating medical, psychological and social aspects. Because of their clinical effectiveness, appropriate access to these medicines causes a highly significant reduction in mortality and comorbidities, including those related to the intravenous use of heroin (HIV, HCV infection). From this point of view, in addition to their primary function as medical treatments, these medicines are a key part of a public-health approach to risk and harm reduction. Two medicines in particular, methadone and buprenorphine, have been on the World Health Organisation (WHO) Model List of Essential Medicines since 2005.

To respect their obligations regarding access to healthcare and prevention of discrimination, countries are invited to review their regulations, aiming to rely as much as possible on the ordinary provisions regulating medicines and healthcare professions.

To assist administrative authorities in this process, the Pompidou Group`s Permanent Correspondents mandated a group of health and legal experts to identify criteria for the appropriate use of agonist medicines used in opioid dependence treatment, in line with ethical standards, international law, scientific knowledge and best medical practice.

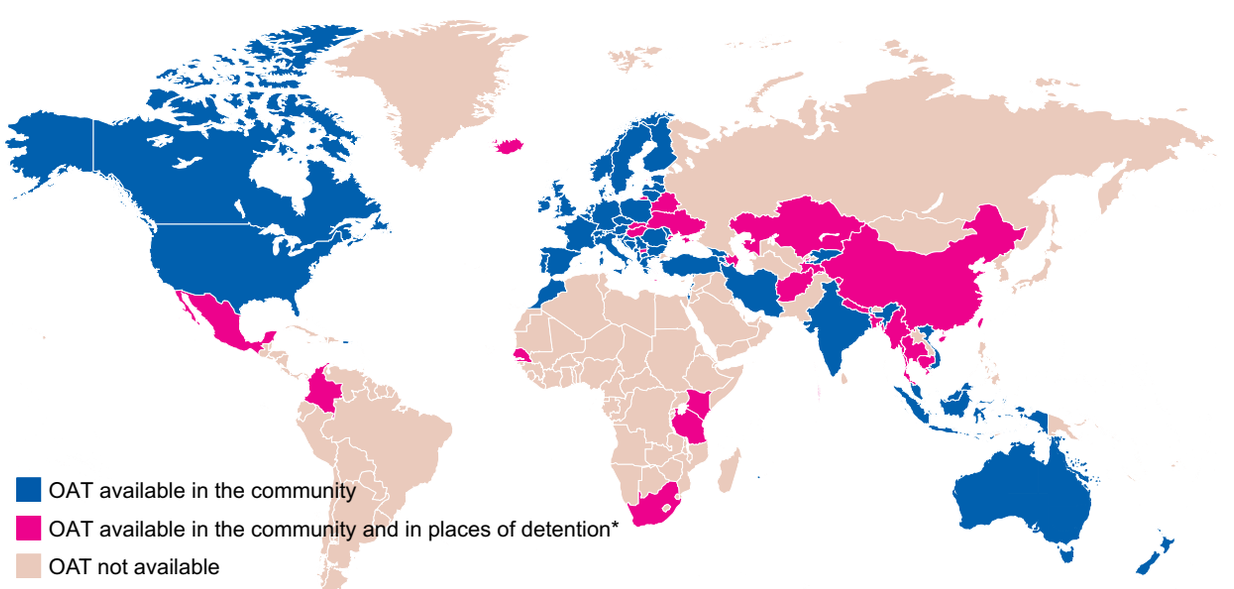
Figure 1 - Proportion of "high-risk opioid users" receiving an OAT (estimation)



NB: Data displayed as point estimates and uncertainty intervals.

EMCDDA 2017, data 2015

Map 1 - Availability of OAT in places of detention



The Global State of Harm Reduction 2016, "Global availability of opioid substitution therapy in the community and in prisons", Harm Reduction International (HRI), London, 2016, Map 1.2., p.15

*For more information relative to the coverage rate and effective availability in penitentiary settings also see Junod V., Wolff H., Scholten W., Novet B., Greifinger R., Dickson C. and Simon O., (2017).

Methadone versus torture: The perspective of the European Court of Human Rights. Heroin Addiction and Related Clinical Problems, Published Ahead of Print, July 18

Pre-existing recommendations

Whilst the legal framework defines the conditions of the treatment, its impact has not been studied comprehensively. Contrary to the abundant literature on opioid prescription and harm reduction measures, there are few publications and, subsequently, few robust recommendations to guide countries in their efforts to revise their legislation. Where such recommendations exist, they are general and difficult to implement in practice.

Two studies of comparative law - one carried out by the EMCDDA and University of Louvain in 2003, involving nine European countries, and the other conducted by the University of Neuchâtel in 2012, including five francophone countries - illustrate the heterogeneity and the inconsistency of regulations, as well as their divergences from ordinary health law provisions. The ATOME project (Access to Opioid Medication in Europe) has documented the central role of legislative and political barriers in reducing access to opioid medicines, as well as other barriers, such as negative attitudes, lack of professional and public knowledge and economic obstacles. Alongside the preparation of WHO clinical guidelines, a study by the Swiss Research Institute for Public Health and Addiction (ISGF) of Zurich University shows that the multiple regulatory contexts result in multiple differing national medical guidelines of varying quality.

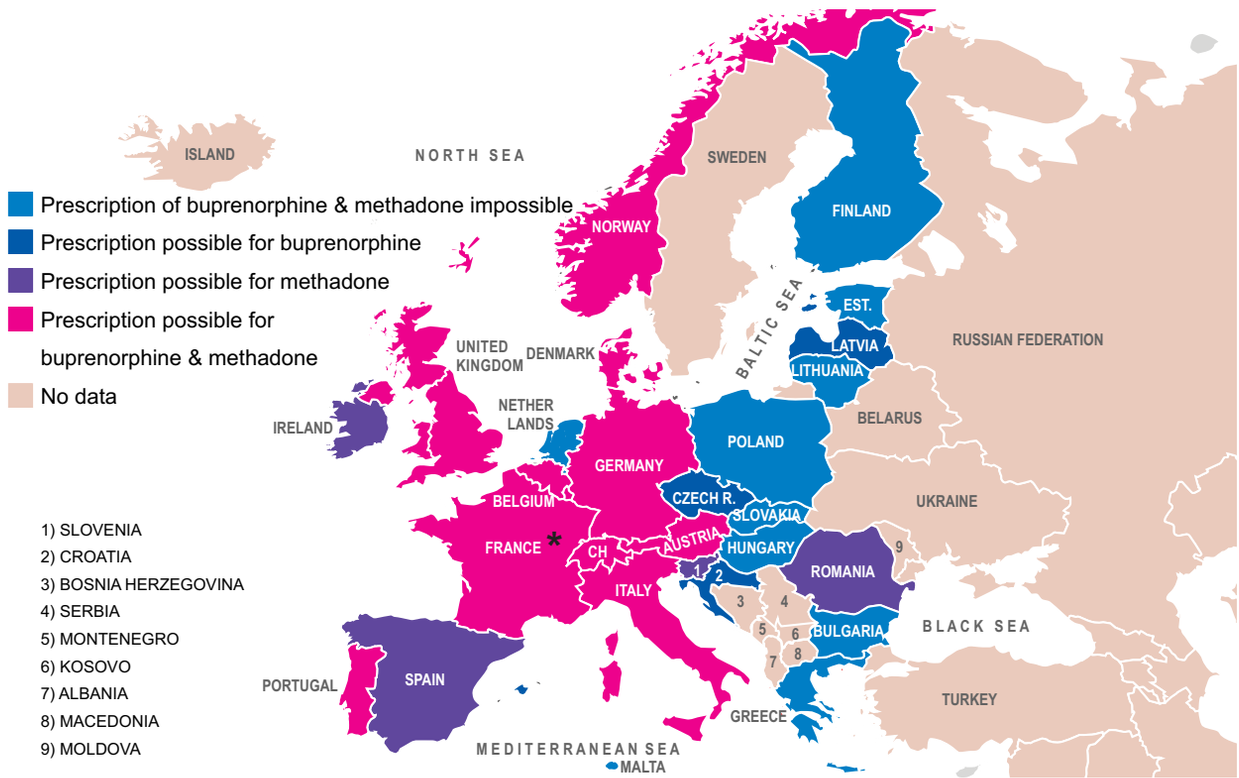
The EMCDDA/University of Louvain report provides several recommendations. The benefit of a “flexible” legal framework is noted, with the lowest possible threshold for access to care, and availability of several opioids (including diacetylmorphine/heroin by injection in specific programmes). The report also notes the importance of ensuring a diverse network of care providers, psychosocial quality monitoring, training beyond that for specialists only and sufficient resources for research.

Furthermore, guidelines established by WHO in 2009 emphasised the need to guarantee the principles of consent and confidentiality, to ensure the availability and accessibility of opioid agonist treatment free of charge, and to implement access to opioid agonist treatment for detained persons. In addition, it is appropriate to integrate opioid agonist treatment into the healthcare system, to ensure the continuous training of the professionals concerned, to allow persons in treatment to take their medicines home (at least for part of the treatment), not to impose a pre-determined term on the opioid agonist treatment and to stimulate monitoring that meets best practices for the evaluation of public policies. These WHO guidelines insist that a breach of the rules of conduct of the health-care institution does not in itself justify treatment discontinuation.

The United Nations (UN) Special Rapporteur on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health (2010, 2015) has also issued several general recommendations on the regulation of opioid prescriptions for opioid dependence syndrome. In particular, the Special Rapporteur prioritises universal and non-discriminatory access to essential medicines and equivalence of care. He points out the risk of discrimination against underage individuals (in particular the risk of depriving children of the right to express their own consent in relation to medical decisions).

In its 2011 and 2014 reports, the ATOME project makes several recommendations concerning the accessibility of controlled medicines regardless of the indication. In summary, it suggests that, to ensure access without discrimination, all legislative or regulatory standards must be the subject of an a priori and an a posteriori review, in terms of the impact upon availability, effective accessibility and quality. It highlights terminology problems found in regulatory documents, including the importance of avoiding confusion between medicines on the one hand, and non-medically used substances on the other. Regarding the training of professionals, the ATOME project proposes that training to prescribe and dispense opioid medicines should be part of the basic curricula for physicians and pharmacists. It also notes the importance of having an ad hoc consultative body to ensure the coordination of actors and the diffusion of pertinent information within a regional or national context.

Map 2 - Countries authorising the prescription of buprenorphine and methadone in a primary care setting



** In France, methadone can only be prescribed in a primary care setting if the primo-prescription has been realised by a specialized centre.*

Table "OST providers", EMCDDA, 2016 and OFSP, 2016

Realisation of the mandate, method for developing the recommendations

The Expert Group comprised participants from the following countries: Algeria, Belgium, France, Greece, Lebanon, Lithuania, Morocco, Portugal, Slovenia, Switzerland, Tunisia and Turkey, as well as representatives from the EMCDDA and WHO. The work benefitted from follow-up from a scientific committee bringing together experts from the participating countries, together with Canada, Israel, Italy, Poland, Spain and the United Kingdom.

Three two-day meetings and a one-day meeting were held in Paris between August 2014 and May 2017. Through discussions and a Delphi survey, the group identified some 60 guiding principles, grouped in 19 sections, which were then the subject of a wide public consultation. The analysis of cross-effects within the principles led to the identification of four key recommendations meant to guide the implementation of national strategies.

Key elements of the guiding principles established by the expert group

The guiding principles have been structured into five parts and 19 sections. The first part is devoted to definitions and objectives. A second part focuses on the right to access opioid agonist medicines used in the context of opioid dependence syndrome. A third part deals with the role of healthcare professionals. A fourth part centres on the role of the authorities. A fifth part addresses national and international collaboration.

I. Definitions and objectives of the guiding principles

The need to review the terminology and to use a vocabulary that is neutral, precise and respectful appears as a prerequisite. The widespread use of the term “substitution” is problematic. The term “substitution” leads to an ambiguity regarding the nature and the effects of prescribed opioid medicines. The Expert Group recommends replacing this term with that of “opioid agonist medicine”, and “opioid agonist treatment”, as a contraction of “treatment of opioid dependence syndrome by an opioid agonist medicine”. The objectives of opioid agonist treatment are first and foremost all centred on the treatment of the individual: reduction of the symptoms of dependence syndrome, improvement of quality of life, decrease in mortality and secondary morbidity, particularly infectious diseases. A medicine that effectively achieves such individual objectives has, subsequently, a positive effect for risk and harm reduction, for health promotion, and finally, for public safety.

II. Right to access opioid agonist medicines and related care

From a normative point of view, anyone with a diagnosis of dependence syndrome must have access to treatment based on the latest scientific and medical knowledge. This treatment integrates in most cases opioid agonist medicines coupled with various psychosocial support measures. Supervised dispensing should be provided if the health status and the risk of diversion justifies it. Respecting medical confidentiality and data protection is crucial. Also of great practical importance is non-discriminatory access for minors (i.e. legally minors, but competent to consent because capable of discernment), for persons who are deprived of their freedom as well as for persons in conflict with their care team. In the latter case, it is essential that the general healthcare system provides a diverse and dense network of infrastructures so as to enable the transfer and the effective continuation of opioid agonist medicines.

III. Role of healthcare professionals

Prescribing and dispensing opioids for any indication including opioid dependence syndrome should be taught as part of the basic training of physicians and pharmacists. Furthermore, as with any healthcare professionals, physicians and pharmacists involved in healthcare accompanying opioid agonist treatment should be the subject of ordinary control by professional disciplinary bodies and by health authorities. In case of breach of professional codes, best practices, or administrative rules, the same consequences should apply regardless of the discipline; unfortunately this is not always the case under most current prior authorisation schemes. Whenever, in order to exercise special control, professional supervision is entrusted to a specialized body (medical or non-medical) for which it is not the usual task, there is a risk of excessive or insufficient control.

IV. Role of the public authorities

The State has the duty to ensure a coherent framework for treatment with opioid agonists, with the aim of ensuring access and quality. When the State establishes a legal and administrative framework for prescription of controlled medicines, it should systematically conduct an a priori impact analysis, not only regarding the possible consequences on access to medicines and treatment, but also regarding the willingness of physicians, pharmacists and other professionals concerned to commit to providing this type of treatment. Indeed, the legal administrative obligations can negatively impact physicians' and pharmacists' willingness to offer these treatments. This is why such obligations should be limited to what is strictly necessary and proportionate to ensure the effectiveness of the treatment and its security to third parties. In particular, prior authorisation schemes are considered disproportionate, the more so because there exists no equivalent system in other areas of medical practice. To prevent double prescriptions or to collect epidemiological data, an a posteriori reporting mechanism represents an alternative solution, if subject to adequate protection of personal data. However, retaining such a declarative system should require prior evidence that less invasive means would be insufficient to achieve the objective. The authorities should ensure that treatments are paid for and that healthcare professionals are duly remunerated. Finally, the public authorities should make resources available for evaluation and monitoring. Such monitoring should focus on structure and process indicators rather than outcome indicators, since the effectiveness of opioid agonist treatment is no longer to be demonstrated.

V. National coordination and international collaboration

It is recommended that the State designates a dedicated consultative body, bringing together representatives of professionals and users, as well as the different state or parastatal services concerned. These include notably medicine agencies, public-health services, social insurance and professional supervisory bodies. This consultative body should establish links between monitoring data and professionals' feedback so as to establish operational recommendations. In addition, each State should participate in the updating of high quality international guidelines, such as WHO guidelines. Furthermore, States should invest in the promotion of these international guidelines and refrain from producing new ones at the national level. In order to secure the comparability of data, States should agree on a set of minimum common indicators and should co-fund intergovernmental agencies with the expertise to process and publish this data.

Table 1 - General Structure of the guiding principles

Part	Section	Main messages
I- Definitions & objectives	1 - Definitions 2 - Objectives of the principles 3 - Objectives of opioid agonist medicines	Primary objectives of opioid agonist medicines centred on the person and the fundamental right to access to essential medicines. Opioid agonist treatment scientifically recognised for opioid dependence syndrome as well as a risk and harm reduction measure.
II- Right to opioid agonist medicines and related care	4 - Fundamental right to healthcare 5 - Non-discriminatory access 6 - Free and informed consent 7 - No discrimination due to the simple fact of receiving opioid agonist medicines 8 - Continuity of care	Respect for the principle of non-discrimination de jure and de facto justifying monitoring and ad hoc measures. Compliance with the principle of equivalence of care. Right of access to treatment for minors. Guaranteed continuity of the medicine even in the case of an impasse in the provider-person in treatment relationship No delay to the start of treatment once the indication has been established.
III- Role of the professionals	9 – Indication, prescription, dispensing, coordination 10 – Training of Physicians 11 – Training of Pharmacists 12 - Supervision	Competence to implement opioid agonist treatments expected from all physicians and pharmacists at the end of basic training; Right to prescribe granted to any physician. First-line monitoring of healthcare professionals by professional bodies (professional or disciplinary law); Importance of support measures alternative to sanctions (e.g., mentoring, group exchanges, supervision/intervision).
IV- Role of the authorities	13 - Availability and quality of opioid agonist medicines 14 - Proportionality of the framework 15 - Financing and remuneration 16 - Training and research 17 - Monitoring and indicators	Authorisation of medicines and pharmacovigilance by the medicine agency. Summary of the Product Characteristics/Product Information providing basic information according to the standards applicable to any medicine. Abolition of prior authorisation schemes. Possibility of declarative systems for the prevention of double prescriptions and epidemiological monitoring (if necessary). Specific mechanisms to remove financial barriers to treatment. Incentives for professionals guaranteeing effective availability of appropriate trained professionals. Guaranteed protection of personal data.
V- National coordination and international collaboration	18 - National consultative body 19 - International collaboration	Body integrating monitoring, professionals, users, state, parastatal, and private bodies to ensure the monitoring of regulatory revision efforts and their impact on healthcare systems. Standardisation of monitoring efforts, public reports. Financing and promotion of international guidelines rather than national guidelines.

Key recommendations for the promotion, initiation and implementation of revision processes in national contexts

A long-term strategy is needed to implement the Guiding Principles while taking into account varying national framework. Based on the strong interdependence between the guiding principles, four key recommendations are put forward: (1) Prescription and delivery without prior authorisation schemes, (2) Effective removal of financial barriers, (3) Coordination and follow-up by a national consultative body, (4) Neutral, precise and respectful terminology.

Prescription and delivery without prior authorisation schemes

This recommendation stems from the analysis of the negative consequences of prior authorisation schemes and from the existence of alternative measures. The legal mechanisms for medicine licensing and for market supervision are sufficient to ensure safety in compliance with the international conventions on controlled substances. Prior authorisation schemes represent, above all, the legacy of a bygone era where opioid agonist medicines were not authorised by the medicine agencies and were off-label prescriptions. Abolishing these prior authorisation schemes will require a careful analysis of political obstacles.

Effective removal of financial barriers

Even in countries with high treatment rates, there are people who use opioids in a risky manner who remain particularly vulnerable and hard to reach. This lack of effective access to care constitutes an ethical challenge and a risk to public health. On the economic front, making these treatments available leads to a proven reduction in direct, indirect and intangible social costs, with savings that largely exceed the overall cost of treatment. A reinforced financial support mechanism is therefore necessary, in-line with what has been developed for other chronic diseases within the healthcare systems.

Coordination and follow-up by a national consultative body

It is recommended to establish an ad hoc national consultative body. Where appropriate, such a body can be created by adapting the mission statement of a pre-existing body. The cost of such a body will be modest compared to the results expected from its work. Such a body enables long-term support for regulating treatment within the ordinary health-law framework, while identifying situations which nonetheless require out-of-the ordinary regulatory measures.

Neutral, precise and respectful terminology

In the field of dependence, many highly ambiguous terms are commonly used by professionals, by administrative services and by international organisations. Elimination of the term “substitution therapy” in favour of the concept of opioid agonist treatment/opioid agonist medicines is an emblematic example of this issue. The terminology used in institutional and regulatory documents should be subject to periodic reviews.

The following pages present two tables summarising the key messages of the guiding principles in addition to the objectives and processes implied by the four key recommendations.

Table 2 - Objectives related to the four key recommendations

1 - Prescription and delivery of opioid agonist medicines without prior authorisation scheme

The therapies involving the prescription of opioid agonist medicines fall under the ordinary rules of prescription and delivery of controlled medicines. Therefore, they do not require a special authorisation for persons in treatment, for professionals or for the infrastructures dispensing treatment. The attribution and division of tasks and competencies between the various actors are the same as for all other forms of authorised therapy including controlled medicines.
This process has implications for the training and supervision of professionals as well as for the approval of the opioid agonist medicines and its pharmacovigilance. Thus, basic knowledge of opioid agonist medicines should be included in the basic training of all stakeholders in the health and social care system. Thus, ordinary disciplinary bodies for the supervision of healthcare professions must also supervise the professionals providing opioid agonist medicines, in the same way as professionals providing other medicines are supervised. Finally, the medicines agencies must be the competent authorities to keep up-to-date records of use (Summary of Product Characteristics/Product Information - SPC/PI) for opioid agonist medicines, taking into account data from pharmacovigilance and other studies. This information must notably clarify how opioid agonist medicines are to be dispensed based on the most recent scientific data.
Prior authorisation schemes are suppressed. Declarative regimes whereby healthcare professionals announce ongoing treatments may be retained, if these regimes are necessary to prevent double prescriptions and/or to facilitate epidemiological monitoring; in any event, strict data protection rules must be followed.

2 - Effective removal of financial barriers

For persons presenting an opioid dependence syndrome, access to treatment must not depend - effectively and practically – on their ability or willingness to pay. Treatment should be provided at no charges at each of the different steps of the treatment (from the first contact to the prescription and delivery of the opioid agonist medicines to follow-up visits). In particular, persons in treatment are not required to advance funds or provide guarantees, regardless of the type of healthcare provider and the type of treatment. Because of public health implications, implementation of this objective may call for special funding, apart from the general scheme of healthcare financing, regime, justified on the grounds of public health.
States must ensure that the effective removal of financial barriers does not lead to a form of rationing. In particular, it must not result in stricter requirements for entry into treatment, nor must it affect the administrative responsibility and/or the remuneration of professionals.

3 - National consultative body for coordination and monitoring

Acting on a clear and specific mandate, a national consultative body monitors the system for the treatment of opioid use disorders and advises the public authorities. In particular, it is responsible for identifying barriers to and for removing them. Where appropriate, such responsibilities can be attributed to a pre-existing body, if its new role is properly defined in an adequate mission statement.
The consultative body includes representatives from people directly affected by the non-medical use of opioids, professionals involved in the treatment and the prevention of opioid use disorders, researchers and public health services, supervisory authorities of healthcare professionals, medicines agencies, pharmaceutical companies, and any other actor relevant to the national context.
To accomplish its mission, the body conducts its work based on research results, has access to pertinent statistics and information, and receives regular feedback from practice. This consultative body enjoys independence with regards to its budget (which must be sufficient) and to agenda settings as well as freedom of speech. The result of its work is subject to the principle of transparency.

4 - Neutral, precise and respectful terminology

The terms employed to designate opioid dependence syndrome, persons in treatment, practitioners, places of care and the medicines used are neutral, precise, and respectful. To prevent prejudice, stigmatisation and discrimination, these terms describe unambiguously the facts, based on scientific knowledge; they respect the personality of persons in treatment, as well as their personal and professional environment.
The term “substitution”, being ambiguous as to the nature and function of opioid agonist medicines, is to be avoided in favour of alternatives focused on the real characteristics of opioid agonist medicines.
While terminology is to take into account international definitions, recommendations and practices, it must be adapted to the language of each linguistic and/or regional community and must be based on an ongoing debate among healthcare professionals, civil society, the persons in treatment and the competent authorities. Such a debate also promotes the dialogue between different disciplines concerned by the field of substance use disorders.

Background and context of the project

1.1 Origin and definition of the mandate

At the "Third French-speaking colloquy on the treatment of opioid dependence", the Swiss Federal Office of Public Health (OFSP) commissioned a comparative study of the legislation governing the prescription of opioid medicines in five French-speaking countries: Switzerland, France, Canada, Belgium and Tunisia (Institute of Health Law, University of Neuchâtel, 2012). This comparison highlighted the disparate nature of the conditions for prescribing these treatments and emphasised the need for recommendations that could make it easier for countries wishing to revise these conditions or create new ones.

In the spring of 2014, with the support of the Secretariat of the Pompidou Group, a group of health and legal experts, guided by a scientific council and by a secretariat commissioned by the OFSP, began work under the 2010-2014 "Assistance for the development, implementation and monitoring of national drug policies" activity programme.

At their 75th meeting in autumn 2014, the Pompidou Group's Permanent Correspondents endorsed this expert group and tasked it with drawing up recommendations concerning the regulations on the prescription of opioids in the treatment of opioid dependence syndrome, referred to below as "opioid agonist treatments" (OATs). The aim of the anticipated recommendations was to enable the administrative authorities to put forward measures for supervising these treatments complying with the standards of good clinical practices, in line with the results of biomedical research and the recommendations of existing international health authorities and upholding the fundamental healthcare rights enshrined in international law.

Under the authority of the Bureau of the Permanent Correspondents, the Expert Group set up in 2014 was enlarged to include other interested countries. Country representatives were appointed by the Permanent Correspondents on the basis of their legal or health expertise in the field of OATs. The fees of the members of the scientific secretariat were covered by the Pompidou Group's voluntary contributions, with the national authorities paying for the travel and accommodation costs of the participants appointed to participate in the Expert Group.

The Expert Group brought together participants from the following countries: Algeria, Belgium, France, Greece, Lebanon, Lithuania, Morocco, Portugal, Slovenia, Switzerland, Tunisia and Turkey, as well as one expert from the EMCDDA and from the WHO. A scientific committee also included experts from Canada, Italy, Israel, Poland, Spain and the United Kingdom (cf. Appendix 5).

Four meetings (seven days in all) were held at the Paris offices of the Council of Europe (CoE). The first was held on 7 and 8 September 2014, providing the opportunity to explore various existing recommendations of the international health authorities and to gather additional data on the practices of the participating countries. The second meeting, on 27 and 28 August 2015, was devoted to the development of guiding principles, which were submitted for public consultation. At the third meeting, on 25 and 26 August 2016 and the fourth meeting, on 11 May 2017, the Expert Group drafted this report.

1.2 Disparate nature of the regulations on opioid agonist treatments

In order to fulfil its remit, the Expert Group drew on three main sources to assess the regulatory aspects. An initial comparative law study was carried out by the EMCDDA and the University of Louvain (EMCDDA, 2003) and covered nine European countries (Austria, Belgium, Finland, France, Greece, Italy, Ireland, Norway and Spain). A second such study was conducted by the University of Neuchâtel Institute of Health Law in 2012 and covered five French-speaking countries (Belgium, Canada, France, Switzerland and Tunisia). Finally, the Expert Group based its assessment on the reports by the EMCDDA's European information network on drugs and drug addiction (Reitox), which are regularly updated via the national focal points of the countries of the European Union (EU) and Norway and uploaded to the EMCDDA's website. The laws of other countries were also consulted in the course of the project.

It has proved difficult to categorise the various existing laws on OATs, although a number of trends are emerging. The following criteria have been taken into consideration: the substances and medicines concerned, the persons or bodies authorised to prescribe a treatment, the demands and limitations concerning the treatment itself, the termination and interruption of the treatment (and any disciplinary sanctions applicable to individuals in treatment who fail to comply with the authorised treatment protocol), and the control and supervision of the treatment by the State. The various laws governing OATs vary in their degree of detail and are based on approaches that come from differing perspectives. For example, although the Belgian, Quebec, Swiss, Lithuanian, Slovenian and, to a lesser extent, French regulations are similar in their public-health approach they differ with regard to whether or not elements of a repressive approach continue to be used, the varying level of commitment to ensuring very tight control of OATs and the degree of detail in the regulations in question.

Moreover, the substances authorised are not the same in all countries. In Portugal and Lithuania, for example, the only substance expressly targeted by a prior authorisation scheme (PAS) is methadone, whereas in Switzerland the treatment is subject to special authorisation in the case of methadone, buprenorphine, slow-release oral morphine and diacetylmorphine (heroin). France, Belgium, Tunisia, Denmark and Slovenia specifically regulate the use of methadone and buprenorphine. The maps of Europe (Appendix 3, maps 3, 4, 5 and 6), taken from the latest data published by the EMCDDA illustrate this situation.

These differences in the substances prescribed lead to additional differences in the content of the regulations. This can be seen in Switzerland, for example, where the legal regime applicable to the use of diacetylmorphine is not identical to that applicable to the other medicines recorded in the "OAT" indication, or in France, where primary care physicians can administer treatments based on the prescription of buprenorphine or methadone but are authorised to initiate only the prescription of buprenorphine, whereas initiating the prescription of methadone is the responsibility of specialised centres.

The various national regulations also differ on more precise points, for example the minimum age for being able to benefit from substitution treatment. However, this is a key issue as minors in some countries are consequently excluded from treatment programmes.

Although most countries lay down a precise framework for OATs based on a PAS, this does not mean that everyone needing treatment is guaranteed access to it. For example, in Quebec, in 2012, less than 25% of people who regularly use opioids non-medically were estimated to have access to OATs, in contrast to coverage rates of above 50% currently observed in Europe (see also Figure 1 above). The regulation of the prescription of opioid agonist medicines (OAMs) therefore primarily raises the key question of the States' positive obligation with regard to the fundamental right to access to healthcare.

1.3 The fundamental right to treatment in international law

The conflict between the right to access to treatment and the policy of punishing the consumption and trafficking of controlled substances is by no means a new one. The first international conventions on narcotics already acknowledged the need to find a balance between access to medicines for medical treatment, especially the treatment of pain, and punishing so-called recreational consumption.[1] In practice, the way in which this compromise has – or has not – been achieved has varied over time and continues to differ from one country to another. For a long time, the emphasis has been on punishment (criminal penalties, also imposed on consumers), even at the risk of jeopardising access to opioids by people who are unwell, especially in the fields of analgesic medicine, anaesthetics or palliative care. In some countries, as we shall see more clearly in Section 1.6, the prescription of opioids is still negligible despite the recognised medical needs. Notwithstanding the recognition of opioid dependence syndrome as a disease, little progress has been made in many countries: the criminal law approach generally predominates; it is often amplified by geopolitical considerations ("war on drugs") or is assumed to fulfil the (explicit or presumed) expectations of the bodies set up by international conventions.

Since the 1990s, a global movement in favour of fundamental rights has called for the current balance to be reassessed, emphasising the right to treatment and stressing the failure of repressive measures (Lines et al., 2017; Taylor, 2007; Valadez, 2014). This right to treatment is enshrined, in various forms, in a large number of declarations and international treaties (see in particular Article 25(1) of the 1948 Universal Declaration of Human Rights and Principle 1 of the World Health Assembly's Declaration of Alma-Ata).[2] Among numerous sources, the most frequently cited international legal basis is Article 12 of the International Covenant on Economic, Social and Cultural Rights (ICESCR, 1966), which states:

"The States Parties to the present Covenant recognise the right of everyone to the enjoyment of the highest attainable standard of physical and mental health.

(2) The measures to be taken by the States Parties to the present Covenant to achieve the full realisation of this right shall include those necessary for ensuring:

(I) A reduction in the stillbirth-rate and in infant mortality, as well as the healthy development of the child;

(II) The improvement of all aspects of environmental and industrial hygiene;

(III) The prevention, treatment and control of epidemic, endemic, occupational and other diseases;

(IV) The creation of conditions which would assure, to all, medical service and medical attention in the event of sickness."

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1 *Without being exhaustive, we cite the following conventions, conferences and protocols, in chronological order: the Shanghai Conference (1909); the International Opium Convention of 1912 (The Hague); the Geneva Opium Conventions (1925); the Geneva Narcotics Manufacturing and Distribution Limitation Convention (1931) / Bangkok Opium Smoking Agreement (1931); the Convention for the Suppression of the Illicit Traffic in Dangerous Drugs (Geneva, 1936); the Lake Success Protocol (1946); the Paris Protocol (1948); and the New York Opium Protocol (1953). More recently, the three principal conventions are: the 1961 Single Convention on Narcotic Drugs (amended by the 1972 Protocol); the 1971 Convention on Psychotropic Substances; and the 1988 Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances.*

2 *Without claiming to be exhaustive, we cite in relation to the right to health: Articles 13, 55 and 62 of the UN Charter; Articles 3 and 25 of the Universal Declaration of Human Rights; Articles 2, 4, 7, 9, 10,11, 12, 13, 15 and 16 of the International Covenant on Economic, Social and Cultural Rights; Article 7 of the International Covenant on Civil and Political Rights; Article 5 of the 1963 International Convention on the Elimination of All Forms of Racial Discrimination; Articles 10.h, 11.f, 12, 14.b, and 14.c of the 1979 Convention on the Elimination of All Forms of Discrimination against Women; Article 33.1 of the 1950 Convention Relating to the Status of Refugees; Article 10.1 of the 1984 Convention against Torture and Other Cruel, Inhuman or Degrading Treatment or Punishment; Article 24 of the 1989 Convention on the Rights of the Child; Article 8 of the 1986 Declaration on the Right to Development; Articles 7.2, 20.2.c, 24 and 25 of the 1989 Convention concerning Indigenous and Tribal Peoples in Independent Countries (ILO Convention 169); Articles 10, 20, 22, 23, 24, 25, 26, 32, 43.4, 52, 65, 66.2, and 82 of the Standard Minimum Rules for the Treatment of Prisoners (Nelson Mandela Rules); Articles 4, 9 and 16 of the 1981 African Charter on Human and Peoples' Rights; Articles 4 and 11.2 of the 1969 American Convention on Human Rights; Articles 2, 3, 8, and 10 of the European Convention on Human Rights; Part I: Articles 3, 7, 8, 12, 13, 14 and 15; Part II: Articles 2.4, 7.9, 8, 11, 12, 13, 14 and 15; Part V: Article E of the European Social Charter; and Articles 1, 11 and 16 of the American Declaration of the Rights and Duties of Man.*

The Committee on Economic, Social and Cultural Rights has provided a helpful explanation of this right in its General Comment No. 14. This Comment states that "[t]he right to health is not to be understood as a right to be healthy. The right to health contains both freedoms and entitlements. The freedoms include the right to [...] control one's health and body [...]. By contrast, the entitlements include the right to a system of health protection which provides equality of opportunity for people to enjoy the highest attainable level of health." Health is generally defined by reference to the definition proposed by WHO, namely "as a complete state of well-being", even though it is accepted that this state is only an ultimate goal. The fundamental international right to treatment must be understood as imposing on States a requirement to take gradual steps to implement it in full. Each State must draw up an action plan to ensure first a minimum state of health of its population and then reaching for an optimum state of health. The WHO has provided concrete assistance by drawing up and updating a list of essential medicines that every country should make available to its population. It includes methadone and buprenorphine (in the indication for the treatment of a dependence syndrome). General Comment No. 14 also sets out four criteria that make it possible to assess measures taken to implement the right to health, namely the availability of healthcare goods and services, their accessibility without discrimination, their acceptability by the individuals and groups concerned and their quality from a medical and scientific angle.

The essential corollary of the right to health is the principle of non-discrimination, according to this principle, States cannot – without relevant reason – create or tolerate inequalities in access to treatment (a relevant reason would be to facilitate access to treatment of particularly vulnerable groups). Also, closely linked to the right to health are the right to court access and the right of political participation. More generally, it is recognised that human rights are closely interrelated, so the realisation of one human right, such as the right to health, requires – or is facilitated by – the realisation of other fundamental rights (for example, the right to education). The concept of social determinants of health has also demonstrated that the state of health of individuals and groups is primarily influenced by non-medical factors, especially socio-economic factors.

There remain two longstanding questions:[3] first, does the fundamental right to access to treatment prevail over other obligations arising under international law? Second, is this right enforceable, that is to say can legal action be taken in national, or indeed international, courts to obtain the corresponding benefits?

In international law, there is no general rule or instrument that set forth a hierarchy between various legal provisions. Some treaties may contain clauses that establish priorities over other treaties, but that is the exception rather than the rule. The general principle remains that each State that enters into a commitment under an international treaty must arrange to comply with it without being able to "invalidate" it by invoking an opposing rule from another treaty. The exception to this principle applies in favour of a small number of so-called "peremptory norms" (jus cogens),[4] which are rules so important that they always prevail, even without being enshrined in a treaty binding on the State in question. The prohibition of genocide and the ban on torture are included in this handful of fundamental norms. These fundamental norms have however not been listed in. At any rate, the right to health as such is not part of the jus cogens. Some legal authors argue further that norms considered "of major importance", above all those that guarantee fundamental rights, including the right to health, should be given priority over others.

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3 Lawrence O. Gostin, Global Health Law, Harvard University Press (2014); Jonathan Wolff, The Human Right to Health, Norton and Company (2012); John Tobin, The Right to Health in International Law, Oxford: Oxford University Press, 2012; Stephen P. Marks. 2013. "Emergence and Scope of the Right to Health", in Advancing the Human Right to Health, ed. José M. Zuniga, Stephen P. Marks, and Lawrence O., Gostin: 1-33. Oxford University Press; Lawrence O. Gostin, J.D., and Devi Sridhar, Ph.D., "Global Health and the Law", New England Journal of Medicine 370 p. 1732 (2014); Jennifer Prah Ruger, Theodore W. Ruger and George J. Annas, "The Elusive Right to Health Care under U.S. Law", New England Journal of Medicine 2015; 372:2558-2563 June 25, 2015 DOI: 10.1056/NEJMhle1412262; Alicia Ely Yamin, "The Right to Health Under International Law and Its Relevance to the United States", American Journal of Public Health. 95(7): p. 1156–1161 (July 2005); Paul Hunt, "Interpreting the International Right to Health in a Human Rights-Based Approach to Health", December 3, 2016, in Papers in Press, Health and Human Rights Journal; Virginia A. Leary, "The Right to Health in International Human Rights Law, Health and Human Rights", Health and Human Rights Journal Vol. 1, No. 1 (Autumn, 1994), pp. 24-56.

4 The foundation of this peremptory norm is generally attributed to Article 53 of the Vienna Convention on the Law of Treaties.

This leads to the second question: enforceability. Most international treaties do not include a mechanism binding on States for guaranteeing their application. For example, most do not establish a court authorised to decide disputes and deliver binding judgments for the State concerned. This is a deliberate political choice, given that States usually prefer not to enter into legally binding international obligations. Despite the lack in most instances of international courts, other supervisory mechanisms may show some effectiveness in practice. For example, numerous treaties oblige States to submit regular reports and/or agree to external inspections (carried out by rapporteurs or independent experts). These reports and external inspections then allow to put forward recommendations, which States, either under international pressure or pressure from non-governmental organisations (NGOs) and the media, often agree to implement, or at the very least to debate. In this regard, it is important to highlight the considerable work carried out by the successive Special Rapporteurs of the United Nations (UN) on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health.[5]

Yet, the fact remains that, if a State refuses to comply with a rule deriving from an international treaty for which no binding enforcement mechanism is provided there is no legal way of forcing its hand, even if the rule in question guarantees a fundamental right, such as the right of access to treatment. For example, if a State refuses to make methadone available to its population then there is generally no international legal mechanism to compel it to do so.

There are however exceptions.

First, some States have gone a step further and recognised not only the higher status (priority) of international law but also its direct applicability by national courts. In such cases, the domestic courts are required give effect to the rules of international law (e.g., access to treatment). Depending on the country, this direct applicability is limited to international rules worded in a sufficiently precise manner so that national courts can readily decide its scope (substance and limits).

Second, in Europe the European Court of Human Rights has adopted a progressive and broad interpretation of the rules emanating from the European Convention on Human Rights (ECHR). Although the latter does not directly enshrine a right to health, several of its freedoms can be relied upon to bring about a somewhat equivalent outcome. For example, the right to life (Article 2), the prohibition of torture and degrading treatment (Article 3), the right to respect for private and family life (Article 8) and the right to freedom of expression (Article 10) can and often are relied upon by individuals in dispute with a State in order to benefit from health-related rights or services.[6] For example, in a recent judgment the Court held that imprisoned persons presenting with an heroin dependence syndrome must benefit from an independent medical assessment of their state of health and cannot simply be forced into abstinence.[7] Such a judgment is directly binding on the defendant country and is also indirectly binding on all other countries in a similar situation. This mechanism is noteworthy because in the context of fundamental rights it is the one most often used and is by far the most effective from a legal perspective.

Finally, these explanations on the scope of the right to health would not be complete without reiterating the major role played by NGOs and civil society in general. Well-targeted pressure exerted by NGOs at the right moment often succeeds in changing minds more quickly, and therefore more effectively, than resorting to often lengthy, costly and, unfortunately, uncertain legal proceedings. For example, an NGO wishing to criticise the lack of a needle exchange programme in a particular country can exert considerable pressure on a State by referring to the report of the General Rapporteur on Health and making judicious use of its media contacts.

To summarise, although the right to health (like other rights) is not absolute in international law and although there is no absolutely binding mechanism for its implementation, the fact remains that its international recognition has had – and continues to have – a major practical impact on States, populations and individuals.

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5 Of fundamental importance is the report of 6 August 2010, A/65/255, which deals with the right to health of dependant persons.

6 See the overview of the European Court of Human Rights judgments which, through Articles 2, 3, 8 or 10, have contributed to the implementation of the right to health: Factsheet on health, July 2017, available at www.echr.coe.int/Documents/FS_Health_ENG.pdf and Factsheet on prisoners' health-related rights, July 2017, available at www.echr.coe.int/Documents/FS_Prisoners_health_ENG.pdf.

7 Wenner v. Germany, 1 September 2016.

1.4 The prescription of opioids in the treatment of dependence syndrome: milestones

It is impossible to separate the specific features of the various regulatory frameworks governing the prescription of opioids from historical, geopolitical or, indeed, socio-anthropological factors linked to the use of opioid substances. The following section recalls a number of frequently mentioned areas of tension, from the widespread use of morphine for medical purposes in the middle of the 19th century to the AIDS (acquired immunodeficiency syndrome) crisis in the 1980s and its subsequent impact for the development of the OATs we know today.

The 19th century saw the establishment of several scientific disciplines (modern psychiatry, psychology, ethnology, sociology, etc.) that accompanied numerous medical advances (discovery of morphine by Sertürner in 1803, invention of the hollow needle by Pravaz in 1841, invention of the hypodermic syringe by Rynd in 1844, invention of the Lüer syringe in the 1860s, and the injection of morphine by Wood in 1853). The creation of these disciplines enabled these discoveries to be recognised and embraced (Cohen & Lloyd, 2014; Foucault, 2014).

In the second part of the 19th century, the violent conflicts involving the use of new weapons (e.g., the war of secession in the United States, the Battle of Solferino, the Crimean War, the Franco-Prussian War, the Greco-Turkish War, etc.) left behind tens of thousands of seriously wounded people who were treated with morphine (Courtwright, 2001). It is therefore understandable that it was sometimes difficult to cease the use of morphine once it had begun, and the concepts of “army disease” and “morphinism” were born. In 1871, the British doctor Francis E. Anstie proposed the long-term prescription of opioids to individuals suffering from morphine dependence syndrome (Berridge and Edwards, 1987). This procedure became the standard in the treatment of “chronic morphinism” (Erlenmeyer, 1883).

In the United States, opioid dependence syndrome is becoming widespread both in marginalised groups and in the middle classes. Numerous drugs containing opioid-based preparations have been popularised as “miracle drugs”, in the absence of any regulatory framework. Alongside various abstinence-based programmes, a large number of clinics were opened and offered treatments very close to the OATs currently employed (Terry and Pellens, 1970). These establishments were subsequently prohibited in the United States by a Federal Government decision dating from 1923 (interpretation of the Harrison Act) (Musto, 1987) because dependence syndrome was not clearly recognised as a disease at that time (Berridge, 2004). There then followed a period of repression during which thousands of health professionals were arrested. In order to relieve the prisons of substance-dependent inmates, institutions which were a combination of prison, hospital and research centre were set up under unclear ethical conditions in the 1930s, such as the well-documented Narcotic Farm in Lexington (Kentucky) in 1935 (Musto, 1987).

The United Kingdom chose a different path. In 1926, under a ministerial remit, the doctor Sir Humphry Rolleston submitted a report by the committee he chaired on the subject of prescribing heroin and morphine in opioid dependence syndrome. The report concluded that their properly supervised long-term prescription was medically appropriate. This prescription practice, which survived until the turn of the 1980s, is accordingly referred to as the “British model” (Lindesmith, 1957).

It was not until 1948 that the United States and Canada began to test the prescription of methadone as a means of managing cessation of opioid use (Lexington). Prescriptions are administered for periods ranging from several days to several weeks, but always with the aim in mind of bringing about the complete cessation of all opioid consumption (“maintenance to abstinence”) (Halliday, 1963; Isbell & Vogel, 1949). It was necessary to wait until 1964 for the initiative of the husband-and-wife team Vincent Dole and Marie Nyswander and the introduction of the long-term prescription of methadone in North America. The underlying concept is that of compensating for a metabolic deficit in the form of “maintenance” treatment (V. P. Dole & M. Nyswander, 1965; Dole & Nyswander, 1966, 1967; Dole, Nyswander & Kreek, 1966; Nyswander & Dole, 1967). Vincent Dole argued that the “ordinary” regulation of medicines containing controlled substances was sufficient to supervise that type of treatment but he was ignored: oversight was entrusted to the law-enforcement services of the all-powerful Drug Enforcement Administration (DEA), a federal agency under

the direction of the Department of Justice, whereas the care of people in treatment was limited to a small number of specialised centres. With some minor variations, this model of the tight control of the prescription of agonists in the treatment of opioid dependence syndrome has been adopted throughout the world, where this type of prescription is not purely and simply prohibited.[8]

In the 1980s, the widespread prevalence of AIDS among people who inject heroin led to these prescriptions being reconsidered as part of new "risk and harm reduction policies", thereby launching the concept of "substitution-based therapy", a hybrid solution consisting of both treatment and making available "substitution products", to adopt the widespread terminology of the 1990s (OFSP, 2013). Several "distribution" experiments took place under basic health conditions that were sometimes hit or miss and were far from the medical model proposed by Dole and Nyswander.[9] These particular arrangements no doubt involuntarily helped to strengthen the development of an ad hoc set of regulations aimed at supervising these initiatives, in settings that very often fell far short of the procedures for ordinary supervision under the aegis of the medicines authorities.[10]

In spite of the limitations inherent in non-mainstream conditions of implementation, a considerable body of research has resulted from the development of OATs under the public-health approach, with the result that methadone and buprenorphine used in the OAT indication were added to the WHO's Model Lists of Essential Medicines, in 2005. Other opioids have been developed for the indication and are the subject of extensive work, especially LAAM, slow-release morphine, the buprenorphine/naloxone combination and, finally, the prescription of intravenous diacetylmorphine. In the following section, the essential insights gained into opioids and their effects, in the indication of OAT, are summarised. The effects specific to morphine are detailed in Appendix 2 of the report.

1.5 The paradox of the harmlessness of opioid medications

1.5.1 Opioid pharmacology

Importance of buprenorphine and methadone for the practice of dependence treatment

Fully understanding the clinical and public health effects of OAT requires some knowledge of opioid pharmacology. All opioids have analgesic and pro-addictive properties, yet what is less well known is that they also have anti-addictive properties. The role of these three properties varies depending on the effects of each opioid, the methods of opioid administration and the environmental and personal circumstances when the medication is taken.

Because the medications methadone and buprenorphine are members of the class of opioids in which heroin is also included, this has led to the misunderstanding that such medications when used for the treatment of opioid dependence syndrome are substitutes for non-medically-used opioid compounds such as heroin. This has contributed to the widespread belief among treatment providers, persons in treatment and society at large that these medications were not treatment for opioid dependence syndrome, but just a way of overcoming the illegality of opioid access and managing its main acute adverse effect of interrupting opioids acutely: the withdrawal syndrome.

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8 In Switzerland, for example, this model was introduced into the Federal Law on Controlled Substances in autumn 1974, by providing for the cantons to submit to special authorisation the prescription, dispensation and administration of narcotics intended for the treatment of dependant persons. The Swiss parliamentary archives state that this provision was unanimously accepted by the commissioners on the proposal of a Geneva deputy "concerning the ease with which certain narcotics issued to sick people on prescription" pointing to several "typical examples of abuse" and arguing that the planned provision would introduce "an extremely useful measure to combat these abuses".

9 On this subject, Vincent Dole stated in 1989: "The difficulty was not that methadone expanded, or that it did so rapidly, but that it expanded faster than medical competence developed. Across the country people who had very little understanding of the pharmacology of methadone, and no comprehension of the wider array of medical and social problems presented by addicts, jumped into the field, feeling that all they had to do was hand out the drug", Dole, V.P. (1989). Interview, in D. Courtwright, H. Joseph and J. H. Des Jarlais, Addicts Who Survived (pp. 331-343). Knoxville, TN: The University of Tennessee Press.

10 In 1992, the Institute of Medicine (IOM) undertook a review of the federal regulation of methadone and LAAM in the treatment of dependence. Their report, issued in 1995, concluded (among other things) that the current regulation by multiple agencies: (1) overemphasises the dangers of methadone diversion; (2) burdens programmes with unnecessary paperwork; (3) constrains clinical judgment; (4) reduces access to treatment; and (5) contributes to premature discontinuation of treatment. The IOM recommended that the current detailed regulations be replaced by practice guidelines and sharply reduced regulations (Rettig and Yarmolinsky, 1995).

This strong belief has contributed to the promotion of prescribing methadone and buprenorphine at minimal dosage and for short periods only. The treatment was conceived as temporary, in anticipation of the cessation of opioid use as such, including those prescribed.

Indeed, the dependence syndrome is not just a matter of using opioids, it is loss of control of the use of a reinforcing compound, i.e. a compound that gives a strong pleasant experience. Short-acting opioids are much more reinforcing than long-acting opioids, because of the rapid onset of the pleasurable effects of the former after being administered. Although methadone and buprenorphine are opioid agonists, their specific pharmacology induces a low-level reinforcing effect that stabilises the physiological processes which are disrupted by the use of rapid and short-acting, reinforcing opioids, such as injected heroin. The use of long-acting opioid medications like methadone and buprenorphine also protects against risks associated with opioid dependence syndrome while facilitating recovery.

What are opioids?

The word 'opioid' has several related and overlapping meanings: there is a botanical, a pharmacological and a chemical sense of the word semi-synthetic opioids (WHO, 2011).

First, in the botanical sense, it includes all natural plant alkaloids obtained from the opium poppy (*Papaver* somniferum L.). These exist in a wide variety: morphine and codeine are mainly used as analgesics, noscapine is an antitussive agent without psychoactive activity, and thebaine and oripavine are only used as starting materials for the production of semi-synthetic opioids.

Second, in the pharmacological sense, it refers to any compound, regardless of its structure, which has the functional and pharmacological properties of binding and activating to an opioid receptor (otherwise termed an agonist to the opioid receptor). They can be semi-synthetic (i.e. a chemically modified natural opioid alkaloid such as heroin, oxycodone or buprenorphine) or fully synthetic (e.g. methadone, which also has no structural relationship to natural opioid alkaloids).

Finally, in the chemical sense, it refers to any natural, synthetic or semi-synthetic compound with a similar chemical structure as natural opioids. These may fully activate the opioid receptor (agonist activity such as heroin and oxycodone), partially activate the opioid receptor (partial agonist or "mixed agonist/antagonist" such as buprenorphine), but may also only bind to the receptor without activating it (antagonist activity such as naloxone and naltrexone).

Endorphins are endogenous opioids, produced by the body. They are found in animals and humans and act on receptors present in the nervous system. These receptors are widely distributed in the nervous system (central and peripheral) and are associated with reward stimuli. They play a central role in establishing habits and responses for survival and pain relief. Three different types of opioid receptors are identified in the body, which are called the mu, kappa, and delta opioid receptor. Most opioids act on all three, but different opioids have a different affinity to each of the receptors.

As such, the opioid endogenous system plays an important role in opioid dependence syndrome, and has also been implicated in the biology of alcohol and cocaine dependence syndromes (Torrens, Fonseca, Galindo & Farre, 2015) as well as as behavioral disorders such as excessive gambling or eating disorders. From this perspective, it makes sense that the opioid endogenous system be the target of pharmacotherapy.

How do opioids exert their activity?

Opioids (in the pharmacological sense) can be classified into full agonists, partial agonists, and antagonists. An agonist is a substance that, when binding to the opioid receptor, activates it and causes a biochemical or cellular response. An antagonist is the opposite of an agonist in the sense that it binds to the receptors, but does not activate them. Once the buprenorphine molecules are bound to the receptors, they block the binding places for the molecules of agonists.

A partial agonist activates the receptor, but does not cause as much effect as a full agonist, and has a ceiling of maximum effect lower than the maximum effect of an agonist.

Examples of opioids

The two main opioid agonist medicines that are most widely available and used in many countries are methadone and buprenorphine. In some countries, buprenorphine is used in combination with naloxon, an opioid antagonist. Other opioids used in OAT are morphine and heroin. In the past the very long acting levoacetylmethadone (LAAM) was also used, but this medicine is no longer commercially available. It was withdrawn because of cardiac side effects. However, it has a therapeutic potential because of its very long duration of action. It may be taken on an every-other-day schedule. New studies assessing its risk benefit ratio would be of interest.

Morphine

Morphine is prescribed primarily as a high-potency analgesic. It is the prototype for opioid agonist actions at the mu-opioid receptor. The typical effects of mu-opioid activation are described in appendix 2.

Diacetylmorphine (heroin)

Diacetylmorphine is synthesised from morphine by acetylation. At the end of the 19th century, it was marketed with the brand name Heroin, which is still often used. It is twice more active than morphine at equivalent doses due to its higher lipophilic properties. As a consequence, it has a very strong euphoric effect making its dependence-producing potential very high. This was not known when initially introduced in human medicine. Heroin itself has no intrinsic opioid activity; it is a prodrug and in humans, it is metabolised to active opioid compounds: 6-monoacetylmorphine (6-MAM) and morphine. The effects of heroin are the same as other mu-opioid agonists. Heroin has an average half-life in blood of 3 min after intravenous administration; the half-life of 6-monoacetylmorphine in humans appears to be 3–10 min. This rapid onset of euphoria and its short duration potentiates the dependence-producing potential of heroin.

Methadone

Methadone is a semisynthetic opioid agonist that is used in the chronic treatment of pain and in opioid dependence syndrome to manage craving and withdrawal. It has a low euphoric effect making it suitable as a medication for opioid dependence syndrome. Methadone is an agonist at mu-, delta-, and, to a lesser extent, kappa-opioid receptors. Methadone also displays N-methyl-D-aspartate (NMDA) receptor antagonist properties that makes it useful for morphine induced hyperalgesia.

Methadone is usually administered as a racemate: a 50:50 mixture of (R)- and (S)-methadone. (R)-methadone has a higher affinity for opioid receptors and an increased analgesic potency than the (S)-enantiomer. Although (R)-methadone is believed to account for most, if not all, of the therapeutic effects of methadone maintenance treatment, the racemate, called (R,S)-methadone, is normally used in treatment due to its lower production costs.

There are two important adverse events related to methadone: the risk of respiratory depression and the risk of cardiac rhythm disorders related to QT interval prolongation attributed to the S-isomer.

Methadone is rapidly absorbed after an oral dose, it can be detected in the blood at 15–45 min after oral administration, and peak plasma concentrations occur at 2–4 h after dosing. It has a half-life of 15 – 60 hours. The oral bioavailability of methadone was found to be around 70–80 %. Methadone binds highly to plasma proteins, including albumin, lipoproteins, and mainly to alpha-1-glycoprotein. Methadone is extensively metabolised in the body. All this contributes to methadone having many pharmacological interactions with many medications.

Buprenorphine

Buprenorphine is a semisynthetic opioid. It is primarily active at the mu-opioid receptor as a partial agonist and as a kappa antagonist with a ceiling effect. Buprenorphine alone or in combination with naloxone is available in many countries for the treatment of opioid dependence syndrome to manage craving and withdrawal. norbuprenorphine is a major metabolite of buprenorphine in humans, with activity at the mu-opioid receptor.

Initially developed as an analgesic, buprenorphine has shown to be equally effective as morphine for pain management. It is 25–50 times more potent than morphine (i.e., for an equally strong effect, for buprenorphine a 25 – 50 times lower dosage is needed than for morphine). Buprenorphine has a high affinity but a low intrinsic activity at mu receptors and displaces full opioid agonists from the receptors. For this reason, and because of buprenorphine's higher affinity for the mu receptor, full agonists like heroin cannot displace it and therefore will not bind to the receptors already occupied by buprenorphine. This will be protective if the full mu-acting opioid has strong euphoric effects. The user will not feel the effect of, for instance, heroin, and this will protect him from craving and relapse.

In the event that buprenorphine is administered after use of full agonists (e.g., heroin, morphine or methadone), buprenorphine will displace the full agonist from the receptors and take its place, but with a reduced activation of the receptor. This will be experienced by the user as acutely precipitated withdrawal syndrome.

Owing to its ceiling effect, increasing doses in humans beyond 32 mg sublingually has no greater opioid agonist effect. Two important properties of buprenorphine are relevant: its apparent lower severity of withdrawal signs and symptoms on cessation, compared with heroin, morphine or methadone, and its reduced potential to produce a lethal intoxication when used alone in opioid-naive or intolerant persons because of its partial agonist properties.

Buprenorphine has poor gastrointestinal bioavailability and fair sublingual bioavailability. Blood plasma concentrations peak within 1–2 h after oral or sublingual administration. Buprenorphine has a long duration of action (24–48 h) when administered on a chronic basis, not because of its pharmacokinetic profile but because of its very slow dissociation from mu-opioid receptors.

Possible interactions with other medications like antiretrovirals are less than with methadone.

1.5.2 Clinical effectiveness in treating opioid dependence syndrome

The two main opioid agonist medicines that are most widely available and used in many countries are methadone and buprenorphine.

Many studies have, so far, proven the clinical effectiveness of these two medications. Types of outcomes measures are not identical across studies. Primary outcomes are mainly treatment retention and use of opioids measured by urine drug screen or self-reported use and secondary outcomes include a number of variables such as physical health, psychological health, employment, adverse effects.

In the Drug Abuse Treatment Outcomes Studies (DATOS), persons in treatment in the outpatient methadone treatment group showed a drop in heroin use from 91% in preadmission to 31% at 5-year follow-up and a 10% increase in full-time employment at 5 years (Hubbard, Craddock, & Anderson, 2003). In the Australian Treatment Outcome Study (ATOS), persons in treatment receiving either methadone or buprenorphine showed a drop of past-month heroin use, at 3-year follow-up, from 99% to 34% (Teesson et al., 2008). A systematic Cochrane review demonstrated that methadone maintenance therapy, compared with either placebo maintenance or other non-pharmacological therapy, appeared statistically significantly more effective in retaining persons in treatment and in the suppression of heroin use as measured by self-report and urine/hair analysis (Mattick, Breen, Kimber, & Davoli, 2009).

Many countries have both methadone and buprenorphine registered for the medications of opioid dependence syndrome. Clinicians have to choose which one to use according to different parameters. It was highlighted that the efficacy of methadone maintenance is perceived as superior to that of buprenorphine, probably because methadone has been used for a longer period of time and thus has a large body of research supporting its effectiveness and because of the pharmacological properties of methadone, being a full-opioid agonist. Authors also reported a document by Verster and Buning (2005) stating that this perception of methadone's superior efficacy "has not been universally accepted primarily because of factors such as suboptimal buprenorphine dosing, slow induction protocols, and incongruities in study designs that may be biased in the interpretation of study results" (Maremmani & Gerra, 2010).

A double-blind randomised trial comparing methadone and buprenorphine showed similar results concerning positive opioid urine tests but a higher retention rate for methadone which can be due, according to the authors, to inadequate induction doses with buprenorphine (Petitjean et al., 2001).

In a meta-analysis, high doses of methadone (higher than 50mg/d) were more effective than low doses in the reduction of non-medical opioid use and significantly more effective than low doses of buprenorphine, but similar to high doses of buprenorphine (superior to 8 mg/day) for both parameters (Farré, Mas, Torrens, Moreno, & Camí, 2002).

A Cochrane review showed that buprenorphine retained participants better than placebo at any dose higher than 2 mg but only high-dose buprenorphine (≥ 16 mg) was more effective than a placebo in suppressing non-medical opioid use measured by urinalysis. Authors concluded that if fixed medium or high doses of buprenorphine are used, buprenorphine and methadone appear no different in treatment retention and in suppression of non-medical opioid use (Mattick, Breen, Kimber, & Davoli, 2014).

Since buprenorphine non-medical use occurs, the buprenorphine/naloxone (bup/nal) formulation is used in some countries to mitigate this risk. The literature appears to indicate that in non-medical use of morphine, hydromorphone or methadone, parenteral bup/nal can precipitate withdrawal and it has less diversion liability than buprenorphine alone (Jones et al., 2015). Parenteral bup/nal did not precipitate withdrawal in bup-maintained individuals but was self-administered less frequently than buprenorphine or heroin and subjective ratings of “drug liking” and “desire to take the drug again” were lower for buprenorphine/naloxone than for buprenorphine or heroin (Comer et al., 2010).

In May 2016, the U.S. Food and Drug Administration (FDA) approved the first long-acting, subdermal buprenorphine implant for the treatment of opioid dependence syndrome. This implant is approved for persons already stable on other forms of buprenorphine and will provide a sustained release of buprenorphine for a period of six months. For persons stable on a sublingual dose of buprenorphine, the use of buprenorphine implants showed no inferiority in remaining a responder compared with continued sublingual buprenorphine (Rosenthal et al., 2016).

For opioid dependence syndrome among pregnant women, a review study found no significant differences between buprenorphine and methadone when assessing for treatment retention, reduced substance use, child health status and neonatal mortality, although authors insisted on the need of further studies with adequate sample size (Minozzi, Amato, Bellisario, Ferri, & Davoli, 2013). A systematic review and meta-analysis showed lower risk of preterm birth, greater birth weight and larger head circumference with buprenorphine treatment during pregnancy compared with methadone treatment, and no greater harms (Zedler et al., 2016).

Slow-release oral morphine (SROM) has been proposed as an alternative treatment. It showed to be a clinically useful alternative treatment in subjects not tolerating methadone or with inadequate withdrawal suppression (Kastelic, Dubajic, & Strbad, 2008). In a randomised cross-over, non-inferiority study versus methadone, SROM appears to be at least as effective as methadone in treating persons previously treated with methadone (Beck et al., 2014).

For a sup-group of persons with heroin dependence syndrome, for whom the abovementioned OAT options have not been successful, it has been shown that an OAT prescription of pharmaceutical heroin, administered intravenously, reduced cravings and the use of heroin in non-medical settings, in comparison with the prescription of methadone (Blanken, Hendriks, Koeter, van Ree, & van den Brink, 2012; Ferri, Davoli & Perucci, 2005; Ferri, Davoli & Perucci, 2011; Nielsen et al., 2016). The Swiss programme of prescribing pharmaceutical heroin is the most successful experiment in this field; since the middle of the 1990s, the programme has been used in approximately 20 specialised centres in German-speaking Switzerland and Geneva. While the programme today is institutionally well-established, scientific work dedicated to it focuses primarily on the effects on public health; clinical effects, particularly on the addictive pleasant sensations, have not yet been studied.

1.5.3 Effects on public health and public safety

The overall burden associated with opioid use disorder and injecting substance use is well documented to be very high. It extends to the user environment, through family and friends, but also impacts society at large through cost. Injecting drug use has been strongly associated with HIV, accounting for 30% of HIV infections in Europe, and up to 80% of cases in some countries in Eastern Europe. Once it enters a drug-using population, HIV can spread rapidly, and new epidemics of HIV infection mediated by intravenous drug use are occurring in some East European countries and Russia. Unsafe injecting practices associated with injecting substances use have also led to a global epidemic of hepatitis C. In Europe individuals with opioid dependence syndrome have been found to have an annual mortality of 2–4% per annum, or 13 times that of their peers. This increased mortality is primarily due to lethal intoxications, violence, suicide, and smoking and alcohol-related causes. Opioid dependence syndrome per se is associated with a significant reduction in quality of life as meaningful activities become replaced by time spent intoxicated or seeking opioids. In addition to medical comorbidity associated with injecting substance use and violence, people who use opioids non-medically have high rates of psychiatric comorbidity – in particular, depression and post-traumatic stress disorder. Many illegal activities are related to non-medical opioid use and it is estimated that half or more of people who use opioids non-medically are engaged in criminal activities other than just the fact of using an controlled substance.

It has been estimated that non-medically used controlled substances and non-prescribed medications, most of which are opioids, cost the United States more than $193 billion per year (McLellan, 2017). These costs are due primarily to lost productivity by working people using substance and criminal justice costs for drug-related crimes. Despite the extraordinary costs, morbidity, and mortality associated with the non-medical use of psychoactive substances, it has been and is still at a global level, widely overlooked.

During the past 20 to 30 years, research has documented that methadone and more recently buprenorphine treatments counteract almost all of these negative effects. This is due to the fact that these treatments reduce opioid use through injection and, consequently, the spread of HIV, HCV and other infectious diseases (Gowing, 2011; MacArthur, 2012; Mattick, 2014). It also decreases mortality and criminal activity related to non-medical opioid use, even in persons that continue to use some non-medical opioids while in opioid agonist treatment. Access to methadone and buprenorphine increases access, compliance and response to other treatments such as HCV and tuberculosis treatments (Moatti, 2000; Roux, 2008, 2009).

Studies have attempted to assess the cost-effectiveness of opioid agonist treatment with methadone and buprenorphine. A diversity of models has been used and most studies focus on healthcare costs and not on societal costs more broadly, such as productivity loss or costs of drug-related crime (Chetty, 2017). Costs to individuals and impacts on family and social networks have been overlooked. Connock et al. (2007) reviewed the clinical effectiveness and cost-effectiveness from 11 economic evaluations of opioid agonist treatment (eight with methadone and two with buprenorphine). They found that both treatments were cost-effective compared to no treatment (methadone incremental cost-effectiveness ratio (ICER) £13,697/quality-adjusted life-year (QALY), buprenorphine ICER £26,429/QALY).

As part of an ongoing economic analysis of California's treatment programmes, Krebs et al. (2017) estimated the State's expenditures related to crimes committed by 31,000 persons in treatment during a median 2.3-year follow-up period. During the follow-up, the persons participated in time-unlimited opioid agonist treatment and/or 21-day detoxification programmes. Costs of each crime were assessed including victims' injuries and property, income, and other losses. Analysis indicated that the persons generated fewer crime-related costs on days when they were in treatment than on days after they left treatment. Persons who received opioid agonist treatment generated $126 per day less, on average, and persons who received detoxification generated $141 per day less, in crime-related costs when they were in treatment compared to after they left. However, over a period of 6 months, persons in opioid agonist treatment would be expected to be more often in treatment than those that initiated a 21-day detoxification programme. Based on the medical histories of the persons in treatment in the sample it was estimated that those who initiated opioid agonist treatment spent a median of 161 days of the 6 months in treatment, and those who initiated 21-day detoxification spent a median of 19 days in treatment. Because persons who initiated opioid agonist treatment spend a larger

portion of the 6 months in treatment, the time when crime-related costs were reduced, they would generate significantly lower total crime-related costs: $9,774 versus $27,324, or a saving of $17,550. Hence, the costs of opioid agonist treatment are more than offset by the reduction in crime alone. In addition, opioid agonist treatment produces savings by reducing healthcare costs and improving worker productivity, among other means. The authors suggest that their findings likely underrepresent the actual societal costs of crime and, consequently, the savings that treatment can yield. In the study total costs were driven by the number of individual interactions with the criminal justice system, for which there was data. However, many crimes do not result in arrest, and these costs were not captured. Consequently, the real savings due to treatment are much higher.

This strong positive impact of treatment is due to the fact that the frequency and quantity of non-medical opioid use are related to all the above-mentioned side effects and the global burden. Hence, partial decrease in frequency or quantity of non-medical opioid use has a positive impact on public-health and crime indicators even for those who do not achieve total abstinence from non-medical opioid use. Taking all this together, regardless of the individual benefits expected from individualised treatment, there is a very strong societal and financial benefit to making opioid agonist treatments accessible to people who use opioids non-medically that have problems related to use. From this perspective, access to treatment should be timely, easy and unconditionally long-term. Similar findings are reported for chronic medical conditions. Comparisons with blood hypertension and diabetes have been suggested (McLellan, 2000, 2012, 2014). Nevertheless, opioid agonist treatment should not be used only for its societal impact, but for the benefit of the individual's personal health. From this perspective, treatment effectiveness may need to be individually tailored to the specific medical needs of each person in treatment. This might include better understanding of what characterises dependence syndrome, and the specific long-term modulation effect of methadone and buprenorphine upon craving, in addition to psychotherapy and counselling (Auriacombe, 2017).

1.6 Main barriers to accessing opioid medication

According to WHO, 5.5 billion people live in countries with little or no access to controlled medicines, particularly opioid medications (WHO, 2009). Several studies have thereby demonstrated that these medications are used very little in the treatment of moderate to severe pain (Duthey & Scholten, 2014; Seya, Gelders, Achara, Milani & Scholten, 2011). Although methadone and buprenorphine are on the WHO model list of essential medicines, Mathers et al. (2008) point out that, in many countries, one or the other - or even both - of these substances are not available for OAT (Stone & Sander, 2016). Yet Mathers et al. (2008) believe that 16 million people worldwide inject controlled substances and many others administer them through other means. Access to opioids for OAT, and consequently access to OAMs, is therefore as restrictive as opioid access for pain management.

Above all, politicians would like to prevent the non-medical use of opioids, dependence caused by their consumption and the diversion of opioid medications, even if this is at the expense of access to substances, despite being essential to medical practice. As a result, the availability of opioid medication for medical treatments has gradually decreased worldwide (see also Chapter 1.2).

WHO responded by recommending that all policies for psychoactive substance control be based on the fundamental principle of "balance", namely a double obligation for governments to establish a monitoring system that guarantees a sufficient availability of controlled substances for medical and scientific purposes, while simultaneously preventing non-medical use, diversion and trafficking. This principle is based on the objectives mentioned in the preambles of the Single Convention on Narcotic Drugs, as amended by the 1972 Protocol (regulating in particular the use of methadone), and the International Convention on Psychotropic Substances (regulating in particular the use of buprenorphine) (WHO, 2011).

In 1989, the International Narcotics Control Board (INCB) recommended paying close attention to the overreaction of some governments with regard to the "problem of drug abuse" when "[…] the reaction of certain legislators and certain members of the judiciary, fearing the development and the spread of drug abuse, led to the enforcement of laws and regulations which could, in certain cases, create additional obstacles to the availability of opiates" (INCB, 1989). The INCB has regularly repeated its recommendation over the years, the last time being in its 2016 report (INCB, 2016).

The various parameters in the availability of controlled medications have been defined by the WHO. These definitions should help to analyse the use of opioids in different countries.

Availability: the amount of a medication present in the distribution points of a defined area and for the population living there at the time when access is needed.

Provision: the extent to which a medication can effectively be obtained by these persons, taking into account potential regulatory, social or psychological obstacles.

Financial accessibility: the extent to which a medication can be obtained by these persons, at a cost that does not put them at risk of suffering serious negative consequences (e.g., inability to meet other basic human needs) (WHO, 2011).

In other words, the medication should be found in pharmacies; it should be possible to obtain the medication in pharmacies; and the person being treated should be able to afford it. In order for the person in treatment to be able to really benefit from the medication these 3 conditions should be fulfilled (Scholten, 2013).

Other authors add two other dimensions to this concept of access to care: adequacy and acceptability (Obrist et al., 2007) or sometimes accommodation and acceptability (Penchansky & Thomas, 1981; Wyszewianski, 2002). The idea of acceptability is an important aspect, particularly for access to ODT.

The report will use the term “access” to include these different parameters.

Obstacles that can restrict access are usually organised into four categories:

- legislative or political obstacles
- obstacles in knowledge
- obstacles linked to societal attitudes
- economic obstacles

In practice, every country has obstacles limiting access to controlled medications, including opioid medications. In many countries, these obstacles are also serious enough to prevent most of those who are ill from receiving the appropriate treatment when they need it.

The findings of the ATOME project (Access to Opioid Medication in Europe), which took place between 2009 and 2014 and was financed by the EU, showed that there were obstacles in the 12 western European countries included in the study (Larjow, Papavasiliou, Payne, Scholten & Radbruch, 2016; Radbruch, Jünger, Payne & Scholten, 2014).

Firstly, the lack of knowledge is the main obstacle in most countries, as universities do not often offer or offer very little teaching on opioid medication and on the field of dependence syndrome. Subsequently, many health professionals do not know how to deal with these medications at the end of their studies (see also Chapter 4.2).

Secondly, obstacles of a legislative nature have been noticed in the 11 countries where legislation was available for assessment and ten of those showed potential obstacles specifically affecting access to OAMs for persons with an opioid dependence syndrome (Vranken et al., 2016). In most of the countries studied, the measures taken are stricter than those required by international conventions, to the detriment of those who are ill. Consequently, legal provisions sometimes restrict the possibilities of medical treatment to the extent that it is completely impossible to offer the therapeutic option that wouldbe the most prudent, scientifically.

Thirdly, negative attitudes have been observed amongst health professionals, persons in treatment and society. These attitudes are most often based on incorrect knowledge of opioid medication or the disorders associated with dependence syndrome and are also influenced by the use of inappropriate terminology by authorities, health professionals and the media. These terms may be derogatory, disrespectful towards the person affected, or even openly rude, imprecise and/or judgmental (Scholten, 2015).

Lastly, economic obstacles have been noticed in several countries examined by ATOME, often in the form of insufficient funding of health services.

The WHO recommended guidelines to eliminate obstacles to opioid access, which have been used as reference material in the preparation of these recommendations by the Pompidou Group (WHO, 2011). Several other publications are available, which review the obstacles to opioid access, the majority concerning the treatment of pain, but apply to OAMs (Cherny, Baselga, de Conno, & Radbruch, 2010; Milani & Scholten, 2011).

1.7 Issues associated with barriers to accessing opioid agonist treatment

A review of the various obstacles to opioid access identified three distinctive challenges for public policies concerning OAT.

1.7.1 Quality and training

Defining quality of care

With regard to the extent of the obstacles to accessing healthcare, the quality of treatments is usually a secondary issue. However, it is easily argued that quality is closely linked to access through the common denominator of training. Clearly established quality of care standards are an important aspect in allocating resources and defining expectations in education and training. According to WHO, quality of care can be defined as: an approach guaranteeing that every person cared for receives a combination of diagnostic and therapeutic procedures that will ensure the best result in terms of health, in line with the current state of medical science, at the best cost for the same result, with the least iatrogenic risk and the best level of satisfaction in terms of procedures, results and human contact within the healthcare system.[11]

Quality of care refers to several levels of judgment: the quality of contact between professionals and the person being cared for, the quality of diagnoses and treatments, the quality of the process in a healthcare facility and decisions to invest in the organisation of care. One of the main objectives of the approach to disorders associated with the consumption of substances remains the increased ability to reach those who need to be taken care of the most by expanding the coverage of services. Quality also means using the most recent empirical knowledge, reducing discrimination and negative attitudes, and, more generally, respecting fundamental rights and professional codes.

Diverse clinical guidelines

Various works (Haasen et al., 2004; McLellan, Carise & Kleber, 2003) have shown numerous shortfalls in the quality of treatment, particularly with regard to the low professional status of healthcare providers. A review of 26 national clinical guidelines (Uchtenhagen et al., 2005) concerning OAT brings to light several inappropriate guidelines. A total of 22 out of 26 national guidelines studied included eligibility criteria for treatment, for example, a minimum duration of three years living with dependence syndrome before beginning treatment, a minimum age (25 years in some countries) and previous failures in treatments to bring about a cessation of consumption. Nine national guidelines mentioned various contraindications, for example, pending imprisonment, an alcohol problem and living with dependence for just a short period. At least eight out of 26 sets of guidelines gave incorrect instructions for dosage; only one set mentioned that knowledge of the pharmacokinetics of methadone presupposed personalised dosages. Several sets of guidelines also established criteria for ending treatment; particularly, two sets of guidelines advocate ending treatment in the event of a positive urine test.

11 Quality of care (definition in French): http://www.santepublique.eu/qualite-des-soins-definition/ (visited on 03.08.2016).

Among the 26 national guidelines, not one single area has been identified as having uniform recommendations There are some differences that particularly standout, in addition to the examples already mentioned, with regard to settings (private/public), the type and content of information for medical staff and persons in treatment, transport rules, supervision measures, funding of care, conditions for infrastructure, and quality assurance.

Developing international standards

The EQUS study (Study on the Development of an EU Framework for Minimum Quality Standards and Benchmarks in Drug Demand Reduction) analysed various guidelines from EU member states; it highlighted a lack of legal, ethical, economic and care coverage standards, a lack of empirical data for the proposed standards in the different countries and also a major deficit in monitoring for structural and outcome indicators (Uchtenhagen & Schaub, 2011).

This EQUS study concluded by stating the need to continue efforts in developing international standards, both to perfect the situation in countries with the highest standards and to highlight the needs not covered in some national contexts. The EQUS study also highlighted the importance of standards for the exchange of knowledge and the development of training methods for new practitioners in the domain.

The EU has renewed its efforts in this area (European Union, 2015). At the same time, the WHO and UNODC have made available for public consultation a report containing proposed international treatment standards (UNODC & WHO, 2016). With regard to OAT, these standards use the main themes from the WHO international guidelines published in 2009. Lastly, several countries have developed specific quality assurance systems in the field of dependence, such as the Swiss regulation QuaThéDA (Quality, Therapy, Drug, Alcohol) (FOPH, 2012).

The importance of training professionals "involved on a timely and occasional basis"

The efficiency and effectiveness of services depend on the availability of skilled staff. In turn, their competence depends on knowledge and solid basic skills, in addition to know-how and interpersonal skills acquired through on-the-job mentoring, all of which result in the quality of the relationship between health professional and the person in treatment. With regard to disorders associated with dependence-producing behaviour, professionals must also be able to address ambivalence without being judgmental, to maintain self-efficacy and to direct persons in treatment to different professional help options and self-help (Miller & Rose, 2013; Feldstein, Apodoca, Gaume, 2016; Daeppen, 2016).

A very large group of people is affected by dependence syndrome. Most people with opioid dependence syndrome come into contact, often before anyone else, with professionals involved on a timely and occasional basis: social services, emergency medical services, primary care physicians and professionals only periodically involved such as paramedics, various technical professionals, staff from judicial or civil administrations and security personnel.

In Europe, a general shortfall in professionals' knowledge has been identified. Dependence is rarely incorporated into basic and ongoing training in these different sectors (Pompidou Group, 2014).

Most often, there is little or no coordination between the training opportunities for the different sectors; if there is coordination, it is often organised by NGOs (Uchtenhagen, Stamm, Huber & Vuille, 2008). Similar shortcomings have been reported in the United States (cf. Pompidou reference document p.11 or more recent).

In 2011, the Pompidou Group established a working group, following a call by the Mediterranean network for co-operation on drugs and addictions (MedNET), with the task of developing a reference framework for education and training in policies and practices relevant to the field of dependence syndrome. Eleven recommendations were made.

- The objective of training and education in substance use disorders should be taken on board by international organisations such as UNODC, WHO and the EU. Education and training on substance use disorders should be embedded into a national Drug Policy. Education and training on substance use disorders should also be embedded into a national education system through national action plans developed either by the education, health or research departments.
- Education and training on substance use disorders should be based on national needs and also on changes occurring at international level.
- Education and training on substance use disorders should be updated regularly to include the new elements that come to the fore.
- Education and training should be evidence based and therefore the curricula should evolve accordingly.
- Education and training on substance use disorders should be adapted to national priorities.
- Education and training on substance use disorders needs to be evaluated.
- Education and training on substance use disorders requires proper funding and qualified human resources.
- Education and training on substance use disorders needs to be adapted according to the different requirements of respective target audiences.
- Education and training on substance use disorders needs to take into account the complexity of the substance phenomenon and provide for multi-disciplinarity.

The need to train physicians and pharmacists

The literature review by Ayu et al. identifies a lack of training in medicine relating to substance use disorders at undergraduate level, where substance disorder is generally under-represented compared to other chronic diseases such as diabetes. At post-graduate level, it is generally not taught or covered very briefly in specialisations other than psychiatry. O'Brien and Cullen showed that despite the increase in the prevalence of disorders associated with substance use, the number of hours allocated to teaching on substance use disordershas not increased in Ireland. In addition to enhancing the ability to screen for disorders associated with substance use, training raises students' awareness of the burden of dependence and strengthens their skills in communicating with people who use substances. In this respect, Kothari et al. (2011) stress the development of knowledge and skills acquired in short-term training programmes. Ayu, Schellekens, Iskandar, Pinxten, and De Jong (2015) note that the benefits linked to basic training on opioid use disorders are felt at all levels of teaching.

The rationale behind teaching substance use disorders rests on the fact that all physicians should have the basic skills to identify, refer or treat people who use controlled substances, in the light of the high prevalence of disorders associated with substance use and the high number of cases of psychological comorbidities associated with use (Ayu et al., 2015). The basic training of pharmacists should also include training in dependence, because they see the persons in treatment the most often and are often the first point of contact when there is a problem (Arnaud, Dubois-Arber & Gervasoni, 2011).

The lack of training leads to a well-known problem of under-diagnosis. Physicians and pharmacists are often incapable of correctly identifying users, which leads to the latter not being treated or receiving inadequate care.

In addition to university training, several studies have shown that the fact of physicians and pharmacists having a negative perception of people who use substances − caused, for example, by the link between consumption and criminal activity − perpetuates a reluctance to properly treat these persons in treatment (Goodair & Crome, 2014; Muscat, Stamm & Uchtenhagen, 2014; Rao et al., 2016; Rasyidi, Wilkins & Danovitch, 2012). According to O'Brien and Cullen (2011), students are sceptical of the effectiveness of treatments and medical interventions related to dependence syndrome. The analysis of scientific literature highlights the link between this stigmatisation and scepticism and a lack of qualifications in the field.

Structure and content of teaching dependence-producing behaviour in medicine

Recurring characteristics of the teaching of dependence-producing behaviour in medicine include its fragmentation, diverse content and lack of coordination between the different branches involved (Ayu et al., 2015; Ritter, 2014). In addition, teaching often focuses on specific substances rather than an interdisciplinary approach towards dependence-producing behaviours (Broers, 2016; Ritter & Bischoff, 2014). Furthermore, the shortage of healthcare facilities for this type of disorder reduces the opportunities for students to practise, without which they are not adequately trained (O'Connor, Nyquist & McLellan, 2011; Rasyidi et al., 2012). Lastly, various authors, including Ayu et al. (2015), report difficulties in implementing a programme after the curriculum has been produced, for example, due to a lack of time in students' timetables.

There is a consensus on which basic skills every physician should have in the field of dependence-producing behaviour. The basic skills are screening, brief intervention (for example, during a conversation) and referral to treatment (SBRIT). Ritter and Bischoff (2014) complement this list with professional objectives such as the ability to diagnose, manage and monitor a treatment, along with the knowledge of psychological and physical comorbidities associated with substance use. In addition to these professional objectives, there is a personal objective for a future physician to identify substance use and a societal objective to prevent all stigmatisation of people who use psychoactive substances. Another important aspect is the interdisciplinary nature necessary in teaching.

According to the American Society of Health System Pharmacists, basic training must include specific and comprehensive knowledge on the safe and effective use of medications and their negative side effects if used inappropriately. Teaching must pass on the skills to enable pharmacists to judge the suitability of pharmacotherapy and to advise and monitor the effects of the medication, while taking on a role to prevent, educate and assist.

Ayu et al. (2015) suggest that the field of dependence-producing behaviour should be prioritised in the same way as other chronic diseases in curricula. Those responsible for teaching should also improve their competence in the field in order to provide quality teaching based on the most recent scientific knowledge. To increase students' interest and offer them career prospects, specialised study programmes should be established. Special attention should be given to primary healthcare, since this is generally the first point of contact between a person suffering from a dependence syndrome and a healthcare professional. For Ayu et al. (2015), one problem that has not been resolved is knowing how to adapt a curriculum on the medicine of dependence-producing behaviour to different fields, taking into account the local context and the training needs of different sub-groups of professionals involved to varying degrees.

1.7.2 Non-medical uses and diversion of prescribed opioids

Definition and distribution

Non-medical use by persons in treatment prescribed opioid medication for their treatment includes practices that respond to very different needs: self-medication (from relevant to non-relevant, to treat different physical, emotional or mental health problems) or occasional recreational use. Literature similarly distinguishes between "non-medical use", whereby "state of the art" dosage and delivery methods are not complied with and "diversion", which involves the illegal resale of medication on the black market. Diversion and non-medical use occur in all health and medication prescription systems, yet, in the context of OAT, it represents a unique issue, because restricted access to treatment increases the value of this medication on the black market (Becker, Murphy & Grossman, 2004; Johnson & Richert, 2015b; Wakeman & Rich, 2017).

The extent of diversion and non-medical use is difficult to estimate and the literature reflects this in the lack of reliable monitoring data relating to these two phenomena. Some research has tried to establish a number of prevalence rates of non-medical use (from 18 to 81% of people receiving treatment) along with a diversion rate (less than 10% of people receiving treatment) (Alho, 2015; Johnson & Richert, 2015a; Launonen, Alho, Kotovirta, Wallace & Simojoki, 2015). However, in the absence of structured monitoring and using a clearly defined logical framework, the results are difficult to interpret because they greatly depend on the national regulatory context (Alho, 2015).

The risks to the population and to individuals associated with the non-medical use of prescribed opioids and their diversion differ. With regard to individuals, these two phenomena tend to increase mortality from accidental acute intoxication and the risk of transmitting infectious diseases, along with other negative effects linked to administration by injection (Alho, 2015). With regard to the population, non-medical use and diversion, in particular, may convey a negative image of OAT and those who prescribe them, which can consequently harm the public image of these services (Alho, 2015).

Strategies to reduce diversion and non-medical use

While non-medical use and diversion cannot be completely avoided, a number of measures may help limit their impact.

Trained staff available to ensure prescriptions at the appropriate dose

According to the literature, approximately 70% of non-medical use could be for self-medication (Alho, 2015). Above all, this figure indicates that access to OAT must be ensured for those who need it. Measures that restrict access to treatment incite those in need to turn towards diverted medication and illegal markets. Several studies have shown that inability to access OAT significantly fuels diversion (Alho, 2015). Access to quality healthcare and to an appropriate dosage dispensed by trained staff eliminates one of the causes of non-medical use and diversion (Alho, 2015).

Covering treatment costs

As explained in Chapter 1.6, accessibility also includes the financial aspect of treatment. The cost of treatment must be economically affordable for the person in treatment, in order for a person suffering from opioid dependence syndrome to give up the risks and disadvantages linked to self-medication and to stop obtaining supplies from the black market. In addition, the studies show that with regard to controlled substances, the harsher the (monetary) restrictions, the more the black market thrives. Economic research suggests that due to the difficulty in obtaining opioid medication, the demand on the black market increases nearly proportionally to the restrictions imposed on legal access (Becker et al., 2004; Crane & Rivolo, 1997; Miron, 2003).

Measure to prevent double prescriptions

The literature shows that a certain amount of the diversion of opioid medication is carried out through “doctor shopping”, in other words when a person seeks help from several physicians at the same time to obtain two or more prescriptions (Reimer et al., 2016). The problem can be eliminated if the prescriber uses a counterfoil book, as this would produce a shared list of names and the opioid medications prescribed.

Taking medication under supervised medical supervision

Combating diversion can be aided through a system of supervised medication administration, including a minimum number of times the treatment must be taken under supervision. However, it must be taken into account that too much monitoring is counterproductive as it dissuades those needing treatment from asking for it and discourages persons already in treatment from continuing. It can damage the quality of the relationship between the person in treatment and the healthcare professional. Lastly, supervision is rarely very effective (Mjåland, 2015). It is therefore necessary to find the right balance so that anti-diversion measures do not create obstacles to accessing healthcare that then increases the risk of diversion.

Ensuring medical confidentiality

Under certain rules, medical confidentiality may be breached, for example when personal information is made available to the judicial authorities. This risk dissuades those needing OAT from seeking assistance and pushes them towards self-medication via the black market. Ensuring confidentiality increases the number of people receiving treatment and significantly reduces the requests for medication outside the medical setting.

Summary of issues linked to non-medical use and diversion

To summarise, although there are real harms linked to non-medical use and diversion and an effort must be made to reduce these problems, the competing risks should be weighed up between the principle of beneficence and the principle of nonmaleficence. Although there is a lack of usable specific data, a healthcare measure that includes low diversion rates and low non-medical use rates can be considered as a balance between the two principles and less harmful than a restrictive context that fuels the black market and its associated risks (stigma, crime, degradation of the substance making it more harmful) (Harris & Rhodes, 2013; Richert & Johnson, 2015; Wright et al., 2016). Non-medical use and diversion therefore need, above all, a public health approach based on an optimum reduction in the number of problems. In relation to this, they should be an integral part of the monitoring system, as will be further discussed in Chapter 5.1

1.7.3 Register of those receiving treatment and data protection

One of the main consequences of current prior authorisation rules is that registers are produced, leading to issues with regard to data protection and the negative effects that the possible shortcomings (real or imaginary) may cause for access to healthcare. In addition to confidentiality, the existence of these registers raises the question of their explicit aim and proportionality, when taking into consideration the alternative methods of achieving the desired objectives (see also Chapter 4.1).

According to the analysis of data submitted by the Reitox national focal points to the EMCDDA, the majority of member states and Norway (22 countries) have only one specific registry recording OAT treated persons. Six countries have two registries where OAT treated persons data is recorded, while the Netherlands has three registries where OAT treated persons data is recorded. These registries are often located in National Health Departments or Institutes or in National Medicines Agencies. Interestingly, in 11 countries, OAT treated persons data are recorded as part of the general national substance treatment monitoring registry where, for example, data on treatment demands for all individuals entering substance treatment are recorded. It can be considered that in these countries an overall database monitors substance treatment clients, including persons receiving OAT. In four countries, a certain data flow exists between the OAT registry and other substance treatment monitoring databases due to the existence of unique client identification codes which allows the merging of the databases. In seven countries, no flow of data between databases is possible due to the absence of unique identifiers.

2

Method of drafting recommendations

The identification of key themes for and the drafting of recommendations are based on several components: documentary research, the Delphi approach, public consultation and a survey completed by an Expert group in order to evaluate the combined effects of the key recommendations identified.

2.1 Sources

Three sources of information were analysed to provide material for the drafting of the guiding principles. (1) Research of scientific literature focusing on the framework conditions of the prescription of OAM by using databases that index the main scientific journals relating to addictive behaviours and public health, with additional research via the search engine "Google Scholar", in order to access non-indexed publications, in particular reports or book chapters (grey literature). (2) An online questionnaire sent to each expert in order to gather information specific to each participating country. (3) Hearings with specific experts. The survey materials for participants and the outcomes of the discussion are available upon request from the project secretariat.

Member of the group of experts participating in the hearings:

Laura Amey − *Substitution treatment for opiate dependence. Study of the regulations in some francophone countries*

Alessandro Pirona − *Establishing the minimal vs. optimal list of indicators for monitoring treatment programmes that include OAT*

Abdallah Ounnir − *Control measures for substances and the pre-eminence of the right to health*

Willem Scholten − *The Results of the ATOME Project in Relation to Opioid Agonist Treatment for Dependence*

Experts invited to the hearings:

Jean-Michel Costes, Gambling watchdog, Ministry of Finance, France – *Free thinking on Section 17, "monitoring and indicators" the guiding principles*

Rachel Gooch, Yacine Hadjiat, Mundipharma International, United Kingdom; Mundipharma France − *Sharing an Industry Perspective: Selling Medicines Within the Context of Opioid Agonist Treatment (OAT)*

Mohamed Farah, Karine Laurent, Corine Sedilot, Reckitt Benckiser Pharmaceuticals, a subsidiary of Indivior PLC, France − *Dealing with opiate dependence using buprenorphine: the French context; a pharmaceutical laboratory's point of view*

Marc Reisinger, European Opiate Addiction Treatment Association (EUROPAD), Belgium − *Access to opioid agonists: treatment or regulation?*

Ambros Uchtenhagen, Research Institute for public health and addiction, WHO Collaborating Centre at the University of Zurich, Switzerland − *Opioid Substitution Therapy for Opioid Dependence. An analysis of national guidelines*

Ahmed Youssef, Health Care in Detention Program, International Committee of the Red Cross (ICRC), Switzerland – *Prison Health, Public Health*

2.2 The Delphi method

The decision was made to use the Delphi method to arrive at the guiding principles from the considerable information collected.

2.2.1 Choice of method

The recommendations were formulated using the Delphi method, which places importance on the provision of justification for the responses given (Baillette, Fallery and Girard, 2013).

The Delphi method is a research tool that aims to anonymously gather and produce an opinion from a panel of independent experts on a given subject (in particular, see Day, 2005; Ekionea, Bernard and Plaisent, 2011; Heiko, 2012). Using a questionnaire, it structures panel discussions around an issue. The questionnaire is given to the group several times and then amended depending on the latter's assessments and comments until a consensus is reached or at least a near consensus. Equal importance is given to each of the participants' comments. This process is repeated as many times as necessary.

In addition to reaching a consensus, the importance given to the provision of justification (Kuusi, 1999) is an aspect that focuses on comments made by participants over the successive rounds, in order to identify the arguments for the preparation of the next round and for the final reasoning of the consensus reached using this method.

2.2.2 Preparatory survey

An anonymous online questionnaire was sent out twice before the first meeting of the Expert group (August 2014). It was completed a third time (with non-anonymous replies) during the first meeting in Paris on 7 and 8 September 2014.

Participants

12 experts from the working group (the full composition of which is given in the appendix) participated in this phase of the survey. The participants included a pharmacist, six physicians, four legal experts in the field of health and an administrative head of public health from the following countries: Belgium, France, Greece, Lebanon, Morocco, Switzerland and Tunisia.

Questionnaire

A questionnaire was produced after identifying eight fields of regulation linked to the implementation of OAT and 10 pre-existing recommendations in two reference documents: the report on "Psychosocially Assisted Pharmacological Treatment of Opioid Dependence" (WHO, 2009) and the report on "Ensuring balance in national policies on controlled substances: guidance for availability and accessibility of controlled medicines" (WHO, 2011) by the ATOME project (Access to Opioid Medication in Europe).

Each item was evaluated using a Likert scale to assess the extent to which the experts agreed with the content of the suggested recommendations (1 = strongly disagree; 10 = strongly agree), in addition to how important they considered the different fields of State intervention identified (1 = unimportant; 10 = very important). In addition, an empty text field for each item provided space to write comments and possible suggestions to rephrase the recommendations being examined. The online questionnaire was carried out using Sphinx software.

Procedure

The results of the preceding round were returned to the experts in a document containing a histogram for their personal responses in each field, accompanied by all the comments given, and indicated the previous response of the expert in question. A consensus was considered to have been obtained when a recommendation earned an average score above nine and/or a standard deviation smaller than one. Recommendations that received a lower score were rephrased on the basis of the comments.

2.2.3 Identifying guiding principles

The Delphi method was applied in August 2015 when a different anonymous survey was sent out in two rounds. A third, non-anonymous round took place during the meeting on 27 and 28 August 2015.

Participants

16 experts participated in the survey, including a pharmacist, six physicians, four legal experts in the field of health and four administrative heads of public health from the following countries: Algeria, Belgium, France, Greece, Lebanon, Lithuania, Morocco, Portugal, Slovenia, Switzerland, Tunisia and Turkey.

Questionnaire

Based on the outcomes of the preparatory survey and the discussions at the first meeting in September 2014, the project drafting group (cf. impressum) drafted a summary document to formulate guiding principles from existing recommendations. This document was then divided into 40 items to be used in a new survey using the Delphi method. Each item was investigated using a 10-point Likert scale to assess the extent to which experts agreed with the content of the suggested recommendations (1 = strongly disagree; 10 = strongly agree). There was an empty text field and the survey was once again carried out using Sphinx software.

Procedure

In the second and third rounds, the outcomes were returned according to the same methods as in the preparatory survey. This time, a consensus was obtained between the experts when the average was higher than 8 and the coefficient of variation (standard deviation divided by the average) lower than 0.5 (Von der Gracht, 2012). The content of the 40 items tested in this manner was amended in line with the comments of each expert, in order to obtain a version that was as close as possible to the opinion of the entire panel of experts. At the end of the second meeting of the Expert group, the drafting group organised the 40 items into five sections and 60 subsections under the document title “Guiding Principles”. They were ready to be subjected to a larger consultation procedure.

2.3 Public consultation

Between 15 March and 15 May 2016, an advanced version of the “Guiding Principles” was made public specifically for consultation. The Guiding Principles, in their draft form, were initially presented at the 77th meeting of the Permanent Correspondents of the Pompidou Group (November 2015 in Oslo) before being sent out twice, to the Expert group and to the Scientific Council of the project.

The “Guiding Principles” were published in French and English for consultation on the websites of the Pompidou Group (PG) and the Lausanne University Hospital (CHUV). Through the intermediary of the participants from the Expert group, 117 national and international organisations concerned were proactively asked, including:

- administrations
- non-governmental organisations
- professional bodies of physicians and pharmacists
- professional associations
- pharmaceutical companies producing medication registered as OAMs

Fifteen detailed responses were sent to the contact addresses:

Belgium	Ministry of Justice
	Alternatives to drug addictions (ALTO)
Morocco	Focal point of the national programme combating addiction (DMNT)
	Directory of epidemiology and Fight against Diseases, Ministry of Health
	Directory of Medication and Pharmacy of Morocco dealing with the control of narcotics
Norway	SERAF, Norwegian Centre for Addiction Research, University of Oslo
Mexico	General Directorate for Global Issues, Directorate for Drugs
	Permanent Mission of Mexico to the Council of Europe, Strasbourg
International	International Drug Policy Consortium (IDPC)
	International Centre for Ethnobotanical Education Research & Service (ICEERS)
	International doctors for healthier drug policies (IDHDP)
Slovakia	Ministry of Health of the Slovak Republic, Department of Anti-Drug Strategy, Coordination and Drug Monitoring
	Slovak Ministry of Health for the Treatment of Drug Dependencies
Switzerland	Federal Office of Public Health (FOPH)
	Professional umbrella organisation of pharmacists

All the responses received pointed out the appropriate structure and content of the document. The only requests made were for clarifications and more details on specific technical aspects. There were no requests to remove sections of the text or questions expressed on the general content chosen for establishing the guiding principles. The detailed report on these responses can be found in the appendix in the summary of the third meeting of the Expert group. Members of the public can access it via the project secretariat.

2.4 Survey of the recommendations' combined effects

In the 60 or so guiding principles that were outlined, the drafting group noticed that three of them played a prominent role and deserved to be highlighted: (1) an end to prior authorisation, (2) the removal of financial barriers to accessing care; and (3) the establishment of a national advisory body. These three have been highlighted as key recommendations, because their implementation causes the greatest impact on the other guiding principles.

In order to assess the degree of consensus relating to the expected effects of the three key recommendations, the members of the Expert group were anonymously consulted through online questionnaires in July and August 2016 before the third meeting. Each respondent was asked to consider the possible anticipated effect of each key recommendation on the guiding principles, grouped together as 20 items this time, as a categorical variable of "strongly negative", "rather negative", "no effect", "rather positive" and "strongly positive". Each question included an empty text field. Out of 13 respondents, eight left at least one comment. Approximately 60 comments were recorded, which were taken into consideration in the drafting of the reasoning presented in Chapter 4 of the report.

The outcomes confirmed a strong level of consensus in the Expert group on the interdependence of the guiding principles and the particularly significant impact of the three key recommendations on the other guiding principles. A summary of the outcomes is in the appendix. The detailed report appended to the summary of the third meeting is available to the public via the project secretariat. During the third meeting of the Expert group, a fourth key recommendation was established: the use of neutral, precise and respectful terminology throughout the guiding principles.

3

Guiding Principles for regulations relating to opioid agonist treatment

Part I: definitions and objectives of the guiding principles

Section 1: definitions

1.1 The terms used in the Guiding Principles are defined as follows:[12]

(I) **equivalence of healthcare**: the principle that persons held in detention or subject to other measures restricting freedom should have access to healthcare equivalent to that provided to the general population.

(II) **basic training for physicians and pharmacists:** university training including the entire required curriculum for general professional qualification.

(III) **indicator:** qualitative and quantitative data providing information on the conditions or the performance of a public policy or a programme.

(IV) **medication(s):** any substance or composition that can be administered to a person with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions.

(V) **agonist medicine(s) used in the treatment of opioid dependence syndrome (OAM(s)):** medicine with marketing authorisation (MA) and whose active ingredient is an opioid. In a person diagnosed as having an opioid dependence syndrome, the main effects include: causing cessation or reduction of opioid consumption, minimising the risk of lethal intoxication and regulating the person in treatment's physiological and psychological state. The main OAMs are methadone, buprenorphine, morphine and diacetylmorphine. They are generally used as part of multimodal treatment, particularly in psychosocial and somatic care. In addition to their main effects, it has been demonstrated that the provision of these medicines affects public health and safety.

(VI) **essential medicine(s):** medicine on a list established by a governmental or intergovernmental agency, defining the minimum medical needs for a basic healthcare system and listing the most effective, the safest and the best value medicines for priority health conditions. With regard to OAM, methadone and buprenorphine are on the WHO model list of essential medicines.

(VII) **controlled medicine(s):** medicine containing controlled substances according to the 1961 Single Convention on Narcotic Drugs, as amended by the 1972 Protocol, the 1971 Convention on Psychotropic Substances and the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances (1988). The controlled medicines most commonly used as OAMs are methadone and buprenorphine.

12 There is a glossary in Appendix 1, accompanied by detailed explanatory notes on the selected terms and terms to avoid.

(VIII) **opioid(s):** substance having a similar pharmacological effect to morphine.

(IX) **reduction/cessation of consumption:** a therapeutic goal to reduce consumption to a level that falls short of the criteria required for a diagnosis of dependence syndrome or use harmful to health (according to the WHO classification of diseases), without necessarily suppressing all consumption.

(X) **opioid dependence syndrome:** a set of physiological, cognitive and behavioural phenomena in accordance with the WHO international classification of diseases. The 10th edition (ICD-10) of this classification system defined dependence syndrome by the fact that three of the following manifestations have occurred together for at least one month or, if persisting for periods of less than one month, should have occurred together repeatedly within a 12-month period: (1) strong desire or sense of compulsion to take the substance, (2) impaired capacity to control substance-taking behaviour, (3) physiological withdrawal state, (4) evidence of tolerance, (5) alternative pleasures or interests gradually being given up and an increase in time being spent on consumption, (6) persistent substance use despite clear evidence of harmful consequences.

Section 2: objectives of the guiding principles

2.1 The objectives of the guiding principles are:

(I) to strengthen the fundamental right of access to care for persons diagnosed with opioid dependence syndrome;

(II) to eliminate and reduce obstacles, especially those of a regulatory nature, which limit access to healthcare and OAMs;

(III) to permit the use of OAM based on the best medical and scientific evidence;[13]

(IV) to define the role of professionals involved in the treatment of opioid dependence syndrome (particularly physicians and pharmacists);

(V) to support and encourage countries introducing OAMs to develop a legislative and administrative framework which takes into account both the following guiding principles and available resources with a view to continuous improvement (see Section 14);

(VI) to ensure the monitoring and adaptation of OAMs regulation, in particular, through structural, process and outcome indicators (see Section 17);

Section 3: primary and secondary objectives of agonist medicines (OAMs) used to treat opioid dependence syndrome

3.1 The objectives of using OAMs are first and foremost person-centred (primary objectives), namely:

(I) to improve the clinical state of persons diagnosed with opioid dependence syndrome:

- to reduce the symptoms of the disease that has been diagnosed;
- to reduce the risks associated with acute intoxication and the risk of lethal intoxication;[14]
- to regulate the emotional state and interpersonal relations;
- to maintain and support social integration (in particular at family, social and professional levels).

(II) to reduce the occurrence of somatic (especially HIV and HCV) and psychological (especially anxiety-depressive disorders and suicidal ideation) comorbidities associated with opioid dependence syndrome.

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13 For further information, please refer to the WHO guidelines (2009): http://www.who.int/substance_abuse/publications/opioid_dependence_guidelines.pdf.

14 The risks include those linked to the random presence of additives in products bought and consumed outside the medical system.

3.2 A treatment which achieves the above objectives also has a positive impact on society (secondary objectives), in terms of public health and public safety.

(I) Public health: reduction in mortality, morbidity and psychiatric and somatic comorbidities, reduction in the occurrence of injection-related transmissible diseases (among persons with dependence but also in the general population) and reduction in mortality attributable to these diseases.

(II) Public safety: reduction in the illicit trafficking of controlled substances and related crime; improvement in both the objective and subjective perception of safety in public and social spaces.

(III) Conjointly:

- reduction in healthcare costs through early treatment and regular monitoring;
- reduction in social costs by supporting an appropriate integration of persons with dependence sydrome into occupational and social spheres and through a reduction in the burden on the judicial and prison systems;
- reduction in indirect costs relating to negative consequences for those close to persons with dependence syndrome (work, school and family environment, in particular with regard to the development of the children of persons receiving treatment).

Part II: right of access to opioid agonist medicines and related healthcare

Section 4: fundamental right of access to healthcare[15]

4.1 Any person presenting with a potential diagnosis of opioid dependence syndrome should be able to have access:

(I) to a healthcare professional capable of diagnosing opioid dependence syndrome, as defined by the medical classification criteria and to a functional and multidimensional assessment of the needs (medical and social) of the person and those close to them (with regard to the training of healthcare professionals, see Sections 10 and 11);

(II) to medical care and medicines, including OAMs, adapted to their health situation and in line with the most recent scientific knowledge (with regard to the medicines approval process, see Section 13);

(III) to medical, psychological and social advice adapted to their situation.

Section 5: non-discriminatory access

5.1. Access to OAMs and related care must be non-discriminatory. Discrimination is defined by any distinction made, particularly in terms of age, gender, sexual orientation, ethnicity, migration status, insurance status, state of health (e.g. persons living with HIV, women who are pregnant or breastfeeding), type of substances consumed, or any situation concerning detention (persons pending judgment, serving a sentence or those held in administrative detention). There must be non-discrimination both in the legal and regulatory texts (de jure) and in practice (de facto). Therefore, if necessary, non-discrimination should be the subject of specific measures, particularly with regard to access for women and sexual or gender minorities.

5.2. A minor (according to the civil legislation of the country concerned) in treatment, capable of discernment, should receive the same access to care and right to medical confidentiality as an adult in treatment who is capable of discernment (see Section 6.3 and with regard to medical confidentiality, see Section 7.2).

5.3. According to the principle of equivalence of care, detained persons or those subject to other measures restricting freedom must be able to begin and/or continue existing treatment in the healthcare facility of their place of detention, if that is their wish. The principle also applies to the delivery of medication and methods to prevent and treat sexually transmitted diseases or diseases transmitted by blood.

5.4. Access cannot be withdrawn due to a person in treatment's inappropriate behaviour, particularly in the case of:

- violence or threats to others;
- trafficking in substances (licit or illicit);
- non-medical use of prescribed substances for personal gain;
- concurrent consumption of other substances (licit or illicit).

The sanctions for violation of the rules of the care setting should be necessary and proportionate; under no circumstances should sanctions interfere with the continuation of the treatment or the quality with which it is administered. In cases where treatment can no longer be administered in conditions in which the safety of the healthcare facility and in particular its employees can be ensured,[16] the person in treatment must be able to be referred as a last resort to another healthcare facility. Where no other care setting is available and there is no other alternative, efforts must be made to arrange for a transfer to a hospital or residential establishment, in all cases with a continuation of OAMs (see Section 8).

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15 The right to healthcare refers to the four parameters defined in the General Observation 14 by the Committee on Economic, Social and Cultural Rights: the availability, accessibility, acceptability and quality of care; also see Appendix 4.

16 Other reference documents include: Framework guidelines for addressing workplace violence in the health sector (International Labour Office, International Council of Nurses, WHO and Public Services International, Geneva, 2002).

5.5. Where a person in treatment hands over or sells his or her prescribed OAMs to another person, this may constitute a criminal offence. However, the penalty imposed must remain proportionate; it should take account of the mitigating or aggravating circumstances specific to the case and more generally, the principle of discretionary prosecution. Committing such an offence should not, in itself, be sufficient reason for the cessation or suspension of treatment, but may lead to a temporary change in delivery methods (for example, under the visual supervision of a professional, possibly including at weekends with the assistance of a pharmacy or a medical on-call service).

Section 6: free and informed consent

6.1. In order to exercise their free choice of treatment (OAMs and related healthcare), the person in treatment must be given clear and comprehensible, written and oral information, provided in the language that they are most fluent in (e.g. giving the person an information leaflet translated into this language).

6.2. OAMs and related healthcare services may not be imposed against the wishes of the person in treatment, including against the wishes of a person being held in detention or subject to other measures restricting freedom.

6.3. Minors capable of discernment should be able to give their own free and informed consent to treatment involving OAMs without the agreement of legal representatives, in line with the rules applicable to any long-term medical treatment offered to a minor.[17]

Section 7: non-discrimination related to being in treatment

7.1. The fact that a person uses OAMs, in itself, should not give rise to any judicial or administrative penalties, or to any negative consequences from a civil rights point of view. Undergoing treatment cannot in any case constitute an offence or indication of committing a crime.

7.2. Professional medical confidentiality must be maintained. Exceptions to medical confidentiality must be based on the consent of the person in treatment, unless confidentiality is lifted in an exceptional case provided for by law. Receiving OAMs does not constitute an exception. This principle also applies to minors who are capable of discernment.

Section 8: organisation and continuation of healthcare involving OAMs

8.1. Access to OAMs (see Section 5) and related healthcare services must be long-term, without interruption (including in the event of hospitalisation, deprivation of liberty or a move from one geographical region to another) and part of an integrated healthcare approach.

8.2. Access must be established immediately, once the medical indication is applied/confirmed by the physician and consent is obtained from the person in treatment.

8.3. Access and its continuation may not be refused on account of:

- the lack of *prior* agreement from another physician, psychologist or social worker;
- the lack of agreement from a judicial or administrative authority required *prior* to or *after* the commencement of treatment.

In contrast, the healthcare professional may be required to send a report to the health authority in order to avoid any duplication of medical prescriptions. This report should be submitted after treatment has begun (see Section 14).

17 This principle in no way questions the fact that healthcare should be organised in a way that supports the involvement, to the greatest extent possible, of relatives in the process of care, the importance of which is highlighted by the results of clinical research.

Part III: role of healthcare professionals

Section 9: indication, prescription, dispensing and coordination

9.1. It is the *physician's* responsibility to decide whether OAMs are indicated and to stipulate how the treatment is to be administered, taking into account the individual situation of the person in treatment, and subject to his or her free and informed consent (see Section 6). This includes the choice of medicine, dosage, specified strength and length of treatment. It also includes any associated measures, such as psychological and social support and screening for transmissible diseases.[18]

9.2. Any physician, regardless of his or her subsequent specialisation, must be able to begin a treatment involving OAMs. The physician may need to be assisted by other healthcare or social care professionals, such as a pharmacist, nurse, psychologist or social worker.

9.3. Following medical prescription, pharmacists must be able to deliver OAMs following completion of their basic training, in their role as manager or employee, regardless of the type of pharmacy (private or public dispensing pharmacy, pharmacy in a hospital, a prison or in a social education reception centre).

9.4. Healthcare (in the broad sense) must be co-ordinated between physicians, pharmacists and, depending on the clinical needs, other healthcare or social professionals, to provide integrated care from multiple disciplines. Healthcare, including the delivery of medicines, can be offered in private physicians` practices, dispensing pharmacies, specialist health centres (outpatient or residential), public or private hospitals and also via healthcare facilities in detention centres.

9.5. As part of an integrated treatment system, primary care physicians and pharmacists should be able to receive assistance from dependence specialists in the different professions involved (medicine, pharmacy, social work, nursing) and/or ad hoc networks.

9.6. When the medicines are dispensed by another healthcare professional working in a medical and social centre, a public hospital, private clinic, medical facility in a place of detention, the rules as mentioned below apply by analogy.

18 For further information, please refer to the WHO guidelines (2009): http://www.who.int/substance_abuse/publications/opioid_dependence_guidelines.pdf

Section 10: training of physicians

10.1. To provide high-quality treatment, special attention must be paid to the training of the healthcare professionals concerned, particularly physicians and pharmacists. Subject to the structure of medical and pharmaceutical studies, the body of necessary skills and knowledge will be passed on through pre-graduate, postgraduate and/or continuing education.

10.2. Training for all physicians, whatever the structure of their medical studies and specialisation,[19] should include basic training in the treatment of substance dependence, specifically including:

- diagnosis of opioid dependence syndrome;
- multi-dimensional and functional assessment of dependent behaviour;
- knowledge of the different treatment options for opioid dependence, in particular the different OAMs and their respective benefit/risk profiles;
- how to conduct an interview with a person using psychoactive substances;
- the ability to arrange for medical care and to initiate the prescription of OAMs;
- the ability to incorporate the treatment in a broader public health context offering a range of prevention, therapy and risk and harm reduction measures;
- knowledge of the legislative and regulatory framework in a broad sense (in particular the administrative formalities and specific financial conditions) for the administration of OAMs.

10.3. Training should be based on the latest medical and psychosocial knowledge.

10.4. At the end of the basic training, the physician should also know which medical specialties, which other healthcare professionals (particularly pharmacists, nurses, psychologists and social workers) and which institutions it is necessary or useful to collaborate with when treating a person with opioid dependence syndrome.

10.5. Basic training shall be kept up-to-date throughout their professional careers through continuous training to incorporate changes at all levels. For this, service-related training and/or specialist training (academic and/or professional) in the field of dependence in general and OAMs in particular should be available for every physician and pharmacist.

Section 11: training of pharmacists

11.1 Basic training for all pharmacists should include teaching in the treatment of substance dependence, specifically including:

- knowledge of the different medicinal options, in particular the benefits/risk profiles of the different medications, including their pharmacodynamic and pharmacokinetic effects, the desired clinical effects as well as adverse effects and interactions with other medications;
- assessment of the state of general health for persons in treatment and, in particular, the state of intoxication;
- knowledge of the legislative and regulatory framework in the broad sense (in particular the administrative formalities and specific financial conditions) for the introduction and administration of OAMs.

11.2. Following their basic training, pharmacists should also know how to collaborate effectively with the prescribing physician, other healthcare professionals (e.g. social workers) and the different institutions and programmes in the network of social and health services.

11.3 The training given should be based on the latest medical and pharmacological knowledge.

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19 Depending on how countries organise their study programmes, some aspects concerning implementation may be part of a common core curriculum on a postgraduate course.

Section 12: supervision of healthcare professionals

12.1. In the same way as all physicians and pharmacists, those involved in providing OAMs shall be subject to regular supervision carried out by professional bodies (disciplinary or professional law). Supervision is above all to ensure compliance with ethical codes and good practice (including informed consent of the person in treatment, regular updating of knowledge, exercise of evidence-based medicine). Disciplinary supervision is in the interests of healthcare professionals, persons in treatment and those close to them and society in general.

12.2. The possible sanctions for healthcare professionals involved in providing OAMs are the same as those which apply to other healthcare professionals.

12.3. Standard professional supervision is, above all, designed to prevent the risks of healthcare professionals' inappropriate conduct, which could otherwise lead to administrative or criminal penalties.

12.4 Physicians, pharmacists and other healthcare professionals shall be subject to administrative sanctions only if their conduct presents or presented a risk to public health or to the health of the persons receiving treatment and those close to them. The intended administrative measure must be deemed appropriate, necessary and proportionate to preclude this risk. These measures may include restrictions on the right of the professional in question to practise their profession.

12.5. The administrative framework must, moreover, be designed to prevent the risks of inappropriate conduct; support measures in place of or combined with sanctions should also be considered (e.g. mentoring, participation in exchange groups, supervision/peer supervision).

12.6. Physicians, pharmacists and other healthcare professionals shall be subject to criminal sanctions only if their conduct – deliberately or through negligence – has endangered public health or safety, or if it has endangered the health of persons who have been identified individually and/or people who are close to them.

Part IV: role of the public authorities

The State is responsible for providing coherent framework conditions to ensure access to high-quality medications and treatments.

Section 13: availability and quality of OAMs

13.1. The State must ensure that:

(I) the necessary and useful OAMs are available on the national market; these medicines shall include as a minimum the OAMs on the WHO list of essential medicines (and therefore, at present, at least methadone and buprenorphine);

(II) the procedures are in place to highlight any potential future needs to ensure a sufficient supply;

(III) these medicines have been duly approved in their territory by one or more specialised agency/agencies (e.g. medicine agency);

(IV) conditions for granting approval are based on current medical knowledge with regard to the safety and effectiveness of the treatment;

(V) information leaflets (SPC/PI or their equivalent with regard to extemporaneous preparations) for approved medicines reflect current medical knowledge, particularly with regard to the permitted therapeutic indications, dosage, composition and length of treatment;

- these leaflets should provide all the necessary clinical, pharmacological and composition information for correctly giving OAM treatment;
- these leaflets should be regularly updated by, and at the initiative of, the authorities and take into account best international practices.

13.2. In cases where the State is unable to ensure a sufficient supply in the country (in accordance with paragraph 13.1 above), it must ensure that:

(I) it is, in practice, possible to import medications that have been approved in other countries (being admitted to the market, through a marketing authorisation procedure, by the medicines agency of the exporting country);

(II) there is the possibility of off-label use of medications when this is clinically justified in the case of a person receiving individual treatment;

(III) it is possible to use non-authorised medication, including extemporaneous or officinal preparations.

13.3. The State, in principle via its medications agency, must monitor the medication market, including OAMs, so as to ensure that the abovementioned objectives are guaranteed in the long-term, especially through standard measures of pharmacovigilance.

Section 14: proportionality of framework measures

14.1. When the State, at any level, establishes the legal and administrative framework for the use of OAMs, it shall pay attention to the prior evaluation of its impact on access to healthcare and medications, as well as on the availability of physicians and pharmacists involved in this form of treatment.

14.2. Specific obligations imposed by the State[20] on physicians and pharmacists should be limited to what is strictly necessary and proportionate in order to ensure safe and effective treatment for the person in treatment, as well as for third parties (in particular relatives and children of persons in treatment).

14.3. As examples, the following are generally considered disproportionate:

- **(I)** the requirement to obtain authorisation prior to the start of treatment (except prescription by the physician);
- **(II)** the obligation to have the treatment, which has been indicated by the physician,[21] subsequently validated by a state authority;
- **(III)** a predetermined waiting time before initiating OAMs;
- **(IV)** the obligation for a physician to receive special training to prescribe OAMs (see Section 10);
- **(V)** the obligation for a pharmacist to receive special training to provide OAMs;
- **(VI)** the obligation to have the person in treatment assessed by two or more different healthcare professionals;
- **(VII)** the imposition of a specific medication, a specific dosage, a specific composition and strength, or a minimum or maximum duration of treatment;
- **(VIII)** a ban on all off-label use of medications;
- **(IX)** security arrangements for the storage of OAMs by healthcare professionals where these generate costs that are incompatible with effective access to OAMs via primary medical care (for example, safety lockers complying with standards that make them prohibitively expensive);
- **(X)** the requirement to include information on the physician's prescription which may impede delivery of the medication, unless there is a clearly established need based on the clinical state of the person being treated;
- **(XI)** a system of OAM delivery that would not fall under the sole responsibility of the healthcare professional tasked with implementing the treatment (with regard to the training of healthcare professionals, see Sections 10 and 11).[22]

14.4. Countries introducing OAMs may need to adopt exceptional measures for a transitional period in order to evaluate feasibility, relevance, accessibility and funding while duly taking into account accessibility to healthcare.

Non-discriminatory access, free and informed consent of the person in treatment and data protection must be guaranteed.

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20 Directly or indirectly, for example, through professional bodies.

21 In contrast, the doctor may be required to report the treatment in order to avoid any duplication of medical prescriptions or to collect epidemiological data.

22 In this respect, the professional must take account of the safety of the person receiving treatment, in particular the risk of diversion or self-medication, as well as the risks to the people they are close to (e.g. accidental access by others, particularly children). Supervised administration is generally necessary at the beginning of the treatment in order to verify the safety and effectiveness for the person in treatment. Following this, supervised administration is justified only if the healthcare professional considers, based on an individual assessment of the person in treatment, that this is the only possible way of minimising the safety risk. For further scientific information, please refer to the WHO guidelines:http://www.who.int/substance_abuse/publications/opioid_dependence_guidelines.pdf

Exceptional measures should be designed as an explicitly transitional device that the State regularly re-evaluates regarding:

- its necessity;
- its consequences (effects) on access to healthcare;
- its funding;
- the difficulties encountered.

All the information collected as part of this evaluation should be anonymous and should not be used for other purposes. The results of this evaluation should be made public.

Section 15: funding and remuneration of healthcare services

15.1. The State must ensure that care delivered by healthcare professionals, OAMs that have received MA in the country and psychosocial support are affordable for persons in treatment in its territory.

15.2. If the cost of the care/follow-up care is not already fully covered by a public health insurance scheme, it should be covered by a free-of-charge scheme for this purpose which guarantees that those on low incomes have full access to them (see Section 5).

15.3. The services provided by physicians, pharmacists and other healthcare professionals must be adequately remunerated, taking into account the workload, the difficulty of delivering the service and the liability incurred. Remuneration should be at a level that ensures the availability of a sufficient number of physicians, pharmacists and healthcare professionals.

Section 16: promoting training, research and innovation

16.1. Within the limits of its financial resources, the State shall encourage innovation, particularly by ensuring the promotion of:

(I) basic, postgraduate and continuous training for professionals working in the field of opioid dependence syndrome, including awareness-raising for those professions involved on a timely and occasional basis;

(II) organisation of healthcare associated with opioid dependence syndrome;

(III) research into medications, care processes and the organisation of care;

(IV) research into comorbidities associated with opioid dependence syndrome;

(V) research into the mechanisms and epidemiology related to opioid dependence syndrome;

(VI) coordination and monitoring activities of the national authority (see Section 18).

In so doing, the State shall encourage a global approach to all dependent behaviours, and therefore not limited solely to non-medical psychoactive substances.

16.2. The State shall ensure that the legislative framework contains no provision particularly likely to restrict the initiation or completion of the innovative projects or research mentioned above.

Section 17: monitoring and indicators

17.1. Each state must evaluate its system for treating dependence disorders (healthcare system, healthcare services and treatment outcomes). Such evaluation comprises of standard monitoring through:

- structural indicators regarding regulatory measures and the availability of healthcare structures, necessary medications and trained professionals needed to provide treatment;
- process and coverage indicators with regard to access to healthcare (non- discriminatory access that is prompt and uninterrupted for anyone within its territory diagnosed with opioid dependence syndrome who has consented to treatment) and relating to the quality of healthcare and professional knowledge (whether they are specialists or involved on a timely and occasional basis);
- outcome indicators on response to treatment, its continuation (including possible side effects), mortality, morbidity and comorbidity, as well as quality of life.

17.2. In this regard, each State must ensure it has the means to regularly obtain data on structural, process and outcome indicators. It is recommended that these indicators are standardised and in line with the EMCDDA epidemiological and healthcare system indicator protocols in order to assure reliability and comparability of the data collected (see Section 17.3).

17.3. The indicators to be collected and the corresponding data must be made public. The data collected should also be made available to researchers, in accordance with the common ethical standards related to consent and the protection of personal data.

17.4. These indicators should then be analysed by the State and other stakeholders in order to optimise treatments and their regulatory frameworks, both nationally and internationally (see Sections 18 and 19). The designated national advisory body referred to in Section 18 shall support these efforts.

17.5. Each State shall make the list of indicators that it collects on OAMs easily accessible; in particular by publishing the list online.

Part V: national coordination and international collaboration

Section 18: national authority for coordination and monitoring

18.1. In order to co-ordinate and monitor the implementation of OAM, the State shall establish a national advisory body, bringing together representatives of professionals and persons working in the field of opioid dependence syndrome, together with representatives from the different fields involved (State, para-statal or private).

Participants of this body include representatives responsible for: the MA of medications, reimbursement of healthcare and medication costs, supervision of healthcare professionals, public health policies, medication manufacturers and social insurance supervisory authorities.

18.2. This body shall be responsible for the regular tasks of:

- **(I)** identifying obstacles to accessing healthcare;
- **(II)** identifying the international directives issued on OAMs and assessing their relevance for the country;
- **(III)** evaluating the relevance of selected indicators, the data collected and the results obtained (see Section 17);
- **(IV)** supporting the efforts to exploit these indicators in order to improve treatments and their regulatory framework;
- **(V)** tracking research results and making recommendations to ensure their implementation;
- **(VI)** on the basis of the above, formulating recommendations to prevent discrimination and to improve access to treatment and quality of healthcare;
- **(VII)** co-ordinating the efforts of various concerned partners.

18.3. The State shall provide this body with sufficient powers and means to perform the above tasks as well as stable funding over time.

Section 19: international collaboration

19.1. In order to facilitate the implementation of OAMs by the professionals concerned, the States shall collaborate to update common international guidelines.

19.2. The state institutions responsible for OAMs (legislative, administrative and judicial) should specifically take into account international directives considered as current recommendations in the light of current scientific knowledge.

The State can further clarify these directives in order to apply them in practice in its territory. It is also free to introduce more favourable conditions for access to OAMs.

19.3. In order to ensure the comparability of collected data, enabling their use for scientific purposes, the States shall agree on the minimum common indicators that they will commit to collecting (see Section 17.2). To this end, they may designate and provide funding for an intergovernmental body which has adequate powers to perform or co-ordinate data collection.

19.4. If a State intends to collect additional indicators (beyond a common minimum list), it shall notify the other States in order to ensure, as far as possible, the international comparability of data.

19.5. On a national level, the tasks of collaboration and communication shall be ensured, in principle, by the body mentioned in Section 18.

Key recommendations and reasoning

4.1 From guiding principles to key recommendations

There are 19 guiding principles' sections, each divided into one to six items. This clearly reflects the authors' desire to cover the various aspects of the consequences of regulating opioid agonist treatment (OAT) and ensure their consistency. Proposing the elimination of prior authorisation schemes, for example, has various effects on several levels and calls for appropriate measures to avoid any adverse consequences.

Anxious to put forward comprehensive arguments justifying the proposed changes, the authors faced a major educational obstacle: the risk of drowning the reader in detailed explanations principle by principle. They have opted for the following solution: choosing four key recommendations and developing their line of argument on this basis, highlighting the effects on the various Guiding Principles. These so-called cross-effects are discussed in Section 5.2, in connection with the implementation of the Guiding Principles. In the present section, the emphasis is on the arguments in favour of these four recommendations and on responses to typical objections.

The four key recommendations chosen relate to the following aspects:

(1) Prescription and delivery of opioid agonist medicines (OAMs) without prior authorisation schemes (PASs)

(2) Effective removal of financial barriers

(3) National consultative body for coordination and monitoring

(4) Neutral, precise and respectful terminology

These four recommendations are framed on very different levels.

The establishment of practices that ensure the safety of prescriptions without PAS (Recommendation No. 1) embodies the paradigm shift underlying the Guiding Principles, which seeks to replace these therapies in the context of the standard regulations and practices of the medical and pharmaceutical fields by abandoning specific past practices.

The aim of covering the actual cost of treatment (Recommendation No. 2) is essentially operational in nature and involves no longer recognising the distinctive characteristic of OAMs in clinical terms but in terms of public health by enabling the rather vulnerable and marginalised group of individuals concerned to have easy access to care and continue to receive treatment.

Making a consultative body available to provide coordination and follow-up is a recommendation (No. 3), which focuses on the functioning of the system as a whole. Its aim is to ensure the monitoring of the necessary reforms and guarantee fine-tuning on the basis of all available data: pharmacovigilance, general insights, epidemiological monitoring, and qualitative feedback from everyone involved in the system, including its users.

Finally, reviewing the terminology employed is a transversal recommendation (No. 4). Both for professionals and for individuals who benefit directly from OAMs, its aim is to ensure a clear, shared understanding while at the same time preventing the stigmatisation that precedes discriminatory behaviour and exclusion.

Each of these recommendations is presented in two parts:

- a description of the desired situation;
- arguments supporting the recommendation, including responses to typical objections.

4.2 Key recommendations

No.1: "Prescription and delivery without prior authorisation schemes"

Desired situation

The therapies involving the prescription of opioid agonist medicines fall under the ordinary rules of prescription and delivery of controlled medicines. Therefore, they do not require a special authorisation for persons in treatment, for professionals or for the infrastructures dispensing treatment. The attribution and division of tasks and competencies between the various actors are the same as for all other forms of authorised therapy including controlled medicines.

This process has implications for the training and supervision of professionals as well as for the approval of the opioid agonist medicines and their pharmacovigilance. Thus, basic knowledge of opioid agonist medicines should be included in the basic training of all stakeholders in the health and social care system. Thus, ordinary disciplinary bodies for the supervision of healthcare professions must also supervise the professionals providing opioid agonist medicines, in the same way as professionals providing other medicines are supervised. Finally, the medicines agencies must be the competent authorities to keep up-to-date records of use (Summary of Product Characteristics/Product Information - SPC/PI) for opioid agonist medicines, taking into account data from pharmacovigilance and other studies. This information must notably clarify how opioid agonist medicines are to be dispensed based on the most recent scientific data.

Prior authorisation schemes are suppressed. Declarative regimes whereby healthcare professionals announce ongoing treatments may be retained, if these regimes are necessary to prevent double prescriptions and/or to facilitate epidemiological monitoring; in any event, strict data protection rules must be followed.

Principal arguments

Today, the medical evidence establishes irrefutably that OATs are the best treatments available and must be implemented over the long term, together with appropriate psychosocial and somatic support. Accordingly, all regulatory measures that will encourage access to this benchmark treatment should be welcomed, whereas those that constitute barriers to it should be carefully analysed to identify any counterproductive effects. The aim is to ensure that measures that interfere with treatment pursue (nevertheless) a legitimate goal and achieve it in a proportionate way, taking account of the interests and rights of the parties concerned (especially the right to health as defined by the UN, cf. 1.3 and in the Appendix). In the case of PASs, the legitimate aim(s) that these schemes are supposed to pursue are generally not spelled out, so that it is difficult, if not impossible, to determine whether or not they have been achieved. Moreover, the previous sections have shown that, even assuming different public-interest goals (e.g. epidemiological monitoring, prevention of diversion), the PAS is an ineffective or disproportionate means of achieving them.

Eliminating prior authorisation schemes improves the availability, accessibility and acceptability of treatments

The absence of PASs enables individuals in treatment to access OAMs more easily and quickly, especially from primary care physicians/general practitioners (in sufficient numbers and based on practical arrangements favourable for those being treated). When there is a PAS, it often has a deterrent effect on physicians who are either not authorised to prescribe or dispense a medicine (concept of availability) or are discouraged from doing so by the administrative constraints to which they must adhere in order to obtain and retain the authorisation (concept of accessibility). For the individual being treated, the PAS also has a deterrent effect when it is subject to constraints, especially schedules or other organisational arrangements, that are either impossible for him/her to adhere to (concept of accessibility) or are too complicated (concept of acceptability). The PAS may also have deterrent consequences for that individual when it is accompanied by a register operated by the authorities, the confidentiality of which is not clearly and effectively guaranteed. If the individual being treated is aware or suspects that his/her identity and medical history may be passed on to other authorities, which could then use that information to his/her detriment (e.g., risk of withdrawal of parental authority over his/her child), he/she will logically be reluctant to accept an OAT.

The existence of a PAS implies that this medical practice is perceived as reserved for specialists who have been duly trained and authorised to that end. Eliminating a PAS sends the opposite message, namely that the treatment is part of the basic responsibility (and therefore training) of healthcare professionals. In many countries, the field of dependence is either not taught or taught very little in the basic training of physicians, pharmacists and the other health and social welfare professions involved (see Section 1.7.1). The obvious consequence of this is that physicians, especially primary care physicians, do not want to provide this service. This creates a vicious circle where, de facto, individuals with an opioid dependence syndrome have no other choice but to turn to specialised bodies set up under the PASs. Conversely, teaching all future professionals how to prescribe and dispense OAMs provides a guarantee of improved availability, accessibility, acceptability and quality.

Eliminating PASs improves the quality and safety of the treatment

The existence of a PAS frequently implies that the supervision of professionals (who treat individuals suffering from a dependence syndrome) is the responsibility of the authorities that have issued the authorisations and no longer that of the ordinary bodies in charge of supervising medicines or professionals (e.g. professional or regulatory bodies). In these precise cases, the virtually automatic effect of eliminating PASs is to reallocate this responsibility to these ordinary bodies. However, the latter are better placed to identify best practices in the light of developments in scientific knowledge. They also enjoy greater legitimacy, especially as they are structurally designed to provide supervision and deal with all cases and disputes involving medicines and healthcare professionals. It is therefore to be expected that such a transfer of responsibilities will improve, or at least contribute to, the quality of the care provided.

The existence of a PAS may also imply that the treatment arrangements are spelled out by the administrative authorities responsible for issuing the necessary authorisation. These authorities typically add further prescription or dispensing requirements not mentioned in the instructions for use (Summary of product characteristics/Professional information, see also Section 1.7.1). These requirements are often not based on clinical studies, pharmacovigilance data or established medical guidelines. In these cases, the virtually automatic effect of eliminating PASs is to (re)allocate the responsibility for regulating the arrangements for prescribing and dispensing OAMs to the medicines agencies. The latter are then obliged to keep up-to-date the information on side-effects, interactions, precautions to be taken and the categories of individuals for whom the treatment is indicated. This update is carried out in accordance with internationally recognised standards. Guaranteeing that correct, precise and up-to-date health information is provided by the medicines agencies increases the safety and quality of treatments.

PASs are not necessary for monitoring treatments

It is sometimes argued that a PAS is necessary to achieve objectives associated with the supervision of this health sector. In particular, PASs are said to enable an overall view of who prescribes, who dispenses and who receives medicines and under what conditions. In this sense, they are a tool for assessing and minimising the risk of diversion. They could be a tool for obtaining quantitative data subsequently used in epidemiological studies and could facilitate the gathering of data sometimes required by international conventions. This line of argument is unconvincing for several reasons.

In practice, data from PASs are rarely systematically exploited, whether with the aim of controlling diversion under criminal law, ensuring epidemiological monitoring or monitoring compliance with conventions. For example, there are few countries in which the IT system and the data it contains are capable of automatically identifying double prescriptions. More generally, well-designed ad hoc surveys enable data considered useful or necessary to be obtained more efficiently and at a lower cost. Such surveys are commissioned and put out to an ad hoc competition among scientists with the appropriate expertise, in order to answer relevant and precise questions, while PASs gather data without any thought given to assumptions to be tested.

The risk of diversion by the person undergoing treatment, especially via a double prescription, can be minimised by less intrusive means. This risk (the individual concerned visits two different physicians to obtain twice the amount of medicine needed and sells half of it) can be avoided using an a posterior reporting system that involves each person in treatment's name being held in a register containing the prescriptions issued for a given individual. In any event, the risk of diversion is relatively low in practice, both in terms of the proportion of people treated and the volume of medicines dispensed (see Section 1.7.2). Furthermore, diversion rarely poses risks to public health since the worst thing that can happen is that it makes a less dangerous substance (methadone or buprenorphine), of better quality than street heroin, available on the black market.

The risk of diversion by the healthcare professional does not provide any further justification for a PAS. Professionals who make a significant contribution to the trafficking of controlled substances are actually a tiny minority. The exception of some countries, like the United States, which is faced with the widespread consumption of so-called "prescription" opioids, indirectly confirms this. It has to be assumed that such abuses largely result from the particularly restrictive nature of these countries with regard to access to opioids, across all indications. These restrictions increase the value of opioids on the black market and therefore the risk of diversion by individuals undergoing treatment, or even by professionals (Scholten, 2017; Scholten & Henningfield, 2016). At any rate, a PAS is not an appropriate way of dealing with these abuses. A physician wishing to make money by selling OAMs to people undergoing treatment only for them to resell them on the black market can easily circumvent the supervision accompanying the PAS by prescribing OAMs with an indication other than that of the OAT (e.g. the treatment of chronic pains). In similar cases, there is no specific check on the physician, even though the diverted medicine is an opioid.

Finally, as far as data to be collected to comply with international conventions are concerned, this condition is already met by other mechanisms. In the case of collecting these data, the conventions do not distinguish OAMs from other controlled medicines. The countries should therefore establish mechanisms for gathering the required information that are mainly based on the ability to track orders and deliveries of every controlled medicine. On the other hand, the international conventions do not require any information to be provided on individuals undergoing treatment. PASs therefore bring together information not required by the conventions.

Eliminating PASs puts an end to an anachronism

For a long time, the treatment of a dependence syndrome has been an area of some controversy, whether among healthcare professionals, law professionals (especially criminal courts), representatives of the social professions (e.g. social workers) and even among individuals in treatment. Only gradually have the effectiveness and legitimacy of treatments been fully recognised, in conjunction with the recognition of a dependence syndrome as a disease. When these treatments began to be proposed, these different groups had many concerns. For example, it was long considered that abstinence was the supreme objective and that OAMs could be an obstacle to achieving it. Some countries continue to stick to this argument, which has been undermined by unanimous medical studies. Imposing a PAS accordingly enabled some of these misgivings to be overcome and to preserve the law-enforcement component of substance control.

However, the fundamental aspect lies in the need to encourage access to OAT for the vast majority of individuals being treated. Even if a person undergoing treatment does not fully comply with the conditions of the OAT proposed or prescribed, it remains in the public and private interest that he/she continues with that treatment given the undeniable benefit for his/her physical and mental health. On a balance of interests, the continuation of the treatment takes precedence over meeting administrative requirements, especially via the imposition of potentially counterproductive sanctions. PASs have in the past been designed to ensure compliance with administrative instructions, making use to this end of the threat of the withdrawal of the authorisation. In view of current medical knowledge, such an aim is anachronistic.

No. 2: "Effective removal of financial barriers"

Desired situation

For persons presenting an opioid dependence syndrome, access to treatment must not depend - effectively and practically – on their ability or willingness to pay. Treatment should be provided at no charges at each of the different steps of the treatment (from the first contact to the prescription and delivery of the opioid agonist medicines to follow-up visits). In particular, person in treatment are not required to advance funds or provide guarantees, regardless of the type of healthcare provider and the type of treatment. Because of public health implications, implementation of this objective may call for special funding, apart from the general scheme of healthcare financing, regime, justified on the grounds of public health.

States must ensure that the effective removal of financial barriers does not lead to a form of rationing. In particular, it must not result in stricter requirements for entry into treatment, nor must it affect the administrative responsibility and/or the remuneration of professionals.

Principal arguments

The particular characteristics of OATs justify a specific financial mechanism

While the aim of the Guiding Principles, taken as a whole, is to put OAT back into the ordinary treatment and healthcare context, it may seem surprising that they can also call for special measures regarding the funding of treatments for individuals needing them. Moreover, such a difference may appear iniquitous compared with other treatments essential for survival or with other groups of people in need of care. However, individuals affected by an opioid dependence syndrome have distinct characteristics, namely: a significant risk of stigmatisation and discrimination, social vulnerability, reluctance to accept help from state systems, whatever their nature, a higher prevalence of high-risk behaviour, of mental and somatic disorders and of other dependence behaviours. All these characteristics have the potential for producing a harm-multiplying effect, both for dependent individuals and for those close to them, especially economically and with regard to the risk of an infectious epidemic.

These specific characteristics have two consequences. Firstly, at the level of the individual they make it considerably harder to enter and remain in treatment. Then, on a collective level they entail costs for the State (direct costs related to the provision of healthcare, social assistance or law enforcement, indirect costs linked to losses of productivity, intangible costs linked to the loss of quality of life) that considerably exceed the total cost of the treatment, including costs linked to associated disorders (see also Section 1.5.3).

Eliminating financial thresholds takes account of the characteristic ambivalence of addictive disorders

It is sometimes argued that there is a moral problem in enabling people to benefit from a more favourable financial regime when they have, as it were, "chosen" to consume substances and therefore taken the risk of finding themselves in a situation of dependence. Not only is this thinking based on a poor understanding of a dependence syndrome, which must be considered a disease where vulnerability is in itself a risk factor but it fails to take account of a consubstantial clinical characteristic of addictive behaviours, namely ambivalence (Miller & Rose, 2013; Feldstein Ewing, Apodoca & Gaume, 2016; Daeppen, 2016). Typically, the individuals concerned focus more on the perceived benefits of their consumption and pay less attention

to the drawbacks, especially for their health, at the very least until the very advanced stages of addictive behaviour, when the drawbacks have become critical (a term also used in clinical parlance is “decisional balance”). This ambivalence explains part of the quasi-structural gap between the existence of a dependence syndrome and the perceived need for assistance (Lipari, Park-Lee & Van Horn, 2016; O’Connor, Sokol & D’Onofrio, 2014). Accordingly, individuals who could benefit from prevention and treatment measures delay committing to them, so it is not very realistic to count on a positive individual cost-benefit calculation of OATs on the part of those to be treated. On the contrary, it is counterproductive not to lower all logistical barriers. In the context of so-called risk and harm reduction policies, this reasoning is also referred to as a “low threshold”.

While it is easy for an outside observer to understand that the individual in treatment would make savings on the amounts he/she spends on the purchase of illegal substances, this is not the way those affected by addictive behaviour would think. Added to this, the current prices of OAMs are far from being negligible, not counting the price of other components of the treatment, such as psychosocial counselling or somatic care. It is unrealistic to expect that an additional financial contribution payable by individuals to be treated could constitute a valid engagement strategy. On the contrary, the existence of financial barriers to be overcome by the individual undergoing treatment risks causing a delay in admission into treatment. This also applies to people in treatment who have the necessary funds but would, for example, have to enlist the help of third parties to access it (spouse, family, legal representative or guardian, etc.) or undertake cumbersome administrative steps to this end.

Eliminating financial thresholds may facilitate confidentiality

The ordinary constraints associated with health insurance are another reason for having to communicate one’s identity and data on one’s state of health to third parties. Accordingly, the existence of specific mechanisms to eliminate financial thresholds can also help to strengthen confidentiality. As already pointed out, it is a crucial component of access to treatment for groups that are potentially stigmatised and discriminated against and, in many cases, in conflict with various authorities or simply with their own friends and family. On the other hand, the beneficial effects expected from the elimination of financial thresholds may be cancelled out if accompanied by additional administrative constraints with an adverse impact on the maintenance of confidentiality.

The costs of OAMs paid by public or para-public bodies are largely compensated for

We have seen in the paragraph entitled “Impact on public health and safety” (1.5.3) that the absence of treatment results in considerable social costs for the community and that, even on the basis of the most conservative assumptions, admission into OAT brings about significant savings over direct costs (especially costs of social and judicial services), indirect costs (loss of productivity, including that of friends and family) and intangible costs (loss of quality of life). The elimination of financial barriers to access to OAMs is therefore likely to result in significant savings for the State, despite a sectoral increase.

It also needs to be reiterated that there is considerable evidence that the increase in the availability of OATs has not led to a drop in demand for help to end consumption and for the costs of therapeutic communities to be covered. However, even these so-called “residential” treatments based on per-day prices close to those charged by hospitals are generally lower than the costs of a period in custody, irrespective of the other factors to be considered when calculating costs.

No. 3: "National consultative body for coordination and monitoring"

Desired situation

Acting on a clear and specific mandate, a national consultative body monitors the system for the treatment of opioid use disorders and advises the public authorities. In particular, it is responsible for identifying barriers to and for removing them. Where appropriate, such responsibilities can be attributed to a pre-existing body, if its new role is properly defined in an adequate mission statement.

The consultative body includes representatives from people directly affected by the non-medical use of opioids, professionals involved in the treatment and the prevention of opioid use disorders, researchers and public health services, supervisory authorities of healthcare professionals, medicines agencies, pharmaceutical companies, and any other actor relevant to the national context.

To accomplish its mission, the body conducts its work based on research results, has access to pertinent statistics and information, and receives regular feedback from practice. This consultative body enjoys independence with regards to its budget (which must be sufficient) and to agenda settings as well as freedom of speech. The result of its work is subject to the principle of transparency.

Principal arguments

The particular characteristics of OAT justify a dedicated body

While considering opioid dependence syndrome as a disease calls for a general effort to standardise treatment regulations, the fact remains that this disease still faces many obstacles (e.g. institutional obstacles, obstacles associated with the costs payable by the State, obstacles due to the hostility of carers and/or the population towards people who use psychoactive substances). These obstacles are greater than those placed in the way of treating most other diseases and disorders. The aim of the consultative body is to assist in the process that should contribute to the standardisation of the treatment of people with addictive behaviour disorders. Only when that goal has been achieved – that is to say when the treatment of the dependence syndrome no longer faces the obstacles mentioned – will it be possible for the body's tasks to be integrated into other government entities or services, as in the case of other diseases or groups of diseases.

A national consultative body is in a better position to bring together the necessary expertise than an ordinary state service

It is sometimes argued that such a body is not necessary as government services already carry out the tasks in question, thereby making it superfluous and redundant.

Unlike a state service in charge of a particular aspect of the subject, such an interdisciplinary and inter-institutional body provides a broader perspective as it incorporates different dimensions.

The consequence of choosing to allocate the responsibilities vested in the consultative body to a specific state-run department is that the State becomes both judge and party to an area in which there is a greater risk of conflicts of interest. Administrative services in charge of prevention, treatment, social insurance, law enforcement, the control of medicines, etc. are often in competition as they represent conflicting interests. By definition, a consultative body has greater room for manoeuvre and freedom of expression and can express views that may conflict with the preferences of one administrative authority or another.

A body such as the one proposed by the guiding principles will also be responsible for taking a long-term view and will therefore by and large be more independent vis-à-vis the political uncertainties with which public administrative departments have to cope. Moreover, a change in government may result in major changes within administrative authorities dealing with dependence, resulting in a loss of expertise and know-how.

A national consultative body facilitates dialogue between stakeholders and contributes to ensuring a coherent policy

As the consultative body has been conceived from the outset as interdisciplinary and inter-institutional, bringing together experts and specialised officials, it provides an opportunity for people who would hardly ever meet to engage in dialogue. The combination of these skills makes it possible to gain an up-to-date overall picture of the issue of dependence. On the other hand, state-run departments are responsible for one specific field (e.g. health policy relating to drugs, social insurance, public order, judicial proceedings, etc.) and have no opportunity to develop this comprehensive and consistent approach.

However, a state policy on addictive behaviours based on incomplete, biased or obsolete knowledge has every chance of ending in disappointing results. The secure knowledge that each representative of a particular field has a possible impact produced by the measures envisaged is important for ensuring the consistency of the process of monitoring the implementation of those measures.

The existence of a specific body motivates and unites the operators involved

Such a body also enables the motivation of professionals responsible for treating individuals suffering from a dependence syndrome to be sustained by providing a single and convenient point of contact for professionals faced with new situations requiring new responses. In the absence of a body that brings together cross-cutting expertise, it is often difficult for an operator in a given sector to find the right person who is able to deal with emerging issues. At the same time, that individual may be asked to participate in the work of the consultative body, either as an expert member or as a third-party expert called upon to assist on an ad hoc basis. The consultative body can therefore enable people working in different fields to be brought together around a unifying project, for example by calling on professional or inter-professional organisations. Furthermore, such a body generally fosters coordination and international co-operation because its experts (especially medical experts) already attend international conferences. Government officials can clearly also participate in these gatherings but in practice rarely do so.

A national consultative body brings about significant savings

Some argue that such a body would be too costly, especially for countries with limited resources.

In some cases, it is not necessary to set up a new body when an existing one is able to take on such a remit.

The cost of an independent body is still low as it brings together a limited number of experts who are appointed on a very ad hoc basis to attend meetings (and, in the case of public service staff, who are in practice often “lent” by their own department). The permanent staff members of such a body are typically limited to a scientific secretariat consisting of one to two part-timers, so the overall cost is not very high and is usually considerably less than the cost of keeping someone in custody for a year.

Accordingly, such a body mainly enables savings to be made by improving the system, for example by promoting the implementation of a number of recommendations identified in this report. For the reasons already mentioned on the subject of eliminating financial barriers, there is considerable potential for making savings.

Table 3 – Criteria to be considered for the proper functioning of a national consultative body

Independence, appointment criteria and affiliation	Its members must be appointed on the basis of their expertise and practical experience and not for political reasons (party representation). The administrative department to which its secretariat is attached must not be authorised to give it any binding instructions, especially in terms of its agenda.
Stable membership	Once appointed, its members will serve a term of several years with no risk of being dismissed by the State on grounds associated with sectoral considerations.
Multidisciplinary and interprofessional approach	The body must be interdisciplinary. The following sectors must be covered in particular: medicine, psychology, nursing, ethics, and law. The fields represented must include care, research, training and prevention. In addition, the body must also be made up of individuals directly or indirectly affected by the subject concerned (e.g. people in treatment or persons close to them).
Chairmanship (chair and vicechair)	These functions must be entrusted to prominent individuals who enjoy broad inter-professional recognition.
Clear, delineated terms of reference	Its terms of reference must be clearly defined in writing. Expiry dates must be specified.
Recourse to third parties	The body must consult outside experts when it does not have the expertise available internally.
Human resources	The body must have the necessary human resources. In particular, it must have a scientific secretariat.
Sensitive nature of the secretariat	Its secretariat must be attached to a state public-health service.
Transparency	The body must regularly publish details of its work.

No. 4: “Neutral, precise and respectful terminology”

Desired situation

The terms employed to designate opioid dependence syndrome, persons in treatment, practitioners, places of care and the medicines used are neutral, precise, and respectful. To prevent prejudice, stigmatisation and discrimination, these terms describe unambiguously the facts, based on scientific knowledge; they respect the personality of persons in treatment, as well as their personal and professional environment.

The term “substitution”, being ambiguous as to the nature and function of opioid agonist medicines, is to be avoided in favour of alternatives focused on the real characteristics of opioid agonist medicines.

While terminology is to take into account international definitions, recommendations and practices, it must be adapted to the language of each linguistic and/or regional community and must be based on an ongoing debate among healthcare professionals, civil society, the persons in treatment and the competent authorities. Such a debate also promotes the dialogue between different disciplines concerned by the field of substance use disorders.

Principal arguments

The commonly used term “substitution” or “substitution therapy” is ambiguous

The term “substitution” literally suggests “the replacement of a drug commonly designated ‘illegal’, i.e. a controlled substance, by a so-called “legal” drug, i.e. one dispensed under the auspices of the public authorities on an ad hoc basis” (OFSP, 2017). Other languages have, incidentally, endorsed the idea of “replacement” therapy (the word Ersatz may be used in German). In the French-language literature from the 1980s, we also find the term “distribution contrôlée” (controlled distribution), with or without medical supervision (“médicalisé”), Mino (1990) refers to “remise médicalisée” (dispensed with medical supervision), while more recently the concept of “medication assisted treatment” (WHO, 2009) has been used. The term “substitution” has sometimes also been associated with non-medical practices aimed at countering withdrawal symptoms, especially through the consumption of derivatives of codeine or opium. The term “substitution” echoes the term “maintenance” popularised in the late 1960s (Vincent P Dole & Marie Nyswander, 1965). It has gradually been associated with the term “treatment” and has come to be used in many institutional and scientific documents, especially under the abbreviation OST (opioid substitution treatment) or SBT (substitution-based treatment). It still appears in numerous texts disseminated by leading intergovernmental agencies, such as the EMCDDA and the WHO.

For a long time controversial among those whose work focused on stopping any consumption of opioids, whether prescribed or not, “OST” has over the years become a symbol of the success of risk and harm reduction policies. The term “OST” now strikes such a positive chord that it reduces the stigma once associated with it, but the fact remains that it conveys an erroneous understanding among the general public based on the replacement of a “street drug” by a “state drug”.

Coupling the word “treatment” with “substitution” is not sufficient to clarify the fundamentally medical-based nature of the “treatments” concerned. Opioid agonist medicines are prescribed with the approval of the medicines agencies following extensive scientific studies and robust pharmacovigilance processes. However, in the context of a dependence syndrome, the term “treatment” or “therapy” has been associated with numerous forms of intervention, both medical and non-medical, based in particular on moral, religious or purely law-enforcement considerations (see also 1.4), the strategy being to try to bring about behavioural changes linked to consumption rather than focusing on “treatment” with the aim of improving the health indices. The concept of “substitution treatment” therefore carries the risk of not being clearly included in its “medical treatment” dimension. The recent spate of deaths in North America linked to the consumption of diverted opioids illustrates this misunderstanding in the public debate about its causes, with prescribed opioids being confused with prescription opioids, which are diverted without being prescribed (Scholten, 2017).

For the non-specialised clinician, the term “substitution” frequently refers to alleviating withdrawal symptoms and/or dysphoria, and to the distinction between “controlled substance consumed in a non-medical context” and “controlled medicine prescribed on the basis of individualised clinical objectives”. However, it is necessary to consider other effects than the prevention of certain harm and the replacement of one molecule by another (Samet & Fiellin, 2015). This misunderstanding is made worse by a body of scientific literature that has in the past mainly focused on the impact on public health rather than on the clinical effects on the individual. There are effects specific to certain opioids, such as methadone and buprenorphine, that alleviate or suppress the hedonic effects of an additional dose of heroin. There are also significant effects bound up with the setting, such as supervised administration at fixed hours, fixed doses or very regular contact with professionals at the beginning of treatment based on guided self-observation (see also Section 1.5 and Appendix 2).

The term “substitution”, which is used in other contexts, such as the consumption of benzodiazepines, tobacco, cocaine or cannabis, covers very different clinical situations. For example, in the case of tobacco, nicotine “substitutes” are mainly used in helping people stop smoking or for the prevention of withdrawal symptoms when the environment temporarily prevents a person from smoking. Benzodiazepines and amphetamine derivatives, such as methylphenidate, are prescribed off-label on the basis of individualised clinical and ethical considerations. The term “substitution” has therefore been employed in the public debate about experiences in the regulation of sales of cannabis for recreational consumption.

For all these reasons, many researchers have expressed reservations concerning the use of the term “substitution” and have proposed various alternatives. In view of the most recent scientific publications, the terminology used in the draft WHO/UNODC document “International Standards for the Treatment of Drug Use Disorders” (UNODC & WHO, 2016) and the position taken up by the professional associations (Scholten et al., 2017), the working group has in the context of the present report opted for the terms “opioid agonist treatment” (OAT) and “opioid agonist medicines” (OAMs).

The language employed has an influence on stigmatisation, which itself impedes access to treatment

The use of certain terms tends to lay the blame for a substance-dependence syndrome on the shoulders of the individual being treated. This usage influences the perception of health professionals. For example, Kelly and Westerhoff (2010) have shown through a randomised study that clinicians presented with cases of “abuse” and “abusers” attributed greater personal culpability and more easily accepted the idea of punishing dependent individuals than those who heard references to a “substance use disorder” and “persons with a substance use disorder”. The language used constitutes one of the elements that shape and reinforce prejudices towards individuals with an opioid dependence syndrome.

The perceptions brought about by the terms employed are not limited to professionals. The words used also influence the public perception of an opioid dependence syndrome, which results in prejudices, stigmatisation and, ultimately, discrimination and exclusion. It is only necessary to think of the current use of such nouns as “drug addict” and slang terms like “junkie”, which reduce the person concerned to his/her behaviour and have negative connotations. Just over 20 examples of problematic terms used are mentioned in the glossary in Appendix 1 to this report.

The replacement of terms that disrespectfully reduce the person affected to his/her disorder is an integral part of other anti-stigma programmes in the field of mental health (Clement et al., 2015; Lauber, Nordt, Braunschweig & Rössler, 2006; Phillips & Shaw, 2013; Sun et al., 2014). It has been shown in connection with autism spectrum disorders or schizophrenia that the general use of terms that do not involve a moral judgment reduces discrimination and fosters access to treatments (Sartorius, 2007).

Ensuring the widespread use of terms that place the emphasis on the individual as a human being (person-first language), describe the dependence syndrome as a condition that affects health and consider OAMs as medicines therefore makes a direct contribution to combating marginalisation and exclusion and fosters access to treatment.

The use of descriptive, precise and standardised terms is conducive to the emergence of an interdisciplinary and international field of knowledge

The work to define and standardise terms used in the treatment of an opioid dependence syndrome, in each area of language, has a significant impact on vocational training and scientific research. This fosters the emergence of an interdisciplinary and international field of knowledge that, in turn, contributes via the media to the emergence of more descriptive, more neutral and more precise language by the users of the treatment system, by professionals involved on an ad hoc basis and, finally, by the general public.

However, whether a specific choice of words is appropriate cannot be determined with absolute certainty since it depends on who uses them and who hears them (see also Appendix 1 to this report). This means that there are variations between different sub-groups and professional networks. This difficulty particularly exists in the case of languages spoken by a very large number of people, such as the official languages of the UN (English, French, Arabic, Chinese, Spanish and Russian) and makes it easy to understand the efforts being made with regard to terminology, both in terms of processes and objectives: merely initiating and continuing a debate on the subject of terminology without precise standard-setting goals leads to often tacit conceptions current among users of these words. Secondly, the opening of structured discussions via the dialogue forums of the various stakeholders is part of a positive interdisciplinary process conducive to the establishment of a regular inventory of obsolete and/or problematic terms in regulatory documents. Bearing in mind the direct and indirect links between the choice of terms, science, and health, the promotion of such a debate ultimately appears closely bound up with the States' obligations regarding access to treatment in general and to OATs in particular.

Implementation in national contexts

5.1 Monitoring / evaluation

5.1.1 General framework for evaluating public policies

It is generally accepted that a public policy is based on a set of decisions, structures and actions initiated by the State or a local or regional authority. The resources allocated (which may vary in nature) enable services to be provided or new ones to be established by involving public, para-public or private stakeholders. The aim of a public policy is to achieve clearly defined basic objectives that seek to change the social situation to solve a problem or improve a situation. These objectives may be placed in order of their importance, for example by distinguishing primary from secondary aims, or staggered over time.

There is a broad consensus today on the need to carry out, in as systematic a way as possible, evaluations of public policies. This work may relate to several dimensions of the policy concerned, especially:

- the method of identifying the needs that a public policy seeks to meet
- the relevance of the policy's objectives in the light of the needs identified
- the level of resources granted
- the output – the relationship between the resources deployed and results obtained, or (efficiency ratio)
- the relationship between the results obtained or "outcome" and the objectives set (effectiveness ratio)
- changes to or elimination of needs established at the beginning (impact)

The assessment of each of these elements needs to be based on a set of indicators in order to make the judgment as objective as possible. The assessment of the impact of a public policy is the most complex task. For example, while it is relatively easy to measure an improvement in the accessibility of opioid agonist medicines (OAMs) or in the quality of treatments (which would be results obtained by a public policy), determining the actual impact on the groups concerned – and on society in general – makes it necessary to consider data on, for example, the vocational integration, housing and family situation of the individuals involved and those close to them.

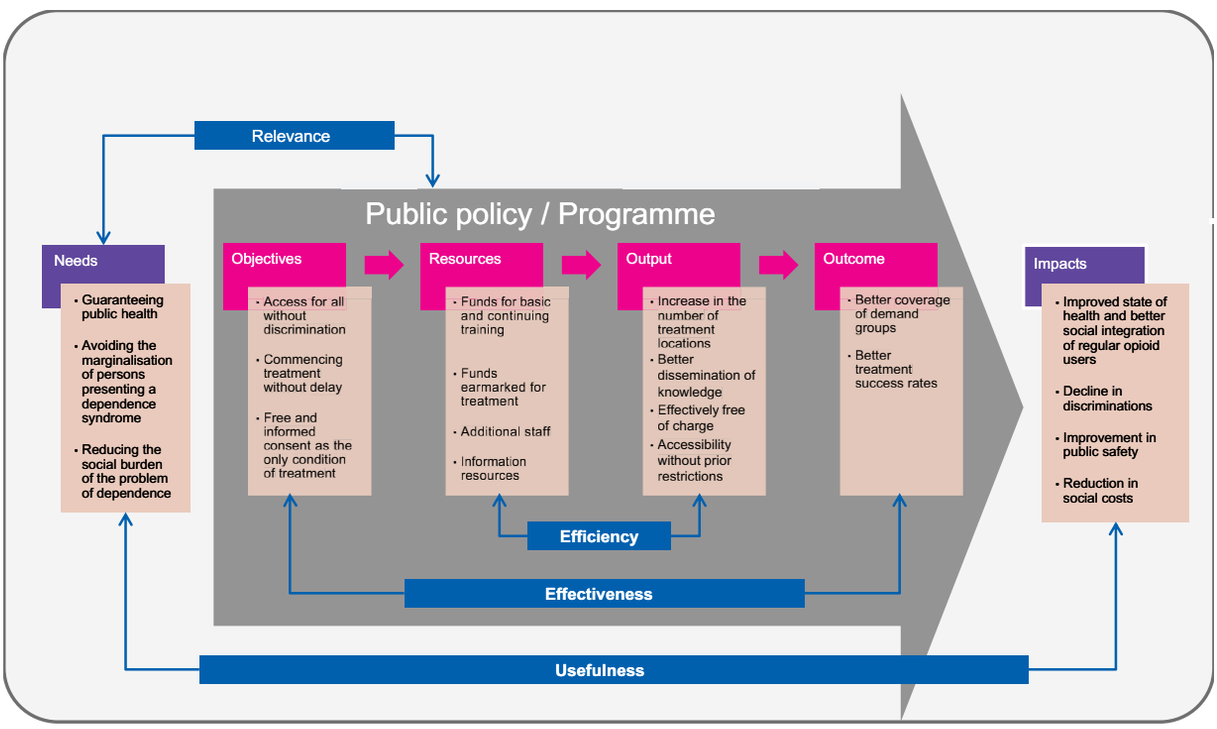
Ideally, the arrangements for making the assessment and the body responsible for carrying it out should be determined at the outset for each stage and each dimension, together with the actual formulation of the public policy concerned – and therefore before its implementation. The methodological discussion should preferably lead to making two central points clear:

- Firstly, the method of comparing the situation that prevailed without the public policy under discussion with the situation after its implementation. Multiple responses are possible, ranging from the local pilot scheme and the parallel implementation of two different schemes, with numerous variants, to the random selection of beneficiaries.
- Secondly, the weighting of the various objectives of a public policy and the means of quantifying them if necessary. This may, for example, mean weighting years in good health differently from years in a situation of invalidity or sickness and defining the figure obtained in monetary terms.

Figure 2 (below) provides a diagrammatic representation of such a process.

These considerations are very theoretical and the situation will differ considerably in practice. As pointed out in section 4.2.3 on the subject of a national consultative body, in most cases the assessment is designed to be an a priori evaluation and entrusted to individuals who will at best document only some of the work undertaken. Moreover, it is usual for state officials appointed to carry out the evaluation to have sectoral interests and this will have a significant impact on the choice of data analysed and putting them into context. It is accordingly important from the point of view of implementation strategies to have a broad overview of existing monitoring systems.

Figure 2 - Framework for the evaluation of public policies applied to OAMs/OATs



Sources and inspiration of figure 2:

International Organisation of Supreme Audit Institutions (INTOSAI) Guidelines on the Evaluation of Public Policies, doc. GOV 9400, July 2016, available at: http://www.issai.org/en_us/site-issai/issai-framework/intosai-gov.htm

Knoepfel P. et al, Analyse et pilotage des politiques publiques. France, Suisse, Canada, Presses de l'Université du Québec, 2015

Conseil d'analyse économique (CAE), "Évaluation des politiques publiques", Notes du conseil d'analyse économique 2013/1, available at the CAE website: http://www.cae-eco.fr/Evaluation-des-politiques-publiques.html

Desplatz R., Ferracci M, "Comment évaluer l'impact des politiques publiques? Un guide à l'usage des décideurs et praticiens", Guide published by France Stratégie, September 2016, available at the France Stratégie website: http://www.strategie.gouv.fr/publications/evaluer-limpact-politiques-publiques

Horber-Papazian K., "Le pilotage et l'évaluation des politiques publiques", presentation at the Autumn University of Swiss political stakeholders, 2010, available at the Graduate Institute website: http://graduateinstitute.ch/files/live/sites/iheid/files/shared/executive_education/Universite_Automne/2010/Katia_Horber_pilo.pdf

Jost S. & Aeby D., Audit de performance ou évaluation des politiques publiques. Comment choisir?, Expert Focus 4/2017, available at the Swiss Federal Audit Office website: https://www.efk.admin.ch/fr/publications/communication-institutionnelle/textes-specialises/1343-audit-de-performance-ou-evaluation-des-politiques-publiques-comment-choisir.html

5.1.2 Taking account of pre-existing monitoring systems

Origins of current monitoring systems

Monitoring of substance disorder treatment in most parts of the globe has to be seen within a wider historical framework of social developments of the substance disorders (e.g. substance disorders epidemics), events associated with these developments (e.g. significant drug-related mortality, HIV infections among people who inject substances, crime), as well as the historical development of substance disorder treatment systems in responding to these social and public health concerns. Although these developments may present fundamental similarities across the globe, it is important to realise that individual countries have responded differently according to individual and sovereign legal, social, economic and political perspectives. Some overarching international conventions and strategies have however led to convergences in this respect, which have also influenced the establishment of common epidemiological drug monitoring instruments and tools. For example, the adoption of the United Nations Conventions[23] has made it compulsory for member states to regularly report on the drugs situation as well as on interventions (EMCDDA, 2010a).

In this context, in 2000, an international expert meeting held in Lisbon led to the adoption of a common reference framework for data collection and monitoring shared by international and supranational organisations, called the Lisbon Consensus.[24] The Lisbon Consensus identifies a number of areas of strategic/policy interest which are monitored using a range of tools and formats, by all supranational and international organisations. Each regional or international drug monitoring network has developed its own model taking into account its specific needs and its institutional environment, but the core data remain the same. In the EU, a reference framework for monitoring the drugs phenomenon including treatment developed by the European Monitoring Centre for Drugs and Drug Addiction is translated into a unique regional data collection network that relies on harmonised and standardised national data collection from national focal points or national drugs observatories (NDOs). In this context, the neutrality and independence of NDOs is paramount for carrying out state-of-the-art data collection and provide factual information necessary for informed policy decisions on the actions and impact of national drug strategies, including the impact of treatment systems. Further information on how to set up NDOs and its tasks is described in Building a national drugs observatory: a joint handbook (EMCDDA, 2010).

National drugs observatories are responsible for covering two main areas through their routine data collection: ‘monitoring the drugs situation’ which covers epidemiology, crime and markets, and ‘monitoring responses’ which covers interventions, law and policies. Selected indicators from these two main areas can provide States with the necessary tools to evaluate their healthcare systems responsible for treating dependencies (Indicator 17.1 in this document: healthcare system, healthcare provision and outcomes). Such evaluation comprises routine monitoring through:

- structural indicators regarding the regulatory measures and the availability of healthcare facilities, necessary medicines and trained professionals needed to provide treatment;
- process and coverage indicators for meeting the needs for access to care (non-discriminatory access, prompt and uninterrupted for anyone within the territory with a diagnosis of opioid dependence syndrome, who has consented to treatment); and relating to the quality of healthcare, and professional knowledge (whether they are specialists or involved on a timely and occasional basis);
- outcome indicators on treatment retention and completion, mortality, morbidity and comorbidity, as well as quality of life.

23 These are: the United Nations Single Convention on Narcotic Drugs, 1961(http://www.incb.org/pdf/e/conv/convention_1961_en.pdf); the United Nations Convention on Psychotropic Substances, 1971 (http://www.unodc.org/pdf/convention_1971_en.pdf); and the United Nations Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances, 1988 (http://www.unodc.org/pdf/convention_1988_en.pdf)

24 The full document can be found on the UNODC website at the following link: http://www.unodc.org/pdf/drug_demand_gap_lisbon_consensus.pdf

5.1.3 Availability, utilisation and access to OAT (structural, process and coverage indicators)

Data and information on the following indicators are necessary to properly monitor and assess treatment availability at national level (structural information) and thereby evaluate national health systems responsible for the treatment of opioid dependence syndrome, including OAMs:

Institutional framework

- Policy (National strategic goals and objectives with regard to treatment, including OAMs);
- Organisation
- Institutions, bodies, organisations, involved in the main areas of drug treatment provision
- Financing or funding of drug treatment

Availability and access

- Availability of main (or most common) treatment arrangements by outpatient and inpatient setting (including in custodial settings) as well as number of people receiving drug treatment by setting (see Figure 3 below).
- Availability of main OAMs
- Availability of target group specific treatments (e.g. gender-specific programmes)
- Utilisation of treatment:

  • Number of people who use opioids receiving (any kind of) substance treatment (across treatment settings and arrangements)

  • Number of problem people who use opioids receiving OAMs. These data are in most countries based on data collected through national registers of individuals receiving OAMs. In some countries where national registers are not available, these data are based on estimation methods, e.g. estimates based on pharmacy sales or reimbursement from national health insurance funds. The establishment of a national monitoring system and/or a national register of individuals receiving OAMs is a way to prevent double-prescription and diversion of the prescribed substances in many countries. While specialised treatment agencies are more likely to be covered by such registries, under-reporting is likely when clients are treated by private medical physicians (e.g. general practitioners). In this case, estimation methods based on, for example, pharmacy sales or health insurance reimbursements can be carried out.

- Access to OAMs:

  • Legal frameworks of OAMs should be documented and regularly assessed as to whether they create barriers to accessing OAMs (see ATOME recommendations)

  • Costs to clients of OAMs (by medication) and of any mandatory intervention (e.g. consultations, counselling) associated with the prescription of OAMs. A basic assessment of the overall out-of-pocket cost for a person in treatment can be performed by calculating the monthly OAM treatment as a percentage of the minimum national income.

  • Waiting times to initiate OAM (at national and local level)

  • Geographical coverage of OAM providers (count) according to needs: For example, number of prescribing physicians per person who uses opioids in a problematic way in need of treatment and per number of OAM treated persons at local, regional and national level.

  • Coverage of the target population (Total OAM treated persons/ estimated number of person who uses opioids in a problematic way). In order to assess whether the current OAM system at regional and national level is adequately reaching the target population and thereby assess whether there are barriers for the target population to access this treatment, it is important to determine the OAM coverage of the target population (see Figure 1 in the “Executive Summary” above). In this way, the number of individuals receiving OAMs on a given day or during a reporting year as a percentage of the estimated number of person who uses opioids in a problematic way should be determined. This calculation should make it possible to determine whether the coverage of OAM is below or within the coverage recommended by international standards (e.g. WHO). Coverage levels of OAMs below 30% should be considered as low, between 30% and 50% as medium and above 50% as high. See the next point for further information on treatment

needs. Additionally, the calculation of the coverage of OAM of the target population may include data on the total number of person who uses opioids in a problematic way receiving any kind of treatment. These estimates provide an indication of the proportion of problem opioid users receiving other treatments than OAT as well as the proportion of person who uses opioids in a problematic way out of treatment (see Figure 4 below).

It should be noted that the scope of treatment monitoring mechanisms within the individual national treatment systems is a major determinant of the quality of treatment data. If large proportions of the system are not covered by monitoring or reporting systems, conclusions on capacity, coverage and performance are difficult to draw, unless a validated methodology to estimate the missing parts is available. When reporting on numbers of clients receiving OAMs in a given year, cases of detoxification treatment should be excluded and reported separately.

Assessing treatment needs

The EMCDDA uses five key epidemiological indicators that have been developed by the Centre in close collaboration with the Reitox network, experts across Europe and with other international organisations competent in the field of psychoactive substances and psychoactive substance dependence syndrome, such as the Council of Europe's Pompidou Group. These indicators underpin the EMCDDA's reporting on trends and developments in the EU drug situation. They are also used for the analysis of the coverage of responses and the assessment of the impact of policies and interventions.

Two epidemiological indicators (Key Indicators) are of direct relevance for the assessment of needs in relation to provision and coverage of OAM, while key indicators on drug-related deaths (DRD) and drug-related infectious diseases (DRID) are relevant epidemiological indicators to assess the impact of OAT and indirectly the need for OAT (prevention of drug-related deaths and infections).

Treatment need is defined by the EMCDDA as the size of the population (or the number of people in a population) in need of specialised treatment on account of their use of psychoactive substances. It is estimated for policy or programme planning and evaluation purposes.

As psychoactive substances users are a population group which is partly hidden due to the lack of social acceptance and the illegal nature of the possession/consumption of those substances, the size of their population cannot directly be measured; it can only be estimated. In addition, estimates by injecting status, gender, age, substance, etc. can provide additional core information on their specific treatment needs. Data from treatment monitoring systems, complementary estimates of the number of clients in treatment and estimates of the need for drug treatment can be combined to estimate treatment coverage. Moreover, multipliers obtained from studies of treatment access among drug using populations can be directly used to describe treatment coverage in this group.

Problem drug use, including problem opioid use

This key indicator collects data on the prevalence and incidence of High-Risk Drug Use (HRDU) at national and local level. "Problem drug use" is defined as 'injecting drug use or long-duration/regular use of opioids, cocaine and/or amphetamines'. As this population group is hidden and difficult to access, this indicator builds on a range of indirect methods that use different existing data sets to extrapolate and produce an estimate of the number of persons who use drugs problematically. One relevant sub-indicator of the HRDU indicator is the High-Risk Opioid Use (HROU) which can be utilised to assess the coverage of particular treatments, especially OAMs, at local or national level (See point above regarding measuring coverage of OAM among the target population).

The data sources employed to calculate the estimates differ in each country and are dependent on the routine information systems used in the country. The methods used to produce prevalence estimates are based mainly on statistical models using drug use related indicators and include mainly:

- a simple multiplier method using police, treatment, mortality or HIV/HCV data, etc.;
- capture–recapture methods;
- extrapolation via multivariate indicator methods

Treatment demand indicator

The treatment demand indicator is used to describe the population of people who use psychoactive substances entering treatment each year and the number continuing in treatment from one year to the next.

In some cases, treated populations are used as a basis to estimate treatment need. This approach has to consider that only a selection of people who use substances in need of treatment enter treatment and that therefore numbers and characteristics are not exactly mirroring the substances users group as such. Besides estimating the overall treatment need, it may be just as important to stratify these treatment need estimates by certain subgroups with different characteristics and needs. Existing estimates by injecting status, age, gender and primary drug are scarce. Monitoring of characteristics of substances users outside of treatment helps to find barriers to treatment.

Drug-related deaths (DRD) and mortality among people who use drugs

The aim of this indicator is to obtain statistics on the number and characteristics of people who die directly or indirectly as a consequence of drug use. Drug-related mortality is a complex phenomenon, which accounts for a considerable percentage of deaths among young people in many countries. This epidemiological indicator has two components: deaths directly caused by controlled psychoactive substances (drug-induced deaths) and mortality rates among people who use substances in a risky manner. These two components can fulfil several public health and methodological objectives, notably as an indicator of the overall health impact of drug use and the components of this impact, identify particularly risky patterns of use, potentially identify new risks, and also assess indirectly the impact and quality of drug treatment systems, including OAT.

Drug-related infectious diseases (DRID)

This key indicator collects data on the extent (incidence and prevalence) of DRID — primarily HIV, hepatitis C and hepatitis B infection — in particular among people who inject psychoactive substances. The data is collected on people who inject psychoactive substances each calendar year using two main methods. These are: (a) surveys of people who inject psychoactive substances that include serological testing and (b) the monitoring of routine diagnostic testing for new cases of HIV, hepatitis C and hepatitis B infection among people who inject psychoactive substances. According to the situation outside Europe, it may be necessary to collect data on other infectious diseases that are related directly or indirectly to psychoactive substances use or people who use them, such as tuberculosis and sexually transmitted infections.

Treatment quality and outcome indicators

Services are expected to fulfil basic quality requirements in terms of providing care to their clients. In addition, the quality of treatment can also be improved by certain processes (e.g. training of staff) and through feedback from outcome evaluations. Treatment outcome can also be indirectly assessed by epidemiological indicators such as mortality and morbidity among the target population.

Minimum indicators in terms of OAT quality and outcome:

- Retention in treatment (e.g. months in OAT)
- Completion of treatment (successful discharge)
- Mortality and morbidities among people who use opioids non-medically in the population and among persons in OAT (see point above regarding DRD and DRID)
- Social integration indicators: stable housing; paid employment; access to education and vocational training.

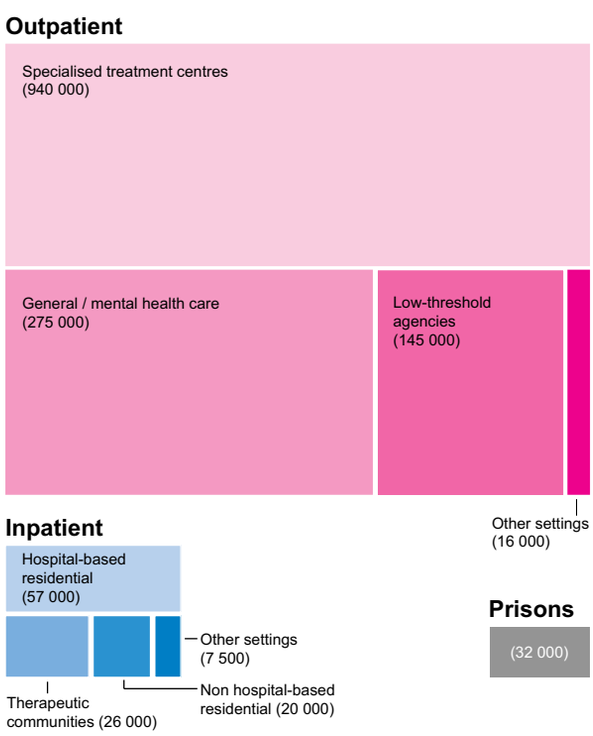
The indicators to be collected and the corresponding data must be made public. The data collected should also be made available to researchers, according to the common ethical standards related to consent and the protection of personal data. It is crucial for institutions, such as national drugs observatories, to establish and make publicly available their internal statistics codes of practice in order to ensure a sound quality

assurance framework for the statistical procedures employed by the institution (see for example: EMCDDA internal statistics code of practice).[25] In order to make data publicly available, NDOs should publish a yearly national report on the drugs situation in their country (or regional reports) as well as presenting the data as national overviews (see Figure 5 below) and in tabulated format (See Table 4 below) on their websites.

5.1.4 Data protection

While data on the number of clients receiving OAM and other indicators to be collected and the corresponding data mentioned here should be made public and available to researchers, it is of utmost importance that clients have the right to privacy. Client data should therefore be collected according to the common ethical standards relating to consent and the protection of personal data. Client data regarding OAM should primarily be utilised for the purpose of assisting practitioners in their daily practice and assessing the clients' therapeutic progress. At a systemic level, client data is necessary to evaluate the process, quality and impact of OAMs. In this respect, central registers of clients can be considered as it supports the prevention of double prescribing at a systemic level and provides more accurate data on clients as it reduces the risk of double counting. However, central registration of clients requires assurance of confidentiality to the clients. According to WHO recommendations, central registrations of clients on OAM can facilitate breaches of privacy and thereby deter people in need of this treatment to access it. WHO recommends that it should be contemplated only if government agencies have effective systems in place for maintaining privacy (WHO, 2009). Unique client identifiers should provide the possibility to accredited governmental agencies of detecting double prescribing, but not the possibility for third parties (law enforcement, researchers) to identify the identity of the clients. The inter-linkage of datasets (e.g. other health registries) should also comply with common ethical standards and be subject to the consent of the clients. An independent ethical committee overviewing the processing of the registry and authorising the usage of client data may be considered.

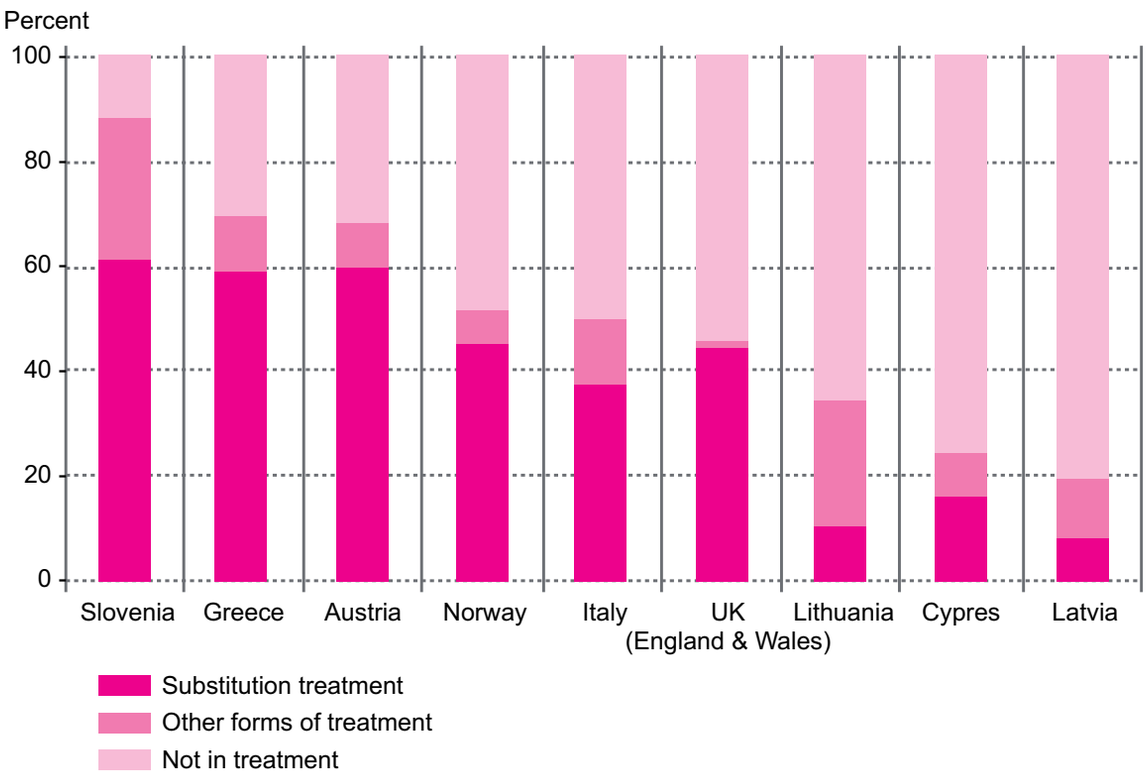
Figure 3 – Number of persons in Europe being treated for substance-related disorders, by setting



Statistical Bulletin 2017 - health and social responses, EMCDDA, 2015. http://emcdda.europa.eu/data/stats2017_en

25 http://www.emcdda.europa.eu/publications/manuals/statistics-code-of-practice

Figure 4 – Proportion of "high-risk opioid users" receiving treatment



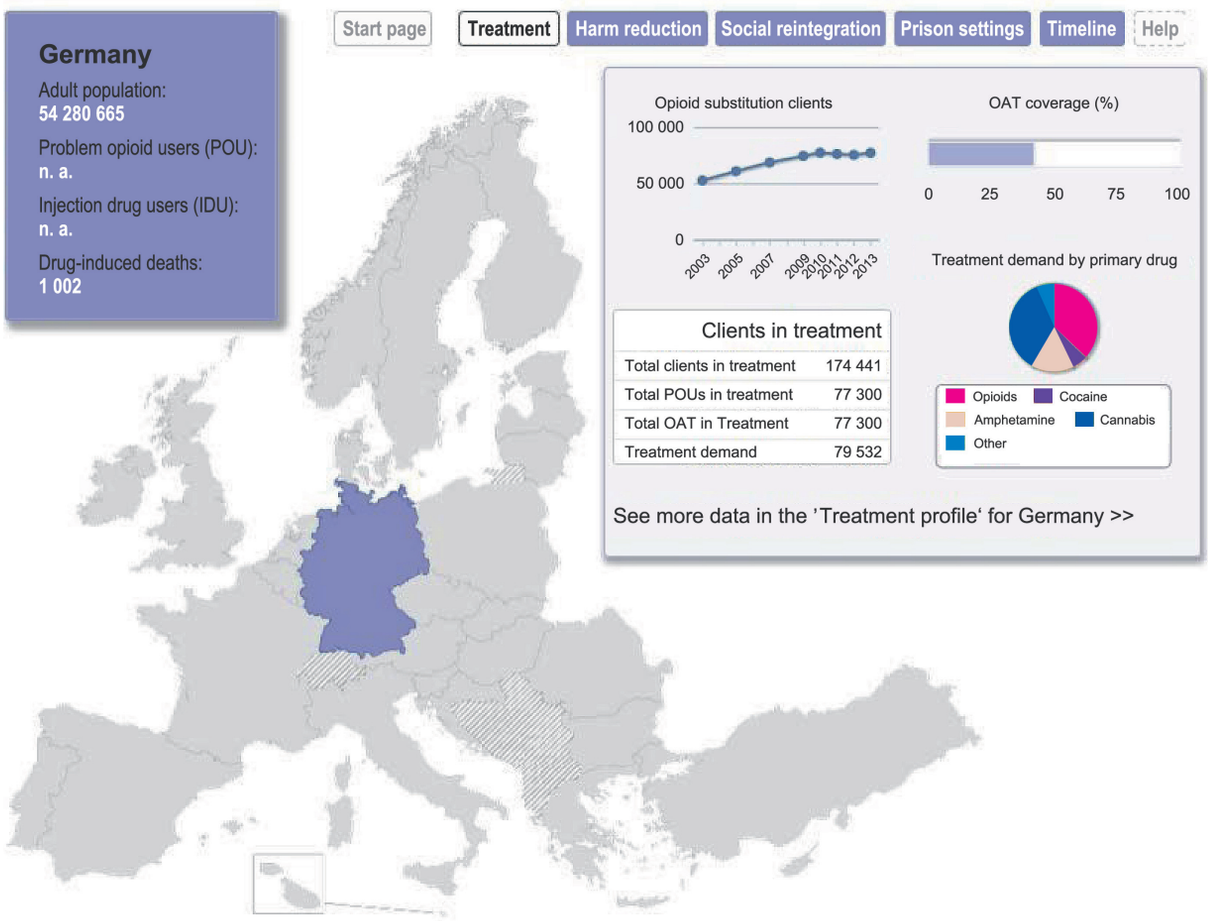
EMCDDA, 2016

Table 4 - Examples of the tables of data available on the EMCDDA website

country	year	Number of methadone clients	methadone share	Number of buprenorphine-based OAT clients	buprenorphine-based OAT share	All OAT clients
Austria*	2014	3599	21%	3784	22%	17272
Belgium	2014	15213	89%	2471	15%	17026
Bulgaria*	2014	3277	96%		0%	3414
Croatia	2014	1999	29%	2244	33%	6867
Cyrus*	2014	33	19%	110	62%	178
Czech Rep.	2014	694	17%	3300	83%	4000
Demnark	2011	6200	82%	1400	18%	7600
Estonia	2014	919	100%	0	0%	919
Finland*	2011	931	38%	1508	62%	2439
France	2014	59467	37%	104975	65%	161388
Germany*	2014	59210	76%	17515	23%	77500
Greece	2014	2631	26%	7595	74%	10226
Hungary	2014	576	77%	169	23%	745
Ireland	2014	9764	100%		0%	9764
Italy*	2014	68385	90%	7579	10%	75964

EMCDDA Statistical Bulletin, 2016 www.emcdda.europa.eu/data/stats2016#displayTable:HSR-3-3

Figure 5 - Example of the country fact sheets available on the EMCDDA website



5.2 Considering the combined effects of the guiding principles

The guiding principles outlined in this document describe the optimum framework conditions for the prescription and delivery of OAM. The principles are broadly interdependent and form a coherent whole, describing their aims and the requirements for their implementation.

With a view to preparing national strategies, this section investigates succinctly how the implementation of each of the recommendations presented above helps specifically to move the framework conditions towards compliance with the guiding principles. While it is impossible in practice to bring a given system into line with this entire set of standards in one sole movement or in a single reform, any change, even if only sectoral, sets in motion a process which goes beyond its formally stated goal. In other words, if the guiding principles are coherent, any partial implementation must imply full implementation in the long term or at least the realisation that other reforms will be needed.

In the introduction to Chapter 4 it was explained why the authors of this report considered it necessary to place emphasis on four key recommendations.

Key recommendation 1

Prescription and delivery without prior authorisation schemes

The main positive influence of the implementation of this recommendation is on free access to treatment (Principles on sections 4, 5, 6 and 7). It strongly encourages the start of treatment without delay (Section 8), considerably reduces the risk of discrimination in access to treatment (by increasing the number of access points) or discrimination due to the fact of receiving treatment (by extending competence to administer such treatment to all physicians) and helps to ensure continuity of care even where there is a change in the place of treatment (geographical change or change in the type of treatment establishment).

The lack of specific authorisation schemes presupposes an acknowledgment of a right to access to OAMs equal to that of access to any other form of care, as part of the right to the highest attainable standard of health recognised by international conventions (Section 5). The possibility for all professionals to prescribe and deliver these medicines without specific restrictions or prerequisites helps to secure this right within the general limits set out in chapter 1.3.

Reducing the administrative work required to obtain the necessary authorisations to prescribe or deliver OAMs simplifies the daily lives of the professionals involved. In practice, implementing this recommendation brings about improved respect for proportionality between the nature of OAMs and the specific arrangements applying to them (Sections 12 and 14).

In addition, the application of this recommendation contributes to better integration into the basic training of all practitioners of the knowledge and skills required to prescribe and dispense OAMs (Sections 10 and 11). Lastly, it will make it all the more useful and necessary for there to be a national consultative body (Section 18) capable of defining good practices, conveying the results of scientific research and helping to assess care systems.

Key recommendation 2

Effective removal of financial barriers

The removal of any form of financial obstacle to access to care is also an acknowledgment of the right to treatment of all persons who may be diagnosed an opioid dependence syndrome (No. 4). It also helps to reduce the risks of discrimination in access to treatment (No. 5) by eliminating one of the possible causes of this discrimination (the selection of persons being treated to be admitted depending on their solvency). Unlike the preceding recommendation however, whose aim is to subject the prescription and delivery of OAMs to the general rules in force and hence to standardise them, the effective removal of financial barriers will, in many contexts, call for the establishment of a specific mechanism applying only to this type of treatment. This special approach will not, however, be determined by the nature of the medicines concerned but by that of the target public, who are often on the margins of society and cut off from administrative and health systems (Nos. 2 and 3).

It is possible that the effective removal of financial barriers will facilitate the start of treatment without delay once the indication has been determined and will limit risks of interruptions in treatment when there is a change of place of care (No. 8). Indirectly, the existence of specific financial rules applying only to OAMs is also particularly beneficial for research and innovation in this field, especially where it comes to ensuring continued improvement in the effectiveness of treatment (No. 16). Lastly, the acknowledgment of the distinctive nature of OAMs from the public health viewpoint mentioned above is one of the prerequisites for the establishment of a dedicated national consultative body (No.18).

Key recommendation 3

National consultative body for coordination and monitoring

Fundamentally, the existence of a national consultative body for the coordination and follow-up of treatment involving OAMs assumes that the specific public health features of opioid dependence syndrome are recognised (Nos. 1, 2 and 3). At the same time, the tasks of such a body, which are to solve the problems raised by the special rules governing OAMs, may be partly reduced in scope as the framework conditions fall closer into line with those described in the Guiding Principles.

In the long term, having a specific body has effects in the different areas of recommendations 1 and 2. The activities of such a body have a positive influence, mainly affecting the development of healthcare systems, the evaluation of treatment monitoring systems (No. 17), promotion of scientific research (No. 16) and international collaboration (No. 19) through its role as an interface between experiences on the ground and changes in knowledge deriving from research.

More immediately, as forums for exchange, such a body naturally has a positive effect on cross-disciplinary issues such as the use of neutral, non-stigmatising terms in keeping with scientific knowledge (No. 1) and the acquisition of interdisciplinary skills by professionals (No. 9). At the same time, their position at national level, with representatives from various sectors, makes it possible to follow up more effectively on complex issues such as the actual availability on the market of the medicines needed for treatment (No. 13) and the establishment of a specific free treatment scheme (No. 15). Lastly, recognising the contribution of those working in the care chain through proper pay for their activities relating to opioid dependence treatment helps to guarantee adequate care provision.

Key recommendation 4

Neutral, precise and respectful terminology

The use of unambiguous, neutral, non-stigmatising words and expressions has a global impact on the realisation of the guiding principles. In effect, the terminological changes reflect and embody the paradigm change proposed by the guiding principles: by applying the rules of language which have prevailed in other areas to OAMs we help to ensure that they are regarded as an integral part of the ordinary social and healthcare system. When persons in treatment are regarded as human beings suffering from a dependence syndrome and not as individuals reduced to their behaviour or their legal status, and OAMs are seen as medicines for the treatment of a syndrome not “substitutes” for an illegal drug, access to care has already made a great step forward in conceptual terms. Avoiding the use of stigmatising terms also helps to reduce discrimination against persons receiving treatment, as well as professional practitioners (Section II of the Guiding Principles).

Furthermore, the existence in each language area of unambiguous terms in keeping with scientific knowledge and clearly established correspondences between languages is a prerequisite for international exchanges relating both to practices and to scientific knowledge (No. 19).

5.3 Building a national strategy

Key messages:

Regulations on OAMs that comply with the guiding principles have substantial effects on access to care, quality of treatment, professionals' attitudes to this form of treatment and the persons receiving it.

When the opportunity arises to create such a regulatory framework, it is important initially to understand the complexity of these effects and the interactions between them. The aim of this report is to highlight the various facets involved.

Any appropriate strategy must be based on in-depth investigation of the national context. There is no such thing as a standard "one-size-fits-all" strategy.

This investigation should be carried out with all the partners concerned to ensure that it is interdisciplinary and inter-institutional.

The resulting project must take a long-term view and be conducted in a flexible manner so that it can be adjusted to any societal opportunities that may arise. It must be followed-up by a national consultative body.

In terms of content, it should be possible to implement one key recommendation or another depending on the societal context and the institutions or persons in charge of carrying out the project. The project group and/or the national consultative body should be responsible for bearing in mind that the guiding principles must be implemented in a coherent and balanced manner.

In most countries, the prescription of OAM for the treatment of opioid dependence syndrome is subject to legal restrictions, linked among other things to the international system for the control of psychoactive substances. Many of the resulting regulations restrict access to these medicines and to care, such as prior authorisation schemes for treatment.

To comply with their health obligations, and particularly everyone's right to access to essential medicines, the States are invited to amend their regulations, basing themselves as much as possible on ordinary provisions regulating the medicines market and health professionals in the light of these guiding principles.

The aim of this section is to provide some strategic courses of enquiry for the dissemination and implementation of these guiding principles and the four key recommendations.

5.3.1 National regulations: a feature of society

It should be recalled that according to the EMCDDA, of the estimated 1.3 million regular users of opioids in Europe, nearly 650 000 are now prescribed opioids (EMCDDA, 2016).

Average coverage rates hide very wide disparities. Whereas coverage rates in some countries approach 80%, others lie below 20%, and some countries continue to rule out such prescriptions in law or in practice. There are also regional disparities, particularly between urban and rural areas, and disparities among populations already at risk of discrimination such as women, minors, migrants or detained persons.

Despite the scientific evidence and the guidelines drawn up by international health organisations (WHO, 2009 and 2011), political and state authorities are reluctant to integrate the resulting consequences and devise an appropriate legislative and administrative framework for OATs. The reasons probably lie in the mistaken ideas connected with this form of treatment, which are widely elaborated upon in this report (see for example Chapter 4.2.4). This is a feature of society, which should simply be taken into consideration. The strategic considerations and practical measures outlined in the following three chapters must take account of this and provide pointers to devise a strategy for change, which cannot be anything other than flexible and subject to long-term development.

5.3.2 General considerations

As national contexts are specific and every country is at a different stage in the implementation of OATs, ranging from the first steps in the conceptualisation of a national programme to long experience with several OAMs available, there is no such thing as a standard “one-size-fits-all” strategy.

Initially it is important to build up an overall picture of the complexity of the problem and its ins and outs. The aim of this report is to clarify the various facets of the problem and their interactions and interdependences. Chapters 4.2 and 5.2 give examples of the combined effects of the four key recommendations which were identified because of their potential amplifying effect. They are the ideal starting points from which to launch a revision, and this is a very important aspect to bear in mind during this process.

Stakeholders wishing to promote or set up a regulatory framework in line with the guiding Pprinciples set out in this document – whether through the adjustment of existing regulations or the introduction of new legislation – may occupy very different positions in the social fabric. When devising and implementing this strategy of change, it is imperative that they take account of this position. On the one hand, it will determine their legitimacy to act and on the other it will direct them towards one strategic option or another, for example, by choosing to intervene, as a priority, using one or other of the four key recommendations.

The project to devise or amend the relevant regulations should be seen from the outset as an interdisciplinary project, making it possible to take into account the views of the various social bodies involved and the constraints of their various fields of intervention.

Lastly, such projects must be seen as long-term projects, whose stages are dictated pragmatically by the possible steps forward in the light of the current national political, social, economic and cultural context. The guiding principles have been devised overall as ideal objectives which should be held in mind throughout the process. Each country will follow its own path to reach the goals it has set itself. The aim is to devise a realistic project, based on an in-depth assessment of its complexity and the politico-cultural and socio-professional context. The most important thing is to maintain a flexible and proactive approach over the long term and hence to be able to grasp any opportunities that arise in order to move forward pragmatically, step by step.

5.3.3 Assessment of the context

In preparation for the project, a systematic assessment should be made of the initial situation in the country. Here are a number of example questions, which may help with this assessment:

- Who are the partners that can be relied on to support the project in the country and what aspects of the problem are they concerned about or what arguments are they particularly receptive to?
- What knowledge or sources of knowledge are available to support the arguments?
- Who are the potential partners at international level in the form of political, administrative or academic bodies or NGOs?
- Which national or international partners, including the most representative community organisations, can be called on to share their experience in the subject area?
- Who are the key persons in these organisations?
- How do we establish a common line of reasoning for the entire network of partners?
- How do the procedures for the preparation of laws and regulations work?
- How do the procedures for the accreditation and control of medicines work?
- What administrative bodies play a crucial part in this?
- Who are the key individuals involved?

- Is there a national body tasked with monitoring controlled substances policy and, if so, what is its remit and who are the members?
- Are there bodies representing representing people who use psychoactive substances?
- What are the various medical bodies concerned by OATs?
- What research and survey institutes could be interested in OATs?
- Which key bodies and individuals are against OATs and what are their positions and arguments?
- Which of the four key recommendations has the most chance of being implemented?
- Which of the project partners have the greatest legitimacy to act in the national context?
- If a process of construction or adjustment of the legal framework is launched, who will be involved in the project? Is it possible to be part of this process or to follow developments closely so as to be in a position to intervene if the options chosen seem to be at variance with the guiding principles?

When the answers to these questions have been collected it will be possible to prepare a project based on the strategy which has emerged from the discussions and has attracted a consensus among the partners. To devise and run the project itself, it is recommended that the working methods developed for project management be followed.

5.3.4 Moving from strategy to practical measures

Clearly, the project will differ completely in nature depending on whether it is carried out by a state body which has received instructions to adjust or draw up a law or an implementing regulation, or is launched by an NGO, which must begin by raising awareness among political and administrative bodies to give an appropriate legal status to OATs.

The experts involved in the TDOLEG project (see Appendix A5) and the permanent correspondents of the Pompidou Group and MedNET are important resource persons, who can be consulted during the preparatory stage of the project. The countries from which they hail cover practically all the possible scenarios when it comes to the implementation of OATs.

Here are some examples of practical measures which could be taken to launch a process of change and translate it into a project, divided into five areas: research, awareness-raising, training, legislation and terminology.

Research

During a preparatory stage it is important to have reliable data to present to the ministries concerned (generally the ministries of health and justice) or by the latter to political bodies. If there are no such data for the country, the focus should be on the implementation of a research or survey project whose results must clearly centre on the strategic issues identified. The process of establishing the contours of the research design is an opportunity to bring together the persons concerned to involve them in the project. Such involvement is crucial for change to result.

The current project has shown that to date there has been a lack of interest on the part of researchers in the impact of the legal framework and a public policy on the effectiveness and efficiency of OATs. It is essential to launch research and evaluation projects on this subject.

Awareness-raising

Awareness-raising is generally the first step that needs to be taken and it is important to begin by identifying the bodies and actors who are directly or indirectly concerned. The aim of the information to be provided is to disseminate the latest scientific knowledge, to combat the prejudice and untruths conveyed by the social group in question, which shape its attitude, and ultimately to develop a receptive, open and constructive approach towards OATs.

Here are some examples of ways of raising the awareness of the persons and bodies being addressed.

All or part of this report should be disseminated during presentations to national and international colloquies, symposiums, conferences, workshops etc. It is worth systematically finding out the dates and venues of such events and thinking about who would be the most appropriate person to convey the desired message (legitimacy of the speaker in the eyes of the target audience). The form of the presentation should of course be geared to the type of event. It may include PowerPoint presentations and posters summing up the key features, thematic factsheets focusing on particular target audiences and geared to their work culture, clinical scenarios designed to be discussed in workshops, etc.

Awareness-raising can also be carried out by publishing articles in the academic or specialist reviews of the various target audiences and also through articles in the non-specialist press when, for instance, events are reported which illustrate the pertinence of the guiding principles. Account will also be taken here of the principle of choosing the best placed person to address the target audience.

Convergence in the means used will gradually instil a new attitude towards the relevance of the key recommendations and the guiding principles set out in this report.

One example of an important awareness-raising forum which we can look at in more detail is a national symposium. Such symposiums can play a major role, their main objective being to mark milestones in slow societal processes, for example those relating to attitudes to opioid dependence syndrome. By bringing together the various professional stakeholders concerned, symposiums make it possible both to present the current scientific evidence in the various disciplines in question and to hear different viewpoints such as those of street educators, police officers, health professionals, social workers and government legal experts. As a result, each professional body feels recognised and accepted, which is a prerequisite to getting it to participate in a process of change. Such events can also afford an opportunity to alert these professionals to what is being done in other countries which already have some expertise in the matter. By way of example, an event of this sort was held in April 2016 in Algeria, which did not yet have any OAT programmes.

Symposiums of this type play an important part in laying the foundations for new attitudes towards this form of treatment. An effort should be made to choose participants with the greatest possible scientific, political or professional legitimacy among the participants. For example, at the launch of a research project which was to be conducted alongside the establishment of the prescription of diacetylmorphine/heroin in Switzerland, a UK police officer was invited and asked to talk to his Swiss counterparts about the attitude that a municipal police force could adopt to the prescription of pharmaceutical heroin, which was a long-established practice in the United Kingdom. In the area of institutional communication, it is a fact that the person conveying the message is just as important as, if not more important than, its content.

Symposiums can also be useful in countries which have had OAT for many years. It should never be underestimated how much weight can be attached to long-established professional practices, which can prevent new views from emerging in fields of activity which are considered, rightly or wrongly, to have been mastered. How many national or international symposiums have been held by NGOs or state bodies on the impact of regulations on OATs? How many of these events bring together stakeholders in the field social and medical workers, members of the public health and medicines control authorities, legal experts, physicians, sociologists and police officers? How many colloquies on the subject of OATs are designed to break down occupational barriers and the participants' patterns of thinking? While it is understandable that the legal framework is regarded as a fixed component of this system, it should also be questioned and reviewed regularly to check that it is still relevant.

Training

Somewhere along the line between awareness-raising and training lie study visits. Such trips may be arranged for parliamentarians, members of government, members of the authorities or professionals, and programmes should be framed accordingly. Morocco, for instance, sent several delegations of professionals to France and Switzerland when it began training its first teams of health practitioners for its newly established OAT programmes. Irrespective of the knowledge conveyed at whatever level, such trips make it possible to forge solid professional ties and the experts encountered are a key resource which can always be called on.

The prime objective of further training is to pass on new knowledge and skills. The training courses held annually by the Pompidou Group for policy makers are an ideal forum in which to reach out to the management staff of national administrations and promote exchanges between them. Dedicating such a training course to a discussion of the implementation of the four key recommendations and the Guiding Principles should make it possible to lay the foundations for an in-depth investigation in the national administrations concerned. Taking such an approach makes it possible to highlight many aspects of a country's drug policy. This type of training model has proved its worth in Europe and could be taken up in the framework of MedNET for example.

It is also possible to act through the various levels of the national education system, whether at undergraduate, bachelor, masters or postgraduate level, or through further education courses (Certificate, Diploma and Master of Advanced Studies (CAS, DAS and MAS)). The main issue here is to identify training providers and content to determine where it is possible and strategically important to include the subject of OATs and the relevant regulations. As it can be addressed from so many different angles, the range of courses into which it can be incorporated is very wide. Working at the training level is strategically important to give legitimacy to the content. Being dealt with in a basic course in one occupational branch or another or a specialised or masters course affords a different type of legitimacy to the prescription of opioids in general than simply being taught on a professional association's further training course. This does not in any way imply that one is more worthwhile than the other. It is all a matter of context and opportunity. At any rate, over and above the dissemination of knowledge, it is essential to devote time to the question of the participants' attitudes to OATs and the persons to whom they are administered. A module on terminology issues is particularly appropriate in this respect.

Legislation

Many countries have gained long experience in OATs, and their legal and administrative framework has been partially amended. The Guiding Principles make it possible to launch a process of adjustment of this legal framework with the goal of gaining an overall picture of the various aspects of its impact on OATs. To launch this process, and before deciding what the aims of the new regulations will be, it is recommended that the first step be to investigate the effects of the various articles of the law, not only on treatments but also on professionals' and treated persons' attitudes. This process should take place within an interdisciplinary framework bringing together the legal experts tasked with drawing up the new legislation and the various state and medico-social partners involved in the treatment system. All socio-professional groups are profoundly marked by their work cultures and questioning their approach should make it possible to construct a more coherent system, whose ultimate aim is to facilitate access to care with due regard for current ideas about fundamental rights in the health sphere.

Terminology

Both during the legislative process and in the context of the various forms of awareness-raising and training, particular attention will be paid to the terminology employed. The terms used reflect the cultural ideas that underlie the designated subject and some must be reviewed to reflect the current understanding of OATs. The appended glossary lists particularly problematic terms and the alternatives by which they could be replaced. Discussions on these inappropriate terms have an educational value in themselves.

To close this chapter on the implementation of the guiding principles in national contexts, we will point again to the long-term nature of such processes and the fact that they must remain flexible and pragmatic while at the same time being supervised by a national consultative body so as to ensure the overall coherence of the process and its outcome.

Appendices

A1. Acronyms, terminological choices and glossary

Acronyms

English		French	
AIDS	Acquired Immune Deficiency Syndrome	Sida	Syndrome d'immunodéficience acquise
ATOME	Access to Opioid Medication in Europe, WHO project	ATOME	Accès aux médicaments opioïde en Europe, projet OMS
DRD	Drug-related Deaths and Mortality, one of the five key epidemiological indicators, EMCDDA	DRD	Mortalité liée à l'usage de drogues, un des cinq indicateurs épidémiologiques clés, OEDT
DRID	Drug-Related Infectious Diseases, one of the five key epidemiological indicators, EMCDDA	DRID	Maladies infectieuses liées aux droguesun des cinq indicateurs épidémiologiques clés, OEDT
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction (Lisbon)	OEDT	Observatoire européen des drogues et des toxicomanies (Lisbonne)
EQUS	Study on the Development of an EU Framework for Minimum Quality Standards and Benchmarks in Drug Demand Reduction	EQUS	Étude sur le Développement d'un cadre européen pour des normes de qualité minimales et des points de référence concernant la réduction de la demande de drogues
EU	European Union	UE	Union européenne
FOPH	Federal Office of Public Health (Bern)	OFSP	Office fédéral de la santé publique (Berne)
HCV	Hepatitis C Virus	VHC	Virus de l'hépatite C
HIV	Human Immunodeficiency Virus	VIH	Virus de l'immunodéficience humaine
IDS	Institute of Comparative Law (University of Neuchâtel)	IDS	Institut de droit de la santé (Université de Neuchâtel)
INCB	International Narcotics Control Board (Vienna)	OICS	Organe international de contrôle des stupéfiants (Vienne)
ISGF	Swiss Research Institute for Public Health and Addiction (Zurich)	ISGF	Institut für Sucht- und Gesundheitsforschung / Institut suisse de recherche sur la santé publique et les addictions (Zurich)
MAS	Marketing Authorisation System	AMM	Autorisation de mise sur le marché
MedNET	Pompidou Group's Mediterranean Network for Co-operation on Drugs and Addictions, COE (Strasbourg)	MedNET	Réseau méditerranéen de coopération sur les drogues et les addictions du Groupe Pompidou, CE (Strasbourg)
NGO	Non-Governmental Organisation	ONG	Organisations non gouvernementales
OAM(s)	Opioid Agonist Medicine(s)	MAO	Médicament(s) agoniste(s) opioïde(s)
OAT	Opioid Agonist Treatment	TAO	Traitement agoniste opioïde
ODT	Opioid Dependence Treatment	TDO	Traitement de la dépendance aux opioïdes
PAS	Prior Authorisation Scheme	RAP	Régimes d'autorisation préalable
Reitox	European information network on drugs and drug addiction, EMCDDA project	Reitox	Réseau européen d'information sur les drogues et les toxicomanies, projet OEDT
SBIRT	Screening, Brief Intervention and Referral to Treatment	SBIRT	Repérage, intervention brève et orientation au traitement
SPC/PI	Summary of Product Characteristics (or SmPC)/Product Information	RCP/IP	Résumé des caractéristiques du produit/informations professionnelles
SROM	Slow-Release Oral Morphine	MDLP	Morphine orale LP
UNO	United Nations Organisation	ONU	Organisation des Nations unies
WHO	World Health Organisation (Geneva)	OMS	Organisation mondiale de la santé (Genève)

Terminological choices

A glossary is based on the premise that the choice and use of words influences our perception and ideas about the objects, events and abstract concepts they describe. In the medical professions, this is borne out both in the administration of care and the implementation of programmes and services and in the management of departments running national health systems. Terms define concepts and reflect speakers' attitudes, and choosing the best terms will result in the best treatment. To communicate in a professional manner, the terms chosen must be neutral and respectful but unfortunately in the field of dependence syndrome treatment, this basic principle is flouted.

A concrete example which illustrates this problem is the term "physical dependence", which the World Health Organisation withdrew from its nomenclature in 1989 because of the difficulties in defining it, but which is still used by many health professionals despite the fact that it does not in itself reflect the loss of control and the continuation of certain forms of behaviour without regard for the consequences. In truth, for over 25 years, "dependence" has referred to "dependence syndrome", which requires the presence of several symptoms including withdrawal and tolerance effects, although the latter are neither necessary nor sufficient in themselves to establish such a diagnosis. How do we explain such a contradiction in terms to an audience of non-health professionals such as a group of politicians? When they hear "dependence syndrome", they will pick out the word "dependence", which will lead them to the idea of "physical dependence". They will then act accordingly even if it means promoting inappropriate measures, with a disastrous effect on access to the necessary medicines for priority indications.

Another example is the term "substitution therapy", which suggests that an illegal psychoactive substance is replaced by a substance with similar active processes but provided "legally" by state institutions. Specialist professionals know that this interpretation is completely wrong because although the "substitute" medicine belongs to the same class of opioids, it is administered in different ways, at a different frequency and based on opioid properties with different goals. The term "substitution" fuels scientifically and medically incorrect public perceptions. Nonetheless, it is still widely used, even in top-level scientific reviews.

The original languages for the glossary below were French and English. Consequently, unless specifically stated otherwise, the words proposed in the glossary when translated into other languages will be words whose choice was implicitly influenced by these two languages. However, connotations not only depend on the language but also on the regions, the time and the culture in which the terms are encountered. The literal equivalent of a respectful English word in one town may have a negative meaning in another. And terms that were acceptable yesterday will become unacceptable tomorrow and will have to be reassessed as perceptions have changed. As a result, a glossary is only one attempt at a solution, whose outcome at a given time should be constantly reappraised by the persons most directly concerned, namely those who use psychoactive substances and their entourage.

Glossary

Agonist medicine used in opioid dependence treatment (OAM)	Medicine with a marketing authorisation whose active ingredient is an opioid with the main effect, in opiod dependence syndrome, of causing a halt or reduction in the consumption of opioids, of minimising the risk of lethal intoxications and regulating their physiological and psychological state. The main OAMs are methadone, buprenorphine, morphine and diacetylmorphine. They are generally used as part of multimodal treatments, including, in particular, psycho-social and somatic care. Other than their primary effects, it has been demonstrated that making these medicines available has an impact on public health and safety.
Controlled medicine(s)	Medicine which contains substances under control within the meaning of the Single Convention on Narcotic Drugs as amended by the Protocol of 1972, the Convention on Psychotropic Substances of 1971 and the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances (1988). The controlled medicines most commonly used as OAMs are methadone and buprenorphine.
Coverage rate	Proportion of a population eligible for assistance who actually obtain this assistance. For OAT, the coverage rate is defined as the number of OATs actually dispensed in a given geographical area compared to the number of persons in this area with opioid dependence syndrome.
Physicians' and pharmacists' basic training	University education including the entire course required for general professional qualification.
Equivalence of care	The principle according to which detained persons or those subject to other measures restricting their freedom must have access to healthcare which is equivalent to that made available to the general population.
Essential medicine	Medicine featuring on a list established by a government or intergovernmental agency setting out the minimum medical needs for a basic health system, listing the most efficient, safe and cost-effective medicines for priority states of health. Methadone and buprenorphine are OAMs included on WHO's Model List of Essential Medicines.
Indicator	Qualitative or quantitative data providing information on the conditions or performance of a public policy or programme.
International conventions on the control of psychoactive substances	A term referring to the Single Convention on Narcotic Drugs of 1961 as modified by the Protocol of 1972, the Convention on Psychotropic Substances of 1971 and the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances (1988).
Marketing authorisation (MA)	Marketing authorisation (MA) is a prerequisite for any possibility of marketing a medicinal product after an assessment of its quality, safety and effectiveness. In many countries it is also essential before any application for a substance to be included on the list of medicines reimbursed by the health insurance fund. MAs are generally issued by a national medicines agency, although they are also issued by the European Medicines Agency (EMA), which is an EU institution. MAs are official documents made up of a decision and appendices, including the Summary of Product Characteristics/Product Information (SPC/PI) and the person in treatment information leaflet.
Medicine	Any substance or composition that may be administered to a person with a view to establishing a medical diagnosis or restoring, correcting or modifying physiological functions.

Non-medical use	In this document, this term is defined as the use of controlled psychoactive substances outside the context of their prescription as medicines. Non-medical use covers use for recreational or ritual purposes and certain acts of self-medication with no medical justification.
Opioid(s)	Substance with a pharmacological activity similar to morphine.
Opioid agonist treatment (OAT)	Treatment of opioid dependence syndrome which is generally multimodal and multifocal and includes prescription of an OAM for an undetermined period (for the aims of OAT, see Section 3 of the Guiding Principles).
Opioid dependence syndrome	A cluster of physiological, cognitive and behavioural phenomena within the meaning of the WHO's international classification of diseases. According to the 10th edition of this classification (ICD 10) dependence syndrome exists when at least three of the following manifestations have occurred together for at least 1 month or, if persisting for periods of less than 1 month, have occurred together repeatedly within a 12-month period: (1) a strong desire or sense of compulsion to take the substance, (2) difficulties in controlling substance-taking behaviour, (3) existence of a withdrawal syndrome, (4) evidence of tolerance, (5) progressive neglect of alternative pleasures or interests and increased time spent in relation to consumption, (6) persisting with substance use despite emergence of overtly harmful consequences.
Primary care physician	A physician performing general medical activities in a community-based care facility, for example a private surgery or an out-patients' clinic. These physicians are sometimes also called "general practitioners" or "family physicians".
Prior authorisation scheme	Term describing regulations on OAMs which require prior authorisation from an authority or a state medical body for a physician or pharmacist to be allowed to prescribe or continue prescribing and delivering such treatment. Such authorisation may be individual and hence attached to the person in treatment or the health professional, or more general, being linked to the place of care.
Psychoactive substance	A Chemical or natural substance which acts on the central nervous system bringing about changes in perception, feelings, mood and awareness. Psychoactive substances may be developed as medicines used to treat pain, act as anaesthetics or treat insomnia, various mental disorders and disorders linked to the use of such substances in a non-medical context. The closely-related words "psychotropic" and "narcotic" have an essentially historic connotation although they are used in various national regulations and documents. "Psychotropic substances" refers on a legal level to the psychoactive substances listed in the Convention on Psychotropic Substances. "Narcotics" refers on a legal level to the psychoactive substances listed in the Single Convention on Narcotic Drugs of 1961, as amended by the Protocol of 1972.
Reduction / halt in consumption	Describes a therapeutic objective whose aim is to reduce consumption to a level below the criteria required for a diagnosis of dependence syndrome or use that is harmful to health (within the meaning of WHO's classification of diseases) without necessarily eliminating all consumption.
Social costs	Social costs equate to all the adverse consequences for the community linked to a given condition, and the expenses incurred to prevent or remedy it. Accordingly, in the area of substance-related conditions, social costs include medical treatment, residential therapy, survival assistance, prevention and law enforcement costs (direct costs), current and future lost output (indirect costs) and the deterioration in the quality of the life of dependent persons and their families (human costs, also referred to as intangible costs).

Problematic terms, problems related to their use and their alternatives (Scholten et al., 2017)

Problematic terms	Problem	Alternative(s)
Aberrant behaviours	Pejorative, judgmental	Using medication not as prescribed or intended See also in the text.
Abuse	Judgmental and ambiguous; implying wilful misconduct; it negates the fact that substance use disorders are a medical condition	Non-medical use; or: Use In order to avoid too much repetition in a text, at first mention “non-medical use” can be employed, followed by “use” at further occurrences. Note that “harmful use”, “hazardous use”, “recreational use” and “compulsory use” overlap with non-medical use, but are not identical. They can be alternatives only in certain circumstances. If used, these words should be used in a non-moralising manner and well-defined, e.g. the context should make clear to whom the use is harmful and what type of harm is done. Where “recreational use” is employed, this cannot automatically be put on par with “non-medical use”, as it depends on the substance and can be different for each individual user and even differ from one occasion of use to another.
Addict	Not person-first language (reducing the person to one characteristic), pejorative and stigmatising in certain circumstances	Person with substance use disorder, or: person with dependence
Addiction	Pejorative and stigmatising in certain circumstances Addiction comes from Latin “addicere”: to make someone the slave of someone else.	Substance use disorder (as defined in DSM-5) (preferred); dependence (as defined in ICD-10), dependence syndrome. Use of terms in other diagnostic systems is acceptable provided the terms are used as defined
Addictive substance	Not logical to use in certain circumstances (compare the above)	A compound which might promote a substance use disorder; “Substance use disorder producing substance”
Clean vs. dirty (as a test outcome)	Stigmatising, not describing the test result, judgmental	Negative vs. positive test result
Clean vs. dirty (as a person)	Extremely stigmatising, judgmental, not approaching the person as any other person in treatment would be referred to. Will reduce the person’s self-esteem and self-efficacy	A person not using/using psychoactive substances non-medically

Criminal law (when referring to substance control legislation)	The preambles of the Single Convention on Narcotic Drugs and the UN Convention on Psychotropic Substances declare that the conventions have the "health and welfare of mankind" as a primary objective. Different from criminal law, which has as the objective to regulate the prosecution of crimes (e.g. a murder – which would constitute a crime by everybody also without having a law on its punishment), drug law regulates the availability of psychoactive substances. The method of prohibition chosen results in the creation of new crimes as a derivative "only". Most national laws are the implementation of these two conventions and do not intend to create a crime primarily, but do so as the result of the regulation of health effects.	Health law Note that this is related to the concept rather than to the terminology
Dependent, or: dependent person	Not person-first language (reducing the person to one characteristic)	A person with a substance use disorder
Detoxification	Misleading: simplistically representing the dependence treatment as the washing out of a substance	In therapy for cessation (or: reduction) of psychoactive substance use; tapering (off); medically managed tapering from a psychoactive substance
Drug	Ambiguous language; in particular when a controlled medicine is meant, the word interferes with the promotion of its availability	Depending on the context: either medicine or psychoactive substance
Drug users	Not person-first language (reducing the person to one characteristic) Also note that using psychoactive substances is not the same as being dependent on these substances	People who use psychoactive substances (or: People who inject psychoactive substances, if applicable) Note that People who use drugs (PWUD) etc., although in most contexts being clear, is also intrinsically ambiguous.
Drug control conventions	In order to avoid the use of the ambiguous word "drug", referring to the conventions as "drug control conventions" is not recommended. (These conventions do not control medicines)	Conventions for the control of psychoactive substances, or: Substance Control Conventions
"the patient failed treatment…"	It is not the person who failed, but the treatment	The treatment failed, or: the treatment was not efficacious/effective
Illicit substance	Misleading: it is not the substance itself that is illicit, but its production, sale, possession or consumption in particular circumstances in a given jurisdiction	Controlled substance Note that "illicit substance use" can be correct terminology

Junkie, crackhead, speed freak etc.	Pejorative and stigmatising	Person who uses psychoactive substances; person with substance use disorder (depending on the context)
Medication assisted treatment (MAT)	Misleading: misrepresenting the character of this treatment in which effective medicines are at the core	Therapy, opioid agonist therapy (OAT), opioid agonist therapy for the treatment of substance use disorder.
Misuse	Considered judgmental, although less judgmental than “abuse”	See above under “Abuse”
Narcotic	Archaic terminology to refer to a class of substances by an unimportant side-effect of only some members of the class. Narcotic suggests the side-effect “sleep inducing”, but this is called today a “hypnotic”. Furthermore, it is hardly a side-effect of any substance in the Single Convention, and certainly not the main side effect for opioids (which is constipation). Moreover, some substances under this convention are stimulants	Psychoactive substance (or for specific cases: opioid, stimulant, opioid medicines, opioid analgesics, etcetera) The use of “narcotic” is justified if it refers to the list of substances regulated by the Single Convention on Narcotic Drugs, but then it is in the mere sense of a substance listed in a Convention defining its contents as such and stripped of its meaning of “hypnotic”
Opiate	Not in line with chemical nomenclature rules The suffix “-ate” is reserved for salts and esters	Opioid (See page 22 (What are opioids?) for the various meanings of the word “opioid”)
Problem user	Judgmental	Person with substance use disorder (preferred); person with dependence or person in treatment
Physical dependence	Misleading: usually refers to the symptoms of withdrawal and tolerance, which do *not* constitute dependence according to the definition of dependence. Whoever uses the term “physical dependence” must simultaneously tell his or her audience that this is not dependence. Contradictory as this is, it is not very likely that the audience will accept or even understand such a message. It is much easier to use “tolerance” and “withdrawal” and to explain that for dependence at least one of four other symptoms are necessary	Withdrawal and/or tolerance
Substitution therapy, or: Opioid substitution therapy (OST)	Misleading: gives the impression to politicians, civil servants and other lay people that this therapy is replacing “street drugs” with “state drugs” and therefore this language counteracts the availability of therapy	Therapy, Opioid agonist therapy (OAT), opioid agonist therapy for the treatment of substance use disorder

A2. Pharmacological effects of morphine

The main central actions of mu-opioid receptor effect (morphine effects)

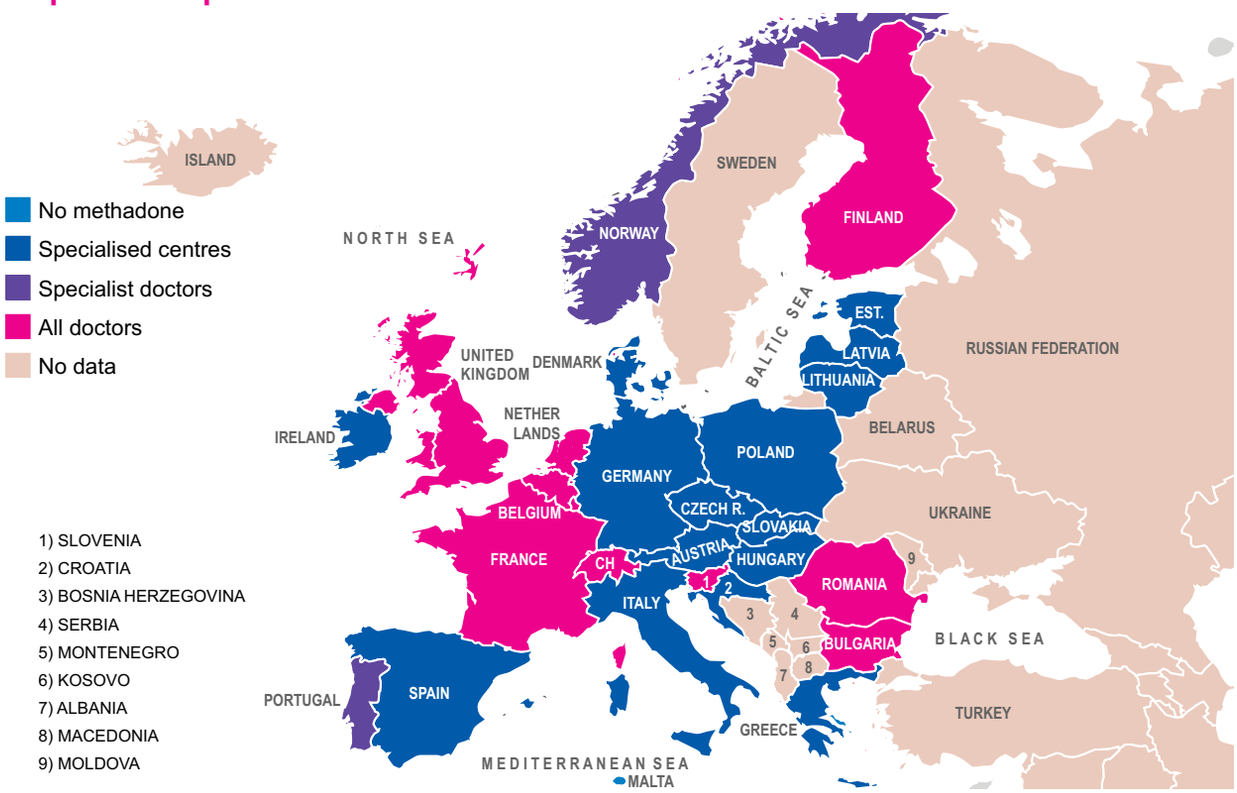
Sedation	Drowsiness, stupor, sleep, and coma. Reduced psychomotor performance. At very high doses, convulsions can appear.
Euphoria	Experience of euphoria, pleasure, and well-being. The short delay for the euphoria effect and its intensity, contribute to the addictive risk of opioids and the abuse potential. This varies largely between opioids from a very high risk for heroin, to a very low risk for opioids such as methadone or buprenorphine.
Analgesia	Reduction in the sensorial and affective components of pain. It can relieve and suppress acute and chronic pain.
Respiratory depression	It reduces the sensitivity to CO_2 and hypoxemia. It reduces the number of breaths per minute and can end in apnoea. This effect is dose dependent. It is the major contributor to opioid mortality.
Antitussive	Depresses the cough reflex.
Miosis	Reduced pupil diameter. This effect does not show tolerance and could be adequate to detect recent use of opioids (naloxone conjunctival test).
Nausea and vomiting	Very frequent at first use.
Neuroendocrine actions	Inhibit the release of gonadotropin-releasing hormone and corticotrophin-releasing hormone, producing a decrease in the luteinising hormone, follicle-stimulating hormone, adrenocorticotropic hormone (ACTH), and beta-endorphin. It also stimulates the secretion of the antidiuretic hormone (ADH).
Muscular tone	Myoclonus is a rare side effect, ranging from mild twitching to generalised spasm.

The main peripheral actions of mu-opioid receptor effect (morphine effects)

Gastrointestinal	Reduction in gastric emptying and in peristalsis and a contraction of the sphincter. Clinically it is related with constipation.
Cardiovascular	Hypotension by its action in the vasomotor centre and by vasodilatation. Also vagal bradycardia has been described.
Histamine release	Feeling of heat, flushing, and pruritus in the face, neck, and upper thorax.
Renal	Increases the tone of the detrusor muscle of the bladder.

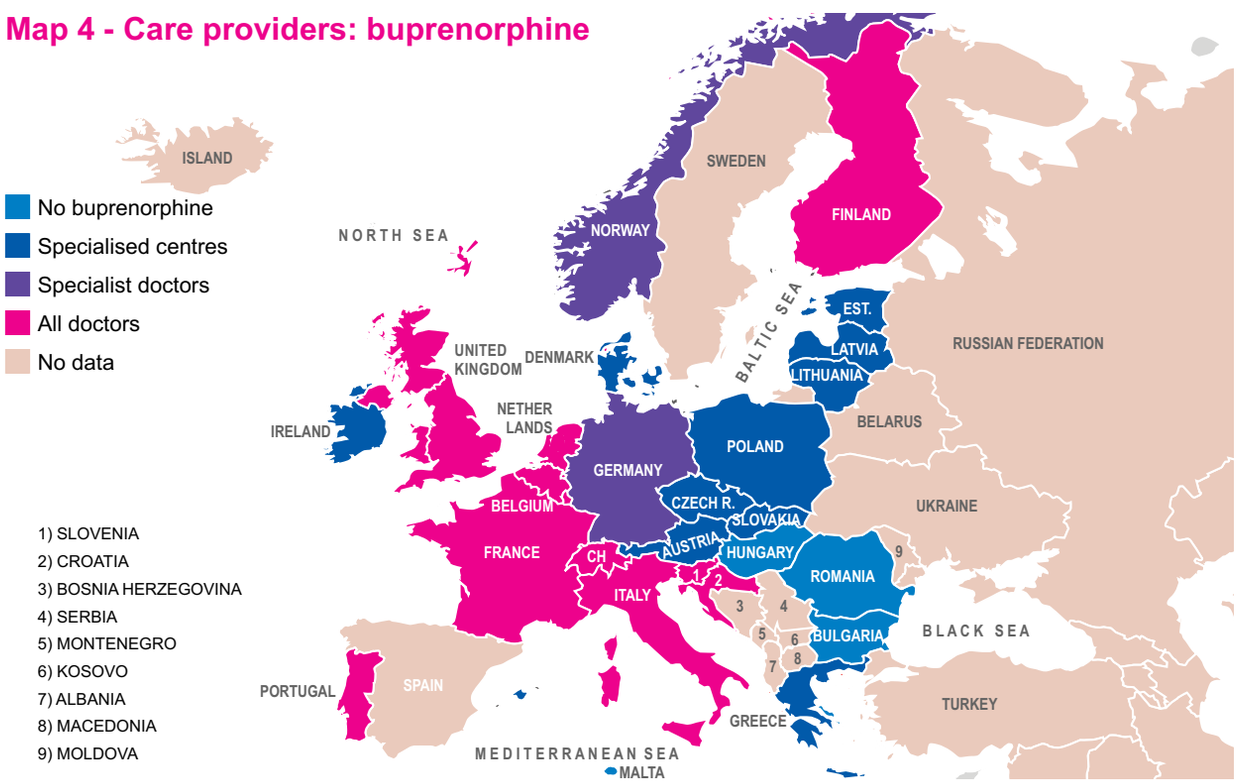
A3. Availability in Europe of the main opioids prescribed for OAT (2016)

Map 3 - Care providers: methadone



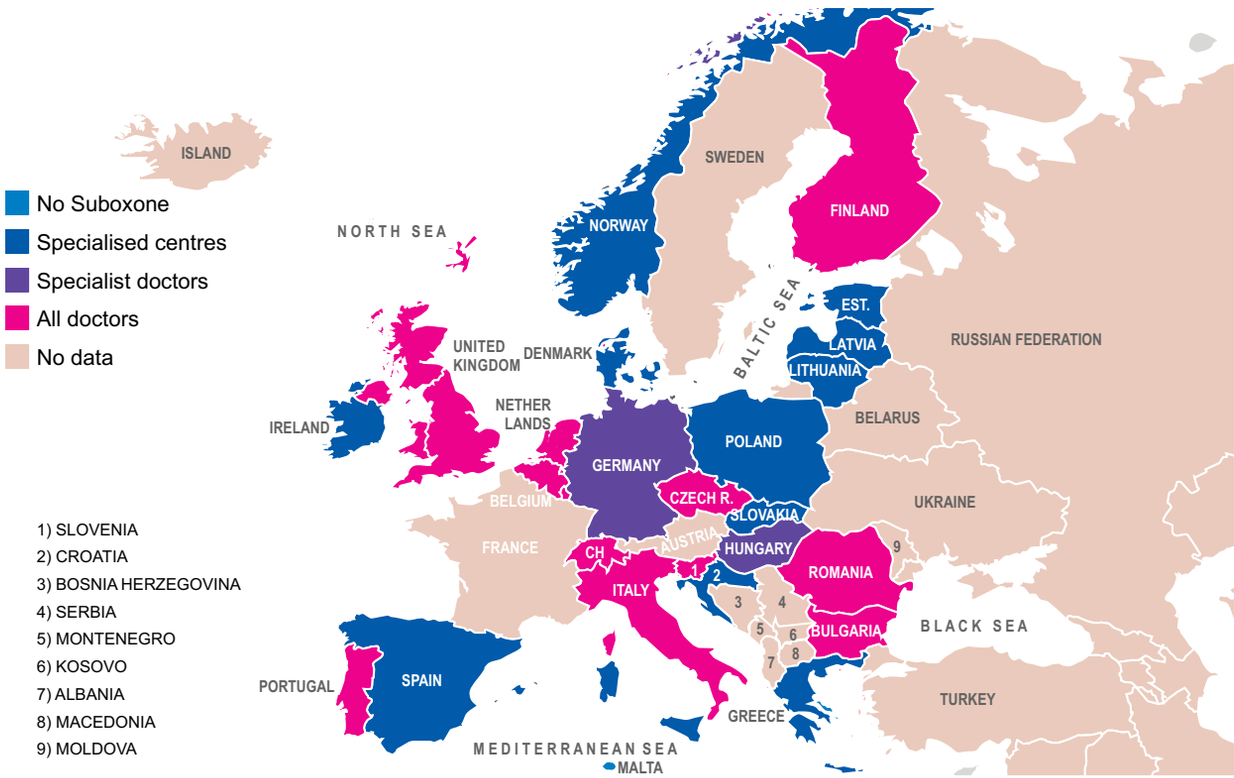
European monitoring center for Drugs and Drug Addiction, treatment providers, 2017; Office fédéral de la santé publique (OFSP), 2017

Map 4 - Care providers: buprenorphine



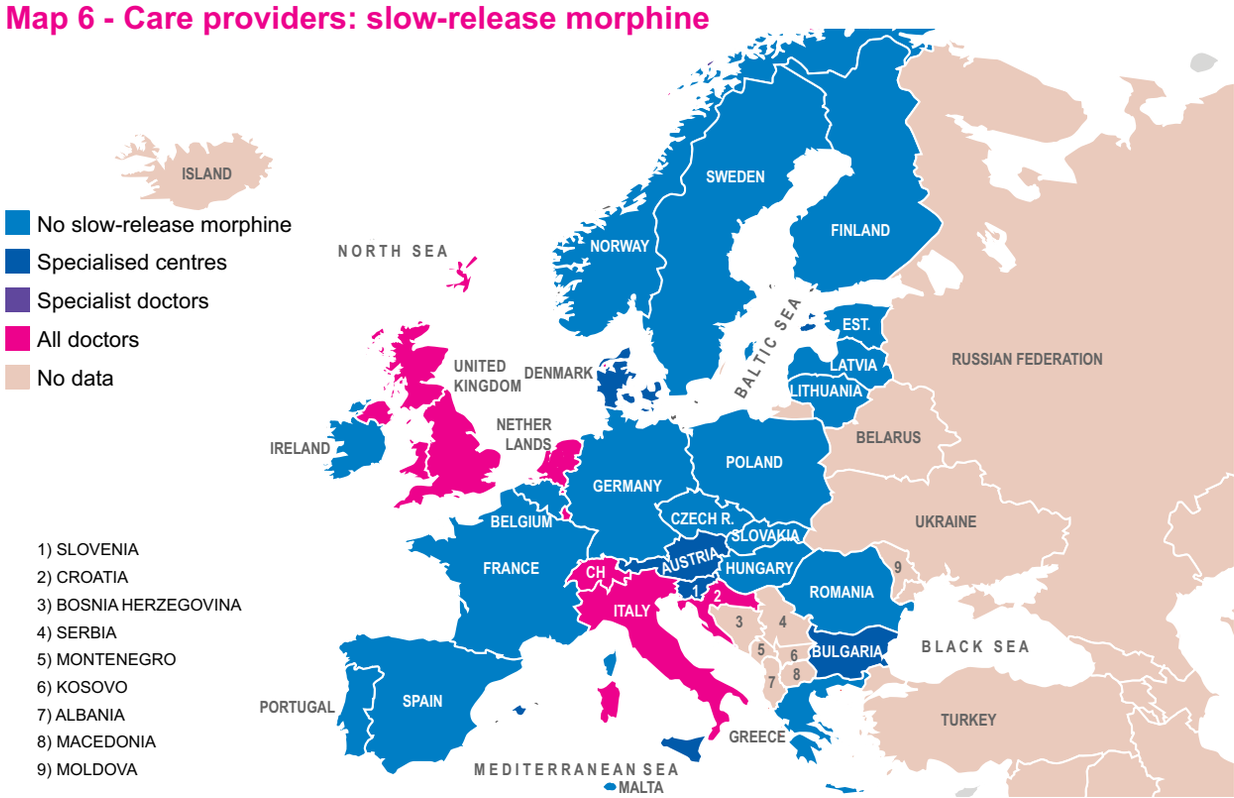
European monitoring center for Drugs and Drug Addiction, treatment providers, 2017; Office fédéral de la santé publique (OFSP), 2017

Map 5 - Care providers: naloxone (Suboxone)



European monitoring center for Drugs and Drug Addiction, treatment providers, 2017; Office fédéral de la santé publique (OFSP), 2017

Map 6 - Care providers: slow-release morphine



European monitoring center for Drugs and Drug Addiction, treatment providers, 2017; Office fédéral de la santé publique (OFSP), 2017

A4. CESCR Article 12 - General Comment No.14: extracts[26]

The right to the highest attainable standard of health (Article 12 of the International Covenant on Economic, Social and Cultural Rights)

1. Health is a fundamental human right indispensable for the exercise of other human rights. Every human being is entitled to the enjoyment of the highest attainable standard of health conducive to living a life in dignity. […]

3. The right to health is closely related to and dependent upon the realisation of other human rights, as contained in the International Bill of Rights, including the rights to food, housing, work, education, human dignity, life, non-discrimination, equality, the prohibition against torture, privacy, access to information, and the freedoms of association, assembly and movement. These and other rights and freedoms address integral components of the right to health. […]

4. […] However, the reference in article 12.1 of the Covenant to "the highest attainable standard of physical and mental health" is not confined to the right to health care. On the contrary, the drafting history and the express wording of article 12.2 acknowledge that the right to health embraces a wide range of socio-economic factors that promote conditions in which people can lead a healthy life, and extends to the underlying determinants of health, such as food and nutrition, housing, access to safe and potable water and adequate sanitation, safe and healthy working conditions, and a healthy environment. […]

8. The right to health is not to be understood as a right to be healthy. The right to health contains both freedoms and entitlements. The freedoms include the right to control one's health and body, including sexual and reproductive freedom, and the right to be free from interference, such as the right to be free from torture, non-consensual medical treatment and experimentation. By contrast, the entitlements include the right to a system of health protection which provides equality of opportunity for people to enjoy the highest attainable level of health. […]

11. […] A further important aspect is the participation of the population in all health-related decision-making at the community, national and international levels. […]

12. The right to health in all its forms and at all levels contains the following interrelated and essential elements, the precise application of which will depend on the conditions prevailing in a particular State party:

a) Availability. Functioning public health and health-care facilities, goods and services, as well as programmes, have to be available in sufficient quantity within the State party. […]

b) Accessibility. Health facilities, goods and services (6) have to be accessible to everyone without discrimination, within the jurisdiction of the State party. Accessibility has four overlapping dimensions:

> i) Non-discrimination: health facilities, goods and services must be accessible to all, especially the most vulnerable or marginalised sections of the population, in law and in fact, without discrimination on any of the prohibited grounds (7).
>
> ii) Physical accessibility: health facilities, goods and services must be within safe physical reach for all sections of the population, especially vulnerable or marginalised groups, such as ethnic minorities and indigenous populations, women, children, adolescents, older persons, persons with disabilities and persons with HIV/AIDS. […]
>
> iii) Economic accessibility (affordability): health facilities, goods and services must be affordable for all. Payment for health-care services, as well as services related to the underlying determinants of health, has to be based on the principle of equity, ensuring that these services, whether privately or publicly provided, are affordable for all, including socially disadvantaged groups. Equity demands that poorer households should not be disproportionately burdened with health expenses as compared to richer households.
>
> iv) Information accessibility: accessibility includes the right to seek, receive and impart information and ideas (8) concerning health issues. However, accessibility of information should not impair the right to have personal health data treated with confidentiality.

26 United Nations, Economic and Social Council, United Nations Human Rights Website, 2000

c) Acceptability. All health facilities, goods and services must be respectful of medical ethics and culturally appropriate, i.e. respectful of the culture of individuals, minorities, peoples and communities, sensitive to gender and life-cycle requirements, as well as being designed to respect confidentiality and improve the health status of those concerned.

d) Quality. As well as being culturally acceptable, health facilities, goods and services must also be scientifically and medically appropriate and of good quality. This requires, inter alia, skilled medical personnel, scientifically approved and unexpired drugs and hospital equipment, safe and potable water, and adequate sanitation. […]

16. […] The right to treatment includes the creation of a system of urgent medical care in cases of accidents, epidemics and similar health hazards, and the provision of disaster relief and humanitarian assistance in emergency situations. The control of diseases refers to States' individual and joint efforts to, inter alia, make available relevant technologies, using and improving epidemiological surveillance and data collection on a disaggregated basis, the implementation or enhancement of immunisation programmes and other strategies of infectious disease control. […]

17. "The creation of conditions which would assure to all medical service and medical attention in the event of sickness" (art. 12.2 (d)), both physical and mental, includes the provision of equal and timely access to basic preventive, curative, rehabilitative health services and health education; regular screening programmes; appropriate treatment of prevalent diseases, illnesses, injuries and disabilities, preferably at community level; the provision of essential drugs; and appropriate mental health treatment and care. […]

18. By virtue of article 2.2 and article 3, the Covenant proscribes any discrimination in access to healthcare and underlying determinants of health, as well as to means and entitlements for their procurement, on the grounds of race, colour, sex, language, religion, political or other opinion, national or social origin, property, birth, physical or mental disability, health status (including HIV/AIDS), sexual orientation and civil, political, social or other status, which has the intention or effect of nullifying or impairing the equal enjoyment or exercise of the right to health. The Committee stresses that many measures, such as most strategies and programmes designed to eliminate health-related discrimination, can be pursued with minimum resource implications through the adoption, modification or abrogation of legislation or the dissemination of information. […]

19. With respect to the right to health, equality of access to health care and health services has to be emphasised. States have a special obligation to provide those who do not have sufficient means with the necessary health insurance and health-care facilities, and to prevent any discrimination on internationally prohibited grounds in the provision of health care and health services, especially with respect to the core obligations of the right to health. (16). […]

23. States parties should provide a safe and supportive environment for adolescents, that ensures the opportunity to participate in decisions affecting their health, to build life skills, to acquire appropriate information, to receive counselling and to negotiate the health-behaviour choices they make. […]

28. Issues of public health are sometimes used by States as grounds for limiting the exercise of other fundamental rights. […]

29. In line with article 5.1, such limitations must be proportional, i.e. the least restrictive alternative must be adopted where several types of limitations are available. Even where such limitations on grounds of protecting public health are basically permitted, they should be of limited duration and subject to review.

30. While the Covenant provides for progressive realisation and acknowledges the constraints due to the limits of available resources, it also imposes on States parties various obligations which are of immediate effect. States parties have immediate obligations in relation to the right to health, such as the guarantee that the right will be exercised without discrimination of any kind (art. 2.2) and the obligation to take steps (art. 2.1) towards the full realisation of article 12. Such steps must be deliberate, concrete and targeted towards the full realisation of the right to health (20). […]

32. As with all other rights in the Covenant, there is a strong presumption that retrogressive measures taken in relation to the right to health are not permissible. […]

33. The right to health, like all human rights, imposes three types or levels of obligations on States parties: the obligations to respect, protect and fulfil. In turn, the obligation to fulfil contains obligations to facilitate, provide and promote (23). The obligation to respect requires States to refrain from interfering directly or indirectly with the enjoyment of the right to health. The obligation to protect requires States to take measures that prevent third parties from interfering with article 12 guarantees. Finally, the obligation to fulfil requires States to adopt appropriate legislative, administrative, budgetary, judicial, promotional and other measures towards the full realisation of the right to health. […]

36. The obligation to fulfil requires States parties, inter alia, to give sufficient recognition to the right to health in the national political and legal systems, preferably by way of legislative implementation, and to adopt a national health policy with a detailed plan for realising the right to health. […]States have to ensure the appropriate training of doctors and other medical personnel, the provision of a sufficient number of hospitals, clinics and other health-related facilities, and the promotion and support of the establishment of institutions providing counselling and mental health services, with due regard to equitable distribution throughout the country.

Further obligations include the provision of a public, private or mixed health insurance system which is affordable for all, the promotion of medical research and health education, as well as information campaigns, in particular with respect to HIV/AIDS, sexual and reproductive health, traditional practices, domestic violence, the abuse of alcohol and the use of cigarettes, drugs and other harmful substances. […]

40. […] The economically developed States parties have a special responsibility and interest to assist the poorer developing States in this regard. […]

42. While only States are parties to the Covenant and thus ultimately accountable for compliance with it, all members of society - individuals, including health professionals, families, local communities, intergovernmental and non-governmental organisations, civil society organisations, as well as the private business sector - have responsibilities regarding the realisation of the right to health. […]

43. In general comment No. 3, the Committee confirms that States parties have a core obligation […]:

a) To ensure the right of access to health facilities, goods and services on a non-discriminatory basis, especially for vulnerable or marginalised groups; […]

d) To provide essential drugs, as from time to time defined under the WHO Action Programme on Essential Drugs;

e) To ensure equitable distribution of all health facilities, goods and services;

f) To adopt and implement a national public health strategy and plan of action, on the basis of epidemiological evidence, addressing the health concerns of the whole population; the strategy and plan of action shall be devised, and periodically reviewed, on the basis of a participatory and transparent process; they shall include methods, such as right to health indicators and benchmarks, by which progress can be closely monitored; the process by which the strategy and plan of action are devised, as well as their content, shall give particular attention to all vulnerable or marginalised groups.

44. The Committee also confirms that the following are obligations of comparable priority: [...]

e) To provide appropriate training for health personnel, including education on health and human rights. [...]

51. Violations of the obligation to protect follow from the failure of a State to take all necessary measures to safeguard persons within their jurisdiction from infringements of the right to health by third parties. This category includes such omissions as […] the failure to protect women against violence or to prosecute perpetrators; the failure to discourage the continued observance of harmful traditional medical or cultural practices. […]

56. States should consider adopting a framework law to operationalise their right to health national strategy. The framework law should establish national mechanisms for monitoring the implementation of national health strategies and plans of action. It should include provisions on the targets to be achieved and the time frame for their achievement; the means by which right to health benchmarks could be achieved; the intended collaboration with civil society, including health experts, the private sector and international organisations. […]

57. National health strategies should identify appropriate right to health indicators and benchmarks. […]

59. Any person or group victim of a violation of the right to health should have access to effective judicial or other appropriate remedies at both national and international levels (30). […]

Notes

6. Unless expressly provided otherwise, any reference in this general comment to health facilities, goods and services includes the underlying determinants of health outlined in paragraphs 11 and 12 (a) of this general comment.

7. See paragraphs 18 and 19 of this general comment.

8. See article 19.2 of the International Covenant on Civil and Political Rights. This general comment gives particular emphasis to access to information because of the special importance of this issue in relation to health.

16. For the core obligations, see paragraphs 43 and 44 of the present general comments.

20. See general comment No. 13, paragraph 43.

23. According to general comments Nos. 12 and 13, the obligation to fulfil incorporates an obligation to facilitate and an obligation to provide. In the present general comment, the obligation to fulfil also incorporates an obligation to promote because of the critical importance of health promotion in the work of WHO and elsewhere.

30. Regardless of whether groups as such can seek remedies as distinct holders of rights, States parties are bound by both the collective and individual dimensions of article 12. Collective rights are critical in the field of health; modern public health policy relies heavily on prevention and promotion which are approaches directed primarily to groups.

A5. Composition of the Expert group and interests

Expert group

Country experts: Peyman Altan (Ministry of Health, Turkey), Laura Amey, (Institute of Health Law, University of Neuchâtel, Switzerland), Evin Aras Kılınç (Ministry of Health, Turkey), Marc Auriacombe (Bordeaux University Hospital, France), Nabil Ben Salah (Ministry of Health, Tunisia), Manuel Cardoso (General-Directorate for Intervention on Addictive Behaviours and Dependencies, Portugal), Mohamed Chakali (Ministry of Health, Population and Hospital Reform, Algeria), Ramzi Haddad (Skoun, Lebanese Addiction Centre, Lebanon), Robert Hämmig (Universitäre Psychiatrische Dienste Bern, Switzerland), Valérie Junod (Faculty of Law, Universities of Geneva and Lausanne, Switzerland), Andrej Kastelic (Centre for the Treatment of Drug Addiction, Slovenia), Dominique Lamy (Réseau alternative aux toxicomanies – ALTO, Belgium), Stamatia Markellou (Greek Organisation against Drugs, Greece), Laurent Michel (CSAPA Pierre Nicole, French Red Cross, France), Abdallah Ounnir (Faculty of Legal, Economic and Social Sciences, Abdelmalek Essaâdi University, Tangier, Morocco), Jallal Toufiq (National Observatory of Drugs and Drug Addiction, Morocco), Didier Touzeau (Paul Guiraud Hospital Complex, France), Evelina Venckevic (Drug, Tobacco and Alcohol Control Department, Lithuania).

Experts from international organisations: Alessandro Pirona (European Monitoring Centre for Drugs and Drug Addiction), Willem K. Scholten (Consultant, proposed by the World Health Organisation).

Representatives of institutions: Marie-Anne Courné (Agence nationale de sécurité du medicament et des produits de santé, France), Kurt Doms (Federal Public Health Service, Belgium), Katia Dubreuil (Inter-ministerial Task Force to Combat Drugs and Addictive Behaviour, France), Elisabeth Pfletschinger (Inter-ministerial Task Force to Combat Drugs and Addictive Behaviour, France).

Observer from the Scientific Council: Miguel Casas Brugué (Vall d'Hebron University Hospital, Spain).

Members of the Scientific Advisory Committee

Marc Ansseau, Nicolas Authier, Thilo Beck, Amine Benyamina, Jacques Besson, Jean-Pierre Couteron, Chin Bin Eap, Jean-Pierre Gervasoni, Edward J. Gorzelańczyk, Christine Guillain, Olivier Guillod, Jennifer Hasselgard-Rowe, Dagmar Hedrich, Bernadeta Lelonek-Kuleta, Louis Letellier de Saint-Juste, Icro Maremmani, Daniel Meili, Haim Mell, Martine Monnat, Marie-Anne Nougier, Marc Reisinger, Michel Reynaud, Ambros Uchtenhagen, Frank Zobel, Serge Zombek, Daniele Zullino.

Other contributors

Rodolphe Aeberhard, Anthony Bamert, Caroline Dunand, Cheryl Dickson, Benoît Gaillard, Dorothy Gütermann, Inès Fernandes, Federico Cathieni, Marc Jeanneret, Dimitri Kohler, Victor Leroy, Selena Lopreno, Sarah Maiolo, Mauro Mayer, Quentin Mottet, Baptiste Novet, Pablo Sanz, Alexander Tomei, Maude Waelchli.

Declaration of interests

When collecting data to establish their profile, the experts were asked if in the past they had either in an individual capacity or through the organisation with which they are affiliated, worked for a laboratory involved in the development or commercialisation of products used for treating dependence syndromes (medicines, biological tests, specific medical materials, etc.).

Marc Auriacombe did not report any personal ties or interests, but he mentioned partnerships between the University of Bordeaux and/or his Foundation with the following pharmaceutical companies: RBPharma, Mundipharma, Lundbeck, DAPharma and Ferrer.

Laurent Michel stated that there had been no interests in the previous two years. He reported that he had, in the past, carried out work for the following pharmaceutical companies: Bouchara, Reckitt and Etypharm.

Willem K. Scholten is an independent consultant and as such, he works on regulations and policies regarding psychoactive substances, including for DrugScience, Grünenthal, Jazz Pharmaceuticals, Mundipharma, Pinney Associates and the World Health Organisation (WHO).

Didier Touzeau said that he had worked for the following pharmaceutical companies: Lundbeck France and RB Pharmaceuticals France.

References

Alho, H. (2015). Opioid Agonist Diversion in Opioid-Dependence Treatment. In El-Guebaly, N., Carrà, G. & Galanter, M. (Eds.), Textbook of Addiction Treatment: International Perspectives (pp. 555-566). Milano: Springer Milan.

Arnaud, S., Dubois-Arber, F. & Gervasoni, J.-P. (2011). Rôle des pharmacies dans la prise en charge des consommateurs de drogue 3e vague d'enquête, 2011: IUMSP (Institut universitaire de médecine sociale et préventive).

Arria, A. M. & McLellan, A. T. (2012). Evolution of concept, but not action, in addiction treatment. Substance use & misuse, 47(8-9), 1041-1048.

Auriacombe, M., Serre, F., Denis, C. & Fatseas, M. (2017). Diagnosis of addictions. In: H. Pickard & S. Ahmed (Eds), The Routledge Handbook of the Philosophy and Science of Addiction. Routledge.

Ayu, A. P., Schellekens, A. F., Iskandar, S., Pinxten, L. & De Jong, C. A. (2015). Effectiveness and organization of addiction medicine training across the globe. European addiction research, 21(5), 223-239.

Beck, T., Haasen, C., Verthein, U., Walcher, S., Schuler, C., Backmund, M. & Reimer, J. (2014). Maintenance treatment for opioid dependence with slow−release oral morphine: a randomized cross−over, non−inferiority study versus methadone. Addiction, 109(4), 617-626.

Becker, G. S., Murphy, K. M. & Grossman, M. (2004). The economic theory of illegal goods: The case of drugs.

Berridge, V. (2004). Punishment or treatment? Inebriety, drink, and drugs, 1860-2004. The Lancet, 364, 4.

Berridge, V. & Edwards, G. (1987). Opium and the People: Opiate Use in Nineteenth-Century England. New Haven, Connecticut: Yale University Press.

Blanken, P., Hendriks, V. M., Koeter, M. W., van Ree, J. M. & van den Brink, W. (2012). Craving and illicit heroin use among patients in heroin-assisted treatment. Drug Alcohol Depend, 120(1), 74-80.

Broers, B. (2016). A concept for undergraduate training in addiction medicine in Switzerland.

Cherny, N. I., Baselga, J., de Conno, F. & Radbruch, L. (2010). Formulary availability and regulatory barriers to accessibility of opioids for cancer pain in Europe: a report from the ESMO/EAPC Opioid Policy Initiative. Annals of oncology, 21(3), 615-626. doi:10.1093/annonc/mdp581.

Cicek, E., Demirel, B., Ozturk, H. I., Kayhan, F., Cicek, I. E., & Eren, I. (2015). Burden of care and quality of life in relatives of opioid dependent male subjects. Psychiatria Danubina, 27(3), 0-277.

Clement, S., Schauman, O., Graham, T., Maggioni, F., Evans-Lacko, S., Bezborodovs, N. & Thornicroft, G. (2015). What is the impact of mental health-related stigma on help-seeking? A systematic review of quantitative and qualitative studies. Psychological medicine, 45(1), 11-27.

Cohen, E. B. & Lloyd, S. J. (2014). Disciplinary Evolution and the Rise of the Transdiscipline. International Journal of an Emerging Transdiscipline, 17, 189-215.

Comer, S. D., Sullivan, M. A., Vosburg, S. K., Manubay, J., Amass, L., Cooper, Z. D. & Kleber, H. D. (2010). Abuse liability of intravenous buprenorphine/naloxone and buprenorphine alone in buprenorphine−maintained intravenous heroin abusers. Addiction, 105(4), 709-718.

Courtwright, D. T. (2001). Dark Paradise: A History of Opiate Addiction in America. Cambridge, Massachusetts: Harvard University Press.

Crane, B. D. & Rivolo, A. R. (1997). An Empirical Examination of Counterdrug Interdiction Program Effectiveness.

Deappen, J. B. (2016). L'accompagnement thérapeutique des patients souffrant d'addictions. Forum médical suisse; 16(18-19):423-426.

Dole, V. P. & Nyswander, M. (1965). A Medical Treatment for Diacetylmorphine (Heroin) Addiction. A Clinical Trial with Methadone Hydrochloride. JAMA, 193, 646-650.

Dole, V. P. & Nyswander, M. (1965). A medical treatment for diacetylmorphine (heroin) addiction: a clinical trial with methadone hydrochloride. JAMA, 193(8), 646-650.

Dole, V. P. & Nyswander, M. E. (1966). Rehabilitation of heroin addicts after blockade with methadone. N Y State J Med, 66(15), 2011-2017.

Dole, V. P. & Nyswander, M. E. (1967). Heroin addiction-a metabolic disease. Arch Intern Med, 120(1), 19-24.

Dole, V. P. Nyswander, M. E., & Kreek, M. J. (1966). Narcotic blockade. Arch Intern Med, 118(4), 304-309.

Duthey, B. & Scholten, W. (2014). Adequacy of opioid analgesic consumption at country, global, and regional levels in 2010, its relationship with development level, and changes compared with 2006. J Pain Symptom Manage, 47(2), 283-297. doi:10.1016/j.jpainsymman.2013.03.015

EMCDDA. (2003). Legal aspects of substitution treatment. An insight into nine EU countries. Catholic University of Leuven, Belgium.

EMCDDA. (2010) Building a national drugs observatory: a joint handbook. Luxembourg : Office for Official Publications of the European Communities.

EMCDDA. (2016). European Drug Report 2016: Trends and Developments. Publications Office of the European Union, Luxembourg. Available online http://www.emcdda.europa.eu/system/files/publications/2637/TDAT16001ENN.pdf.

Erlenmeyer, A. (1883). Die Morphiumscht und ihre Behandlung. Leipzig & Neuwied, Germany: Heuser's Verlag.

European Union. (2015). Council conclusions on the implementation of the EU Action Plan on Drugs 2013-2016 regarding minimum quality standards in drug demand reduction in the European Union. Brussels.

Farré, M., Mas, A., Torrens, M., Moreno, V. C. & Camí, J. (2002). Retention rate and illicit opioid use during methadone maintenance interventions: a meta-analysis. Drug Alcohol Depend, 65(3), 283-290.

Ferri, M., Davoli, M. & Perucci, C. A. (2005). Heroin maintenance for chronic heroin dependents. The Cochrane Library.

Ferri, M., Davoli, M. & Perucci, C. A. (2011). Heroin maintenance for chronic heroin-dependent individuals. The Cochrane database of systematic reviews(12), CD003410. doi:10.1002/14651858.CD003410.pub4.

Feldstein Ewing, S. W., Apodoca, T. R. & Gaume, J. (2016). Ambivalence: Prerequisite for success in motivational interviewing with adolescents? Addiction, 111, 1900-107.

Foucault, M. (2014). Surveiller et punir. Naissance de la prison: Editions Gallimard.

Goodair, C. & Crome, I. (2014). Special Edition: Education and training in addiction medicine. The Canadian Journal of Addiction, 5(3), 27.

Gowing, L., Farrell, M., Bornemann, R., Sullivan, L. & Ali, R. (2011). Oral substitution treatment of injecting opioid users for prevention of HIV infection. Cochrane Database Syst Rev:CD004145.

Groupe Pompidou. 2014. Education et formation aux troubles liés à l'usage de substances. Strasbourg. Muscat, R., Stamm, R. & Uchtenhagen, A.

Haasen, C., Stallwitz, A., Lachmann, A., Prinzleve, M., Güttinger, F. & Rehm, J. (2004). Management of high risk opiate addicts in Europe. Retrieved from

Halliday, R. (1963). Management of the Narcotic Addict. British Columbia Medical Journal, 5(10), 412-414.

Harris, M. & Rhodes, T. (2013). Methadone diversion as a protective strategy: The harm reduction potential of 'generous constraints'. International Journal of Drug Policy, 24(6), e43-e50. doi:http://dx.doi.org/10.1016/j.drugpo.2012.10.003.

Hubbard, R. L., Craddock, S. G. & Anderson, J. (2003). Overview of 5-year followup outcomes in the drug abuse treatment outcome studies (DATOS). J Subst Abuse Treat, 25(3), 125-134.

Hulse, G. K., English, D. R., Milne, E. & Holman, C. D. J. (1999). The quantification of mortality resulting from the regular use of illicit opiates. Addiction, 94(2), 221-229.

INCB. (1989). International Narcotics Control Board Report, 1989 Demand for and supply of opiates for medical and scientific needs. New York, NY.

INCB. (2016). International Narcotics Control Board. Availability of internationally controlled drugs: Ensuring adequate access for medical and scientific purposes. New York, NY.

Institut de droit de la santé (2012). Traitement de substitution à la dépendance aux opioïdes. Etude de la réglementation de quelques pays francophones. Neuchâtel. Amey, L., Brunner, N., Guillod, O.

Isbell, H. & Vogel, V. H. (1949). The addiction liability of methadon (amidone, dolophine, 10820) and its use in the treatment of the morphine abstinence syndrome. Am J Psychiatry, 105(12), 909-914. doi:10.1176/ajp.105.12.909.

Johnson, B. & Richert, T. (2015a). Diversion of methadone and buprenorphine by patients in opioid substitution treatment in Sweden: Prevalence estimates and risk factors. International Journal of Drug Policy, 26(2), 183-190. doi:http://dx.doi.org/10.1016/j.drugpo.2014.10.003.

Johnson, B. & Richert, T. (2015b). Diversion of Methadone and Buprenorphine from Opioid Substitution Treatment: The Importance of Patients' Attitudes and Norms. J Subst Abuse Treat, 54, 50-55. doi:http://dx.doi.org/10.1016/j.jsat.2015.01.013.

Joint United Nations Programme on HIV/AIDS. (2006). Global report: UNAIDS report on the global AIDS epidemic. UNAIDS, Geneva, Switzerland. Available online http://www.unaids.org/en/ KnowledgeCentre/HIVData/GlobalReport/2006/.

Jones, J. D., Sullivan, M. A., Vosburg, S. K., Manubay, J. M., Mogali, S., Metz, V. & Comer, S. D. (2015). Abuse potential of intranasal buprenorphine versus buprenorphine/naloxone in buprenorphine−maintained heroin users. Addiction biology, 20(4), 784-798.

Kastelic, A., Dubajic, G. & Strbad, E. (2008). Slow−release oral morphine for maintenance treatment of opioid addicts intolerant to methadone or with inadequate withdrawal suppression. Addiction, 103(11), 1837-1846.

Kelly, J. F. & Westerhoff, C. M. (2010). Does it matter how we refer to individuals with substance-related conditions? A randomized study of two commonly used terms. International Journal of Drug Policy, 21(3), 202-207.

Kothari, D., Gourevitch, M. N., Lee, J. D., Grossman, E., Truncali, A., Ark, T. K. & Kalet, A. L. (2011). Undergraduate medical education in substance abuse: A review of the quality of the literature. Academic medicine: journal of the Association of American Medical Colleges, 86(1), 98.

Larjow, E., Papavasiliou, E., Payne, S., Scholten, W. & Radbruch, L. (2016). A systematic content analysis of policy barriers impeding access to opioid medication in Central and Eastern Europe: Results of ATOME. J Pain Symptom Manage, 51(1), 99-107. doi:10.1016/j.jpainsymman.2015.08.012.

Lauber, C., Nordt, C., Braunschweig, C. & Rössler, W. (2006). Do mental health professionals stigmatize their patients? Acta Psychiatrica Scandinavica, 113(s429), 51-59.

Launonen, E., Alho, H., Kotovirta, E., Wallace, I. & Simojoki, K. (2015). Diversion of opioid maintenance treatment medications and predictors for diversion among Finnish maintenance treatment patients. International Journal of Drug Policy, 26(9), 875-882.

Lindesmith, A. R. (1957). The British system of narcotics control. Law and Contemporary Problems, 22(1), 138-154.

Lines, R., Elliott, R., Hannah, J., Schleifer, R., Avafia, T. & Barrett, D. (2017). The Case for International Guidelines on Human Rights and Drug Control.

Lipari, R. N., Park-Lee, E. & Van Horn, S. (2016). America's need for and receipt of substance use treatment in 2015. Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration.

Maremmani, I. & Gerra, G. (2010). Buprenorphine−based regimens and methadone for the medical management of opioid dependence: Selecting the appropriate drug for treatment. The American journal on addictions, 19(6), 557-568.

MacArthur, G. J., Minozzi, S., Martin, N., Vickerman, P., Deren, S., Bruneau, J., Degenhardt, L. & Hickman, M. (2012). Opiate substitution treatment and HIV transmission in people who inject drugs: systematic review and meta-analysis. Bmj, 345, e5945.

Mathers, B. M., Degenhardt, L., Phillips, B., Wiessing, L., Hickman, M., Strathdee, S. A. & Toufik, A. (2008). Global epidemiology of injecting drug use and HIV among people who inject drugs: a systematic review. The Lancet, 372(9651), 1733-1745.

Mattick, R. P., Kimber, J., Breen, C. & Davoli, M. (2008). Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database Syst Rev, 2(2).

Mattick, R. P., Breen, C., Kimber, J. & Davoli, M. (2009). Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. The Cochrane database of systematic reviews, 3(3).

Mattick, R. P., Breen, C., Kimber, J. & Davoli, M. (2014). Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. The Cochrane database of systematic reviews, 2.

McLellan, A. T., Lewis, D. C., O'brien, C. P. & Kleber, H. D. (2000). Drug dependence, a chronic medical illness: implications for treatment, insurance, and outcomes evaluation. Jama, 284(13), 1689-1695.

McLellan, A. T., Carise, D. & Kleber, H. D. (2003). Can the national addiction treatment infrastructure support the public's demand for quality care? J Subst Abuse Treat, 25(2), 117-121.

McLellan, A. T., Starrels, J. L., Tai, B., Gordon, A. J., Brown, R., Ghitza, U. & Lindblad, R. (2013). Can substance use disorders be managed using the chronic care model? Review and recommendations from a NIDA Consensus Group. Public health reviews, 35(2), 8.

McLellan, A. T. (2017). Substance Misuse and Substance use Disorders: Why do they Matter in Healthcare?. Transactions of the American Clinical and Climatological Association, 128, 112

Milani, B. & Scholten, W. (2011). Access to controlled medicines The world medicines situation (3rd ed., pp. 1-20). Geneva: OMS.

Miller, W. R. & Rose, G. S. (2013). Motivation Interviewing and Decisional Balance: Contrasting Responses to Client Ambivalence. Behavioural and Cognitive Psychotherapy, 43, 129-141.

Mino, A. (1990). Analyse scientifique de la littérature sur la remise contrôlée d'héroïne ou de morphine. Berne: Office Fédéral de la Santé Publique.

Minozzi, S., Amato, L., Bellisario, C., Ferri, M. & Davoli, M. (2013). Maintenance agonist treatments for opiate−dependent pregnant women. The Cochrane Library.

Miron, J. A. (2003). The effect of drug prohibition on drug prices: Evidence from the markets for cocaine and heroin. Review of Economics and Statistics, 85(3), 522-530.

Mjåland, K. (2015). The paradox of control: An ethnographic analysis of opiate maintenance treatment in a Norwegian prison. International Journal of Drug Policy, 26(8), 781-789. doi:http://dx.doi.org/10.1016/j.drugpo.2015.04.020.

Moatti, J. P., Carrieri, M. P., Spire, B., Gastaut, J. A., Cassuto, J. P., Moreau, J. & Manif 2000 Study Group. (2000). Adherence to HAART in French HIV-infected injecting drug users: the contribution of buprenorphine drug maintenance treatment. Aids, 14(2), 151-155.

Musto, D. F. (1987). The American disease: Origins of narcotic control: Oxford University Press.

Nielsen, S., Larance, B., Degenhardt, L., Gowing, L., Kehler, C. & Lintzeris, N. (2016). Opioid agonist treatment for pharmaceutical opioid dependent people. The Cochrane database of systematic reviews, 5, CD011117.

Nyswander, M. & Dole, V. P. (1967). The present status of methadone blockade treatment. Am J Psychiatry, 123(11), 1441-1442. doi:10.1176/ajp.123.11.1441.

O'Brien, S. & Cullen, W. (2011). Undergraduate medical education in substance use in Ireland: a review of the literature and discussion paper. Ir J Med Sci, 180(4), 787-792. doi:10.1007/s11845-011-0736-y.

O'Connor, P. G., Nyquist, J. G. & McLellan, A. T. (2011). Integrating addiction medicine into graduate medical education in primary care: the time has come. Annals of internal medicine, 154(1), 56-59.

O'Connor, P. G., Sokol, R. J. & D'Onofrio, G. (2014). Addiction medicine: the birth of a new discipline. JAMA Intern Med, 174(11), 1717-1718.

Obrist, B., Iteba, N., Lengeler, C., Makemba, A., Mshana, C., Nathan, R. & Mayumana, I. (2007). Access to health care in contexts of livelihood insecurity: a framework for analysis and action. PLoS Med, 4(10), e308.

OFSP. (2012). Le référentiel modulaire QuaThéDA. Berne, Suisse: Office fédérale de la santé publique. Stamm, R. & Hälg, R.

OFSP. (2013). Dépendance aux opioïdes: Traitements basés sur la substitution. Berne, Suisse: Office fédérale de la santé publique.

Penchansky, R. & Thomas, J. W. (1981). The concept of access: definition and relationship to consumer satisfaction. Medical care, 19(2), 127-140.

Petitjean, S., Stohler, R., Déglon, J.-J., Livoti, S., Waldvogel, D., Uehlinger, C. & Ladewig, D. (2001). Double-blind randomized trial of buprenorphine and methadone in opiate dependence. Drug Alcohol Depend, 62(1), 97-104.

Phillips, L. A. & Shaw, A. (2013). Substance use more stigmatized than smoking and obesity. Journal of Substance Use, 18(4), 247-253.

Radbruch, L., Jünger, S., Payne, S. & Scholten, W. (2014). Access to Opioid Medication in Europe (ATOME). Final Report and Recommendations to the Ministries of Health.

Rao, R., Ambekar, A., Agrawal, A., Pawar, A. K. S., Mishra, A. K. & Khandelwal, S. (2016). Evaluation of a five-day training programme on opioid substitution therapy in India. Drugs: Education, Prevention and Policy, 1-5.

Rasyidi, E., Wilkins, J. N. & Danovitch, I. (2012). Training the next generation of providers in addiction medicine. Psychiatric Clinics of North America, 35(2), 461-480.

Reimer, J., Wright, N., Somaini, L., Roncero, C., Maremmani, I., McKeganey, N. & Alho, H. (2016). The impact of misuse and diversion of opioid substitution treatment medicines: evidence review and expert consensus. European addiction research, 22(2), 99-106.

Richert, T. & Johnson, B. (2015). Long-term self-treatment with methadone or buprenorphine as a response to barriers to opioid substitution treatment: the case of Sweden. Harm Reduction Journal, 12(1), 12. doi:10.1186/s12954-015-0037-2.

Ritter, C. (2014). Substitution maintenance treatment in Ukraine: humanitarian and medical mission 16–21 May 2014. Co-operation Group to Combat Drug Abuse and illicit trafficking in Drugs, Pompidou Group, Council of Europe (https://www.coe. int/T/DG3/Pompidou/Source/focus/P-PG.

Ritter, C. & Bischoff, T. (2014). Enseignement prégradué de la médecine de l'addiction (13.003946 / 704.0001 / -614).

Rosenthal, R. N., Lofwall, M. R., Kim, S., Chen, M., Beebe, K. L. & Vocci, F. J. (2016). Effect of buprenorphine implants on illicit opioid use among abstinent adults with opioid dependence treated with sublingual buprenorphine: A randomized clinical trial. JAMA, 316(3), 282-290.

Roux, P., Carrieri, M. P., Villes, V., Dellamonica, P., Poizot−Martin, I., Ravaux, I. & Spire, B. (2008). The impact of methadone or buprenorphine treatment and ongoing injection on highly active antiretroviral therapy (HAART) adherence: evidence from the MANIF2000 cohort study. Addiction, 103(11), 1828-1836.

Roux, P., Carrieri, M. P., Cohen, J., Ravaux, I., Poizot-Martin, I., Dellamonica, P. & Spire, B. (2009). Retention in opioid substitution treatment: a major predictor of long-term virological success for HIV-infected injection drug users receiving antiretroviral treatment. Clinical infectious diseases, 49(9), 1433-1440

Samet, J. H. & Fiellin, D. A. (2015). Opioid substitution therapy-time to replace the term. Lancet (London, England), 385(9977), 1508.

Sartorius, N. (2007). Stigma and mental health. The Lancet, 370(9590), 810.

Scholten, W. (2013). Access to opioid analgesic: essential for quality cancer care. In M. Hanna & Z. Zylicz (Eds.), Cancer pain. London: Springer.

Scholten, W. (2015). Make your words support your message. J Pain Palliat Care Pharmacother, 29(1), 44-47. doi:10.3109/15360288.2014.997855.

Scholten, W. (2017). European drug report 2017 and opioid-induced deaths: British Medical Journal Publishing Group.

Scholten, W. & Henningfield, J. E. (2016). Negative outcomes of unbalanced opioid policy supported by clinicians, politicians, and the media. J Pain Palliat Care Pharmacother, 30(1), 4-12.

Scholten, W., Simon, O., Maremmani, I., Wells, C., Kelly, J. F., Hämmig, R. & Radbruch, L. (In press). Access to treatment with controlled medicines: Rationale and recommendations for neutral, respectful, and precise language. BMJ.

Seya, M.-J., Gelders, S. F., Achara, O. U., Milani, B. & Scholten, W. K. (2011). A first comparison between the consumption of and the need for opioid analgesics at country, regional, and global levels. J Pain Palliat Care Pharmacother, 25(1), 6-18.

Stein, M. D., Mulvey, K. P., Plough, A., & Samet, J. H. (1998). The functioning and well being of persons who seek treatment for drug and alcohol use. Journal of substance abuse, 10(1), 75-84.

Stone, K. & Sander, G. (2016). The global state of harm reduction 2016. London: Harm Reduction International.

Sun, B., Fan, N., Nie, S., Zhang, M., Huang, X., He, H. & Rosenheck, R. A. (2014). Attitudes towards people with mental illness among psychiatrists, psychiatric nurses, involved family members and the general population in a large city in Guangzhou, China. International journal of mental health systems, 8(1), 26.

Taylor, A. L. (2007). Addressing the global tragedy of needless pain: rethinking the United Nations single convention on narcotic drugs: SAGE Publications Sage CA: Los Angeles, CA.

Teesson, M., Mills, K., Ross, J., Darke, S., Williamson, A. & Havard, A. (2008). The impact of treatment on 3 years' outcome for heroin dependence: findings from the Australian Treatment Outcome Study (ATOS). Addiction, 103(1), 80-88.

Terry, C. E. & Pellens, M. (1970). The opium problem. Montclair: Patterson Smith.

Torrens, M., Fonseca, F., Galindo, L., & Farré, M. (2015). Opioid addiction: short-and long-acting opioids. Textbook of Addiction Treatment: International Perspectives, 467-500.

Uchtenhagen, A., Ladjevic, T., Rehm, J. (2005). A systematic review of existing guidelines. Working paper for World Health Organization. Geneva: WHO.

Uchtenhagen, A., Stamm, R., Huber, J., Vuille, R. (2008). A review of systems for continued education and training in the substance abuse field. Substance Abuse. 29:95-102.

Uchtenhagen, A. & Schaub, M. (2011). Minimum Quality Standards in Drug Demand Reduction EQUS. Zurich: Research Institute for Public Health and Addiction A WHO collaborating center affiliated to Zurich University.

United Nations (2010). Report of the Special Rapporteur on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health (A/65/255).

UNODC. (2007). World Drug Report. United Nations Publications.

UNODC & WHO. (2016). International Standards for the Treatment of Drug Use Disorders — Draft for Field Testing. Vienna: United Nations.

Valadez, M. A. N. (2014). Drug use and the right to health: An analysis of international law and the Mexican case. Mexican law review, 6(2), 201-224.

Vranken, M. J. M., Lisman, J. A., Mantel-Teeuwisse, A. K., Jünger, S., Scholten, W., Radbruch, L. & Schutjens, M. H. D. B. (2016). Barriers to access to opioid medicines: A review of national legislation and regulations of 11 central and eastern European countries. The Lancet Oncology, 17(1), e13-e22. doi:10.1016/S1470-2045(15)00365-4.

Wakeman, S. E. & Rich, J. D. (2017). Barriers to Post-Acute Care for Patients on Opioid Agonist Therapy; An Example of Systematic Stigmatization of Addiction: Springer.

WHO. (2004). WHO/UNODC/UNAIDS position paper: Substitution maintenance therapy in the management of opioid dependence and HIV/AIDS prevention. In WHO/UNODC/UNAIDS position paper: substitution maintenance therapy in the management of opioid dependence and HIV/AIDS prevention.

WHO. (2009). Access to Controlled Medications Programme: Improving access to medications controlled under international drug conventions: briefing note. Geneva: World Health Organisation.

WHO. (2009). Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence. World Health Organisation.

WHO. (2011). Ensuring balance in national policies on controlled substances: World Health Organisation.

Wright, N., D'Agnone, O., Krajci, P., Littlewood, R., Alho, H., Reimer, J. & Maremmani, I. (2016). Addressing misuse and diversion of opioid substitution medication: guidance based on systematic evidence review and real-world experience. Journal of Public Health, 38(3), e368-e374. doi:10.1093/pubmed/fdv150.

Wyszewianski, L. (2002). Access to Care: Remembering Old Lessons. Health Serv Res, 37(6), 1441-1443. doi:10.1111/1475-6773.12171.

Zedler, B. K., Mann, A. L., Kim, M. M., Amick, H. R., Joyce, A. R., Murrelle, E. L. & Jones, H. E. (2016). Buprenorphine compared with methadone to treat pregnant women with opioid use disorder: a systematic review and meta–analysis of safety in the mother, fetus and child. Addiction, 111(12), 2115-2128.

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