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Л. Н. Гумилев атындағы Еуразия ұлттық университеті Тел.: +7(7172) 709-500 (ішкі 31432)  
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Евразийский национальный университет имени Л. Н. Гумилева Тел.: +7(7172) 709-500 (вн. 31432)  
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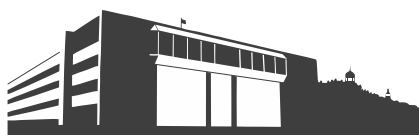
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H. Beshherli<sup>1</sup>, M. Sanatkanuly<sup>2</sup>  
M. Kudabekov<sup>2</sup>, N. Baigabylov<sup>2</sup>

<sup>1</sup>Ankara Haci Bayram Veli University, Ankara, Turkey

<sup>2</sup>L.N. Gumilyov Eurasian National University, Nur-Sultan, Kazakhstan

(E-mail: hayati.besirli@hbv.edu.tr, madi\_01\_15@mail.ru, k-medet@bk.ru, n.baigabylov@mail.ru)

## Methadone use in opioid substitution therapy for drug dependence

**Abstract.** *Anti-methadone hysteria' has reached colossal proportions. It is raging today on the Internet sources specializing in combat drug addiction and popularizing public health. The topic of opioid substitution treatment has long gone beyond the level of scientific discussion. It has become a confrontation between two ideologies. No matter how controversial the assertion about OST may seem, it is necessary to get to the heart of the issue. The article describes the scheme for the use of opioid substitution therapy in Kazakhstan and contains criticism of the maintenance therapy opponents, as well as the arguments of its supporters.*

**Keywords:** *opioid substitution treatment, drug treatment, drug addiction, methadone.*

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### Introduction

According to modern theories, opioid addiction is a disease of the central nervous system in which the biochemistry changes in the active centers (receptors) of the brain. And as a result of this, the need for opiates becomes biologically determined, and very often irresistible. The most competent point of view remains that opioid dependence is a chronic relapsing condition that is difficult to control. It manifests itself as an irresistible attraction (addiction) to drugs despite the negative social and health consequences. Not all cases of addiction are chronic, and that's true. Some people who meet the diagnostic criteria

of drug addiction stop using drugs completely without any medical treatment. However, most people with addiction disorders often relapse after treatment. Moreover, it is considered that such people remain vulnerable for many years or even perhaps the whole of their lives.

It is important to understand that:

- up to 50% of opioid users may suffer from other psychiatric disorders including anxiety, depression, and antisocial disorders;
- one in four opioid users who visit a healthcare organization has a risk of suicide and self-harm;
- almost one in ten people have persistent severe mental health problems which require close touch with psychiatric organizations' specialists.

Inclusion of opioid substitution treatment (hereinafter referred to as OST) in the program has a significant positive impact on the mental, physical, and social condition of such patients.

### Problem statement

OST is a type of long-term combined treatment for opioid dependence. It involves the use of legal pharma drugs that help to prevent withdrawal symptoms (the sweats) and block cravings for illegal opioids. Besides patients receive psychological care and social support. Due to OST patients do not need to look for illicit drugs and do injections of them. And this fact sharply reduces the risk of being infected by HIV, overdose, criminalization, and other negative consequences of illicit drug use. Withdrawal from heroin and similar fast-acting opioids in favor of long-acting opioid medications (for example, methadone) normalizes metabolic processes in the brain over time and allows patients to stop OST in the future in case they are really willing to give it up.

Scientific evidence suggests that a combined approach to medication treatment (OST) and psychological support under constant monitoring works best to treat opioid dependence. Success requires that patients followed the treatment program for a long time (at least 2 years, and sometimes for even more years) receiving all the benefits that such therapy provides. The practice has shown that substitution maintenance therapy (hereinafter referred to as SMT) is the most effective form of treatment for the majority of people suffering from opioid dependence.

### Results and discussion

In Kazakhstan, opioid (maintenance) substitution therapy has been implemented since 2008 with the support of the Global Fund to Fight AIDS, Tuberculosis, and Malaria. From 2008 to 2020, 1 331 patients in 10 regions of the country received treatment as part of the substitution maintenance treatment program (hereinafter referred to as SMT).

*Psychological* support for SMT patients includes motivational interviewing and cognitive-behavioral psychotherapy [1].

*Medication* care for the people taking part in the SMT program is provided by opioid agonists in the maintenance treatment rooms. SMT rooms operate in 15 cities around the country such as Almaty, Uralsk, Atyrau, Aktobe, Semey, Ust-Kamenogorsk, Pavlodar, Ekibastuz, Karaganda, Temirtau, Taraz, Kostanay, Rudny, Lisakovsk, and Kyzylorda. In accordance with the approved standard for the organization of medical and social assistance in the field of mental health to the population of the Republic of Kazakhstan, such rooms provide the following services:

- 1) services under the program of maintenance treatment with opioid agonists including the issuance of drugs, psychosocial counseling in accordance with an approved clinical protocol;
- 2) improving the life quality of and social adaptation of patients with opioid dependence;
- 3) reducing the risk and quantity of illegal drugs and psychotropic substances use;
- 4) reducing the risk of transmission of HIV and other concomitant diseases among people who use injection drug;

**Table 1.** Indications for SMT

Main criteria	Additional criteria
<ul style="list-style-type: none"> <li>- diagnosis (F11.2) Mental and behavioral disorders due to use of opioids, dependence syndrome;</li> <li>- ability to give informed consent;</li> <li>- age over 18 years old.</li> </ul>	<ul style="list-style-type: none"> <li>- established diagnosis of HIV;</li> <li>- established diagnosis of hepatitis B, C, D, G;</li> <li>- confirmed experience of injecting drug use for at least 3 years;</li> <li>- at least two hospitalizations in a hospital with a diagnosis of (F11.2) Mental and behavioral disorders due to use of opioids, dependence syndrome;</li> <li>- pregnancy.</li> </ul>

5) increasing commitment to antiretroviral therapy among people infected with HIV and opioid dependency [1].

Indications for maintenance treatment with opioid agonists are the presence of all main criteria and one of the additional ones listed in Table 1.

Methadone, a long-acting opioid drug, approved for use and registered under the code RK-LS-No121922 is used to provide medical assistance to persons participating in the SMT program in Kazakhstan [2]. The daily dose of methadone hydrochloride is determined by the level of neuroadaptation to opioids with tolerance to opiates while the starting dose is 10 mg, and with established physical dependence – 20-30 mg. The duration of the patient's treatment at this stage is 6 months or more. An optimal dose of methadone hydrochloride is 60-120 mg/day. In case of planned completion/early refusal of treatment, the daily dose of the drug may be reduced on average by 2.5-5 mg per week without severe opioid withdrawal symptoms. During dose reduction, the patient should be regularly examined and there should be adjusted dosages, if clinically necessary. In case of exclusion of the patient, it is recommended to reduce the drug dose daily by 5 mg until reaching 30 mg/day. Further, the daily dose reduction of the drug should be 2 mg until complete cancellation.

In all these cases it is also possible to develop an individual dose reduction scheme for the drug by the attending physician together with the patient. For patients diagnosed with tuberculosis, the initial priority of the service is to treat active tuberculosis, i.e., while the patient is hospitalized, methadone is not available to him. Treatment for patients having viral hepatitis is carried out in combination with other pharmacotherapy without waiting for the onset of opioid withdrawal. Patients with HIV are primarily stabilized with the help of SMT after which they are given antiretroviral therapy. Opioid agonist maintenance treatment with methadone is recognized as the most appropriate for pregnant and breastfeeding patients [3].

According to official data, in early 2020, there were treated 296 people under the SMT program which is only 0.3% of the estimated number of

people who use opioid drugs (94 600 people) [4], 235 of which were men, and 61 women. In addition, the number of people living with HIV in the program is 109 people, and 92 (84%) of them are taking antiretroviral therapy. On July 2021, 326 people have taken part in the program, 117 of which are patients with HIV [5].

According to narcologists, methadone therapy does not cure drug addiction by 100%. At the same time, it makes patients' lives easier. It helps to return them to society, control the risks of contracting incurable diseases, and significantly reduce the crime rate [2]. According to the Mental Health Center, 330 participants completed the program with positive results on a scheduled basis; 127 participants found families; 560 people were employed. There is a decrease in the criminal behavior of program participants: 78% (1038 participants) had criminal experience before being included in the program, and 565 of them had multiple convictions. Over 12 years of the program implementation, 61 participants of the program were convicted [6].

However, opioid substitution treatment is often criticized. In 2010, the Ministry of Healthcare of the Republic of Kazakhstan, and then in 2015 the Prosecutor General's Office initiated checks on the legitimacy of the OST program implementation on behalf of the Security Council of the Republic of Kazakhstan. Then it was recommended to terminate the program ahead of schedule and withdraw patients from the program with a gradual reduction of methadone doses. The monograph Formation and Prospects for the Development of the Institute for Drug Use Level Assessment in Kazakhstan, a study by a group of researchers from the Law Enforcement Academy under the Prosecutor General's Office of the Republic of Kazakhstan, notes the following reasons why further implementation of the OST program is inexpedient:

- failed to reduce the incidence of HIV; the project does not provide for the resocialization of persons being treated;
- no motivation to give up drugs;
- strong aggressive behavior during methadone withdrawal (the sweats);
- no effect on law-abiding behavior education.

It also says that by the protocol decision of the IHS (the interdepartmental headquarters for

coordinating the activities of state bodies aimed at combating drug addiction and drug dealing) meeting in 2018, the Ministry of Healthcare was given a recommendation on the inappropriateness of using OST [5].

In June 2017, the Ministry of Internal Affairs of the Republic of Kazakhstan demanded to stop the implementation of the program. Then was created an Intersectoral Working Group of 17 people. Their task of them was to evaluate the program's effectiveness. The working group prepared a resolution concluding that OST is effective in Kazakhstan and should be continued but some of its members initiated an alternative study with the cooperation of the police. The conclusions of the alternative examination turned out to be predictable. Therefore, in January 2018, the admission of new patients to the opioid substitution therapy centers was temporarily stopped. Meanwhile, the Kazakhstan Union of People Living with HIV appealed to the President not to close the project [2].

Parliamentarians also have repeatedly expressed their opinion against the implementation of the opioid substitution therapy program in Kazakhstan [7]. They believe that an analog of heroin and morphine could undermine national security in the country. In confirmation of this, the following fact was cited in the document 'Expanding the Availability of Opioid Substitution Therapy in the Republic of Kazakhstan in 2010-2014: Review of the Situation, Action Plan and Operational Implementation Plan', that a delay in methadone supply for at least of one day threatens the country with socio-political unrest [2].

Among the arguments of opponents of opioid agonists therapy were also the following:

- the imposition of 'harm reduction programs' by the West and the creation of a new type of drug business with Western money coming to Kazakhstan through non-governmental organizations [2];

- research and clinical trials of methadone in Kazakhstan were carried out in violation of the requirements stipulated by the legislation and in favor of OST [8];

- refusal of the neighboring countries – Russia and Uzbekistan – from the OST program [9];

- use of methadone is not a treatment for drug addicts, it only serves to transfer them to a harder drug that has more devastating consequences [10].

Supporters of maintenance therapy try another argument in favor of the further implementation of the OST program.

Obviously, methadone medicine is a drug. But it is far from the drug use which is threatening with corresponding negative consequences – from overdoses and abscesses to death behind bars or in a hospital. Methadone at an adequate dose does not cause euphoria in patients with chronic opioid dependence. Moreover, it is prescribed under strict supervision, and under controlled conditions, which, unlike street drugs makes this drug safer and more effective for opioid dependence treatment. Also, proper, and stable opioid substitution treatment of the patient usually does not even make him try to get illicit opioids, as methadone blocks the euphoric effect of these drugs. Patients getting supportive treatment do not have physiological or behavioral abnormalities, as happens with street opioids. Among other things, a patient who participates in the OST process learns life-saving skills, whereas a person who uses street opiates uncontrollably becomes indifferent to his or her own health and the health of his or her loved ones.

## Conclusion

Indeed, methadone does not eliminate the addiction, but it allows them to take it under control and significantly improve the life of an addicted patient. Despite the fact that the patient is still dependent on drugs, he acquires the ability to stabilize his mental and physical state, significantly increases his social status, discover new opportunities for himself.

Like any other treatment method, OST is not perfect and, apart from the obvious benefits, also has certain consequences. The main ones have been specified in this article and are actively used by OST opponents to discuss the pros and cons of the therapy. Nevertheless, according to narcologists, the SMT program has demonstrated its effectiveness. The expansion of the program is considered [3].



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**Х. Бешерли<sup>1</sup>, М. Санатқанұлы<sup>2</sup>, М. Құдабеков<sup>2</sup>, Н. Байгабылов<sup>2</sup>**

<sup>1</sup>Ankara Hacı Bayram Veli университеті, Анкара, Түркия

<sup>2</sup>Л.Н. Гумилев атындағы Еуразиялық ұлттық университеті, Нұр-Сұлтан, Қазақстан

### **Есірткіге тәуелділікті емдеуге бағытталған опиоидты алмастыру емінің шеңберінде метадонды қолдану**

**Аңдатпа.** «Нашақорлыққа қарсы күреске» мамандандырылған және қоғамдық денсаулықты насихаттайтын Интернет-ресурстардың кең ауқымында өршіп тұрған «метадонға қарсы истерия» үлкен ауқымға жетті. Опиоидты алмастыратын терапия тақырыбы екі идеологияның қарама-қайшылығы форматына өтіп, ғылыми талқылаудан тыс қалды. ОАТ туралы барлық мәлімдемелер қаншалықты даулы болып көрінсе де, мәселенің мәнін түсіну керек. Бұл мақалада Қазақстанда опиоидты алмастыру терапиясын қолдану сызбасы сипатталады, демеуші терапияның қарсыластарына сын, сондай-ақ оны қолдаушылардың дәлелдері келтіріледі.

**Түйін сөздер:** опиоидты алмастыратын терапия, нашақорлықты емдеу, нашақорлық, метадон.

**Х. Бешерли<sup>1</sup>, М. Санатқанұлы<sup>2</sup>, М. Кудабеков<sup>2</sup>, Н. Байгабылов<sup>2</sup>**

<sup>1</sup>Университет Анкара Наси Баграм Велі, Анкара, Туриция

<sup>2</sup>Евразийский национальный университет им. Л.Н. Гумилева, Нур-Сұлтан, Қазақстан

**Применение метадона в рамках опиоидной заместительной терапии,  
направленной на лечение наркозависимости**

**Аннотация.** «Антиметадоновая истерия», бушующая сегодня на просторах интернет-ресурсов, специализирующихся на «борьбе с наркоманией» и популяризирующих общественное здоровье, достигла колоссальных масштабов. Тема опиоидной заместительной терапии уже давно вышла за пределы научной дискуссии, перейдя в формат противостояния двух идеологий. Какими бы спорными не казались всевозможные утверждения об ОЗТ, необходимо вникнуть в самую суть проблемы. В данной статье описывается схема применения опиоидной заместительной терапии в Казахстане, приводятся критика противников поддерживающей терапии, а также аргументы ее сторонников.

**Ключевые слова:** опиоидная заместительная терапия, лечение наркомании, наркозависимость, метадон.

**Information about authors:**

**Sanatkanuly M. – Corresponding author**, Ph.D. student, Department of Sociology, L.N. Gumilyov Eurasian National University, 6 Yanushkevich str., Nur-Sultan, Kazakhstan.

**Besherli H. –** Doctor of Sociological Sciences, Professor, Department of Sociology, Ankara Haci Bayram Veli University, Ankara, Turkey.

**Kudabekov M. –** Senior Lecturer of the Department of Sociology, L.N. Gumilyov Eurasian National University, 6 Yanushkevich str., Nur-Sultan, Kazakhstan.

**Vaigabylov N. –** Ph.D. in Sociology, Associate Professor, Department of Sociology, L.N. Gumilyov Eurasian National University, 6 Yanushkevich str., Nur-Sultan, Kazakhstan.

**Санатқанұлы М. – корреспонденция үшін авторы**, Л.Н. Гумилев атындағы Еуразия ұлттық университетінің әлеуметтану кафедрасының докторанты, А.Янушкевич көш., 6, Нұр-Сұлтан, Қазақстан.

**Бешерли Х. –** әлеуметтану ғылымдарының докторы, Анкара Наси Баграм Велі университеті әлеуметтану кафедрасының профессоры, Анкара, Түркия.

**Кудабеков М. –** Л.Н. Гумилев атындағы Еуразия ұлттық университетінің әлеуметтану кафедрасының аға оқытушысы, А. Янушкевич көш., 6, Нұр-Сұлтан, Қазақстан.

**Байгабылов Н. –** PhD, Л.Н. Гумилев атындағы Еуразия ұлттық университетінің әлеуметтану кафедрасының доценті м.а., А. Янушкевич көш., 6, Нұр-Сұлтан, Қазақстан.