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# Methadone Treatment for Heroin Dependence

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Additional information is available at the end of the chapter

## Abstract

In substitution therapy for treatment of heroin addiction, methadone is the synthetic opioid agonist of first choice. Methadone doses vary depending on addict profile established by repeated evaluation. It studied a group of 82 patients both male and female, aged between 19 and 47 years, residing in Bucharest, with diagnosis of heroin addiction. They were voluntarily submitted in the methadone substitution treatment at a specialized treatment center for addiction in Bucharest. The study group was characterized in detail, taking into account demographic, comorbid and addiction characteristics, heroin use history, treatment history, and clinical and paraclinical evaluation. The outcomes resulting from the study design on 82 heroin addict patients enrolled into a methadone maintenance program highlighted: lowering of the onset age of heroin use, HVC infection comorbidity, and the extension of the treatment period due to the relapses. The results obtained by clinical, laboratory, and psychological complex evaluations in a correlative approach is essential both in initiating methadone treatment and monitoring the detox period but also in the supervision of methadone maintenance treatment.

**Keywords:** methadone substitution treatment, heroin addiction, addict profile

## 1. Introduction

The opiates, especially the heroin could be the main problem in the matter of drugs at world level, as statistics on the treatment request show. Heroin use dominates the demand for treatment in Europe (around 80% of new opioid-related treatment demands) [1]. However, the opiates consuming is relatively stable at the world level, with an estimated 33 million users of opiates and prescription opioids, according to the latest world report on drugs [2]. European

statistics show that heroin is the most commonly used illicit opioid in Europe, but synthetic opioids such as methadone, buprenorphine, and fentanyl are also misused. The average prevalence of high-risk opioid use among general EU population (15–64 years) is estimated at 0.4%, the equivalent of 1.3 million high-risk opioid users in Europe in 2015 [1].

In addition, opioids remain major drugs of potential harm and health consequences. There are several complications, which are derived from the illicit opioids consumption, among which there are overdoses, transmissible infections, the increase of criminality, reduction of workforce, and general life quality [3, 4].

The addiction to opioids, a complex disease, necessitates a long-term treatment, which mainly consists in the substitution therapy, also called, according to WHO, "agonist pharmacotherapy," "agonist replacement therapy" or "agonist-assisted therapy"; this is a key component of the treatment resources [5]. WHO defines it as the administration under medical supervision of prescription psychoactive substances, which are pharmacologically related to the one producing dependence, to people with addiction, for achieving defined treatment goals.

Several tries of substitution treatments of the opiates addiction took place at the beginning of the twentieth century and they used the morphine. The morphine did not prove to be a corresponding substance for substitution (tolerance used to rapidly install, the patient needed to have several injections per day). Since 1960s, starting with the discovery of the methadone, the substitution treatment began to be reevaluated.

In 2005, WHO added methadone and buprenorphine in the list of essential drugs for the treatment of opioid dependence [6]. This decision was based on numerous studies that have shown that using these two drugs in substitution therapy bring benefits for physical and mental health, improves quality of life, and reduces injection behaviors associated with high risks. Therefore, international guidelines recommend methadone and buprenorphine as first-line medication treatment for opioid dependence [7]. The studies were conducted in countries with different socio-economic conditions and different treatment systems for drug addiction. These studies have shown that therapy with methadone or buprenorphine is safe and effective [5]. The substitution therapy with methadone or buprenorphine gives addicted people the possibility to function normally within their families, jobs, and communities [8]. However, methadone was shown to have higher treatment retention rates than buprenorphine-naloxone, and it is preferred over buprenorphine-naloxone for patients at higher risk of treatment dropout [9].

A standard terminology for the treatment with methadone, classified into four categories, has been proposed:

- Short-term detoxification: decreasing doses for up to 1 month;
- Long-term detoxification: decreasing doses over more than 1 month;
- Short-term maintenance: stable doses for up to 6 months;
- Long-term maintenance: stable dose for more than 6 months.

Usually, the term "substitution therapy" is utilized as an equivalent to "substitution maintenance therapy" [10].

The methadone maintenance therapy (MMT) is an intervention of harm reduction type, because the patient does not become abstinent (i.e., the patient does not cure, i.e., he/she does not give up any substance consumption); instead, a series of positive changes such as managing opioid withdrawal, reducing craving, returning to a job, education, and a family happens [11]. The methadone is orally administrated and due to its half-life, between 24 and 36 hours, it may be administered once a day. Administered in doses of 80–120 mg/a day (adjustments are possible according to each patient), the methadone blocks the euphoric effects of the heroin, and moreover, eliminates the craving for heroin; they are some of the most important factors in case of relapses. Methadone maintenance programs decrease mortality by approximately 50% among persons with opioid-use disorders, decreased prevalence of significant infections such as HIV and hepatitis, decrease crime, reduces illicit opioid use, improve social functioning, and increase the rate of retention in rehabilitation programs [12].

The use of the methadone in the substitution treatment of the patients addicted to opiates is well-documented and its efficacy is well established but responses vary. Despite successful outcomes, the MMT and the influence of methadone pharmacodynamics and pharmacokinetics on dose requirements continue to remain controversial [13]. A relationship between methadone dose and plasma methadone concentration in addicted patients during substitution therapy has been suggested, the plasma level depends on different factors [14, 15]. However, research conducted so far have demonstrated fully and unequivocally follows: patients receiving inadequate doses of methadone will continue to use heroin; these patients do not respond to behavioral therapies or they need maintenance treatment with methadone for long periods; when doses of methadone are tailored and individualized favorable trends are observed in these patients [16, 17, 18]. Optimal treatment can only be determined if one takes into account the factors that determine differences in drug response and only when the dosage is determined based on diagnosis, severity, and stage of the disease and on the presence of other diseases or concomitant therapy. This allows pre-evaluation of efficacy and acceptable toxicity limits. If these assessments are not done properly before treatment, if patients are not appropriately monitored during treatment, there is a risk that the therapy to be ineffective.

In this context, we conducted a study, on a period of a year, on a group of patients with a diagnosis of heroin addiction, who have voluntarily submitted to an addiction treatment center in Bucharest, for inclusion in the program of methadone substitution treatment. The objective of the study was to define the profile of the patient entering the methadone substitution therapy and to evaluate the adherence to treatment.

## 2. Study design

The group to be studied consisted of 82 drug addicts, consumers of heroin; these patients were examined from the psychological point of view at the Addiction Section, were hospitalized and monitored during the detoxification which was carried inpatient, under strict medical supervision, for a period of 10–14 days, then in the outpatient treatment (methadone

substitution treatment). The study was approved by the Ethical Committees of the Centre and the informed consent for the participation in the study was obtained from all patients.

The study group was characterized in detail, taking into account demographic, comorbid and addiction characteristics, heroin use history, treatment history, and clinical and paraclinical evaluation.

Indicators/parameters to be followed: age; sex; occupation; comorbidity; the history of heroin consumption (detailed as follows: recognized consumption age, intravenous heroin consumption starting age, way of heroin administration, other tested/consumed drugs); history of treatment (previous abstinence periods, previous hospitalizations, previous treatments, when starting treatment with methadone, which is currently under, psychological counseling; methadone dose); and toxicological analytic screening aiming at both diagnosing the drug consumption as well as checking and confirming the abstinence along the period of substitution therapy with methadone.

During the hospitalization, the psychological investigation of the patients was made. The description of the mental state, together with monitoring the behavior during the psychological interview, aim at filling in the examination file and applying efficiency and personality tests for the psycho-diagnostic purpose.

Qualitative analytical screening and quantitative assays refers to the immunofluorescence method for the quantitative determination of heroin and their metabolites in urine [19]; it is based on a technique of fluorescence polarization immunoassay using an automatic drug analyzer version TDxFLx (Abbott Laboratories). The results can be expressed either in qualitative (presence or absence of opiates) or quantitative (sample concentration in ng/mL) terms. Detection threshold (cut-off) was established at 200 ng/mL (this being the most widely accepted value). Measurements obtained are used for the diagnosis of heroin use and for establishing the substitution therapy.

## 3. Statistical analysis

To achieve the study, we have used individual medical files, and, for instruments of interpreting data, we have used a series of statistic applications including both the descriptive methods and the analytic ones; the data are centralized in the database EXCEL and SPSS and processed with the available statistic functions, compatible and adequate to the type of the collected data (at nominal, regular and reporting level).

The descriptive statistics, the distribution of the frequencies and the comparisons have been done by means of the program SPSS Statistics, ver. 21; the data of the different parameters are presented as average ± standard deviation (SD). The correlations between the parameters, using the correlation coefficients (Pearson, Spearman, and Kendall) have also been evaluated. The comparisons among the groups under study have been made by means of the Student and Anova tests. All of them have been statistically significant at the level of $p_1 = 0,05$ and $p_2 = 0,01$.

## 4. Results and discussions

We have taken a group of 82 patients, both males and females, aged between 19 and 47, living in Bucharest and diagnosed with heroin addiction (according to ICD-10), who came voluntarily to get a substitute treatment with methadone in a center of specialized treatment of addiction, placed in Bucharest. The group under study has been described in details, taking into account the demographic, addiction characteristics and comorbidity, the history of the heroin consumption, the history of the treatment, the clinical and laboratory evaluation.

### 4.1. Demographic, addiction characteristics, and comorbidities

The complex description of the patients group regarding the demographic, addiction, and treatment characteristics, as well as comorbidities is presented in the **Table 1**.

#### 4.1.1. Indicator: sex

In the selected group, males are predominant; so, the group has included 75/82 patients, respectively 91.5% and 7/82 patients, respectively 8.5% females (**Table 2**), leading to a proportion of 10.71 males/females.

#### 4.1.2. Indicator: age

In the general hypothesis of the study, we have anticipated that, when speaking about the drug consumers, there are clear differences between the average age of the drug consumers who are registered and the onset average age of the drug consumers within the same population, and the results lead to the confirmation and acceptance of the general hypothesis.

Thus, the average age of the patients registered at the beginning of the study was $31.28 \pm 5.15$ years and varied between 19 and 47 years (**Figure 1**), being significantly higher than the average age at the onset of drug use, which was $19.52 \pm 4.35$ years and varied between 11 and 33 years (**Figure 2**) ($p < 0.001$, t-Student). The statistic significant difference was also noticed when the Anova Test was applied ($p < 0.001$).

As regards the age at the onset of heroin use, there is a dramatic remark which says that many of the patients declared their onset under the age of 20, respectively, the most frequent interval, between the age of 15 and 20 (40/82 patients, 48.8%). The study points out the growth of the drug consumption among young people and the decrease of the onset age. Thus, the history of the opiates consumption is a long term one, an average of $11.73 \pm 4.52$ years varies between 3 and 25 years (**Figure 3**). We have pursued, on the other hand, the duration of the drug consumption, previous to the first requirement of treatment. The obtained results, using some specific statistic methods, have shown that the total period of the drug consumption is significantly different, from the statistic point of view ($p < 0.001$; t-Student, ANOVA**),** from the period of the drug consumption until the first methadone substitution treatment, with an age average $6.51 \pm 3.45$ years, varying in the area 1–18 years (**Figure 4**).

| | |
|---|---|
| Proportion according to the sex | 91.5% males; 8.5% females |
| The male/female ratio | 10.71 |
| Age (years) (mean ± SD) | 31.28 ± 5.15 (range:19–47) |
| Age at the onset of the consumption (years) (mean ± SD) | 19.52 ± 4.35 (range: 11–33) |
| Age category | ≤ 20 years old (1.22%); 21–25 years old (9.75%); 26–30 years old (37.8%); 31–35 years old (32.92%); 36–40 years old (14.63%); > 40 years old (3.66%) |
| Age category at the onset of the consumption | < 15 years old (12.2%); 15–20 years old (48.78%); 21–25 years old (31.7%); 26–30 years old (4.87%); >30 years old (2.44%) |
| Length of consumption (years) (mean ± SD) | 11.73 ± 4.52 (range: 3–25) |
| Length of consumption previous Methadone maintenance treatments (MMT) (years) | 6.51 ± 3.45 (range: 1–18) |
| Occupation (% of the patients) | Unemployed 58.83; Employed 41.7 |
| Problems with the law (damnation) (% of the patients) | 17 |
| Daily dose of heroine (g) (mean ± SD) | 1.04 ± 0.74 (range: 0.3–3.3) |
| Way of consuming (i.v. since the onset) (% of the patients) | 78 |
| Concentration of heroine metabolites in the urine (ng/mL) | 1000–30,000 |
| Patients with poly-drug consumption (%) | 52.5 (new psychoactive substances consumption, NPS in 58.14% of cases) |
| Methadone dose (mg) (mean ± SD) | 55.91 ± 26.71 (range: 15–125) |
| Previous MMT (number of treatments) | 5.45 ± 2.14 (range 1–10) (40/82 of the patients) |
| Previous hospitalizations (number of periods) | 8.31 ± 6.06 (range: 1–30) (58/82 of the patients) |
| Psychological counseling (number of meetings) | 9.48 ± 10.48 (range 1–46)(33/82 of the patients) |
| Patients with previous periods of abstinence (%) | 24.4 |
| Patients with comorbidities (Hepatitis C, Hepatitis B, human immunodeficiency virus) (%) | 70.7% (58/82) |

**Table 1.** Characterization of the group under study.

These aspects, together with the typical profile of the drug addict, are set up in essential data, because they contribute to the accurate identification and peculiarity of the target groups, who should be hinted at when starting a prevention or therapeutic program within the drug addiction phenomenon.

The data are in accordance with the official statistics at the national level, which show that the duration of the consumption previous to the first requirement of assistance is longer for the opiates, with an average of 7.4 years and a frequent value of 4 years [20]. The official reports also show that, even though there are beneficiaries who require some medical assistance after

| Parameter | Parameter | Correlation coefficient, statistic significance |
| --- | --- | --- |
| Age | Length of consumption | r = 0.461**; p < 0.001 |
| Age | Length of consumption previous to MMT | r = 0.354**; p = 0.001 |
| Length of consumption | Length of consumption previous to MMT | r = 0.611**; p < 0.001 |
| Length of consumption previous to MMT | Comorbidities | r = 0.409*; p = 0.025 |
| Length of consumption previous to MMT | Methadone dose | r = 0.526**; p = 0.007 |
| MMT numbers | Previous hospitalizations periods | r = 0.655**; p < 0.001 |
| MMT numbers | Number of psychological counseling meetings | r = 0.501*; p = 0.02 |

*Statistically significant correlation.
**Statistically highly significant correlation.

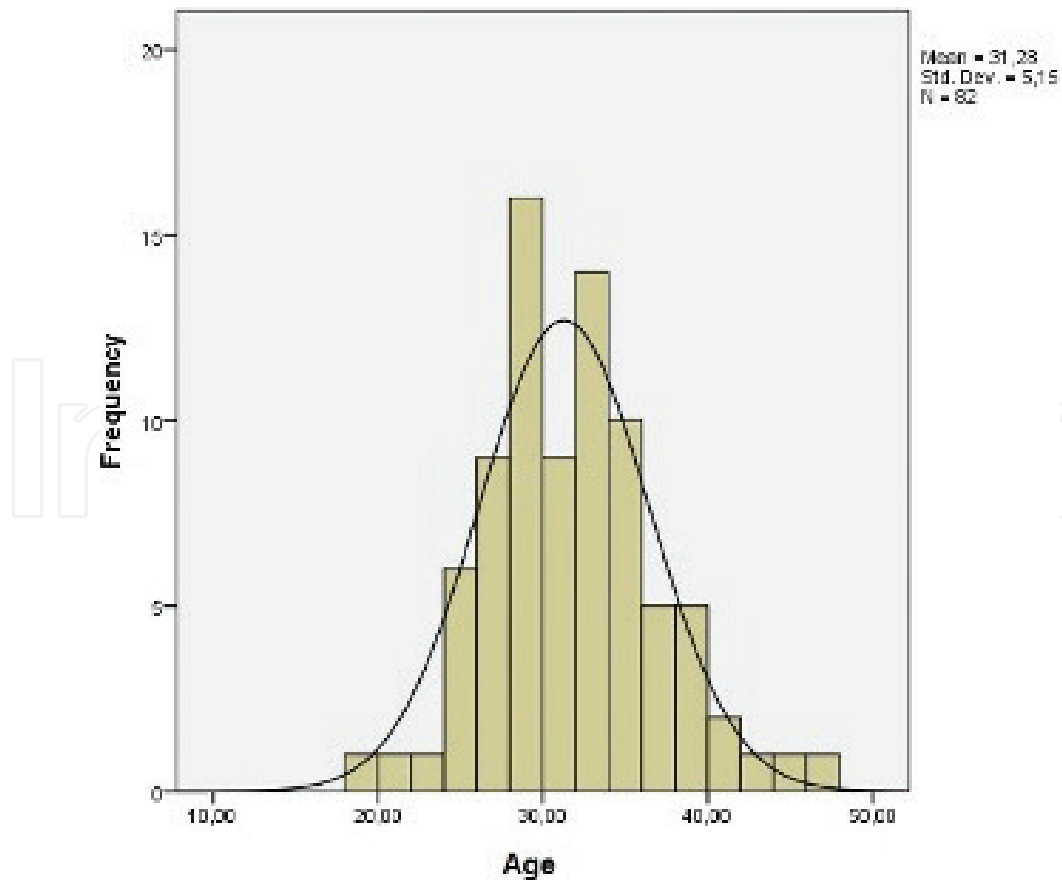**Table 2.** Pearson correlations among the analyzed parameters in the study.



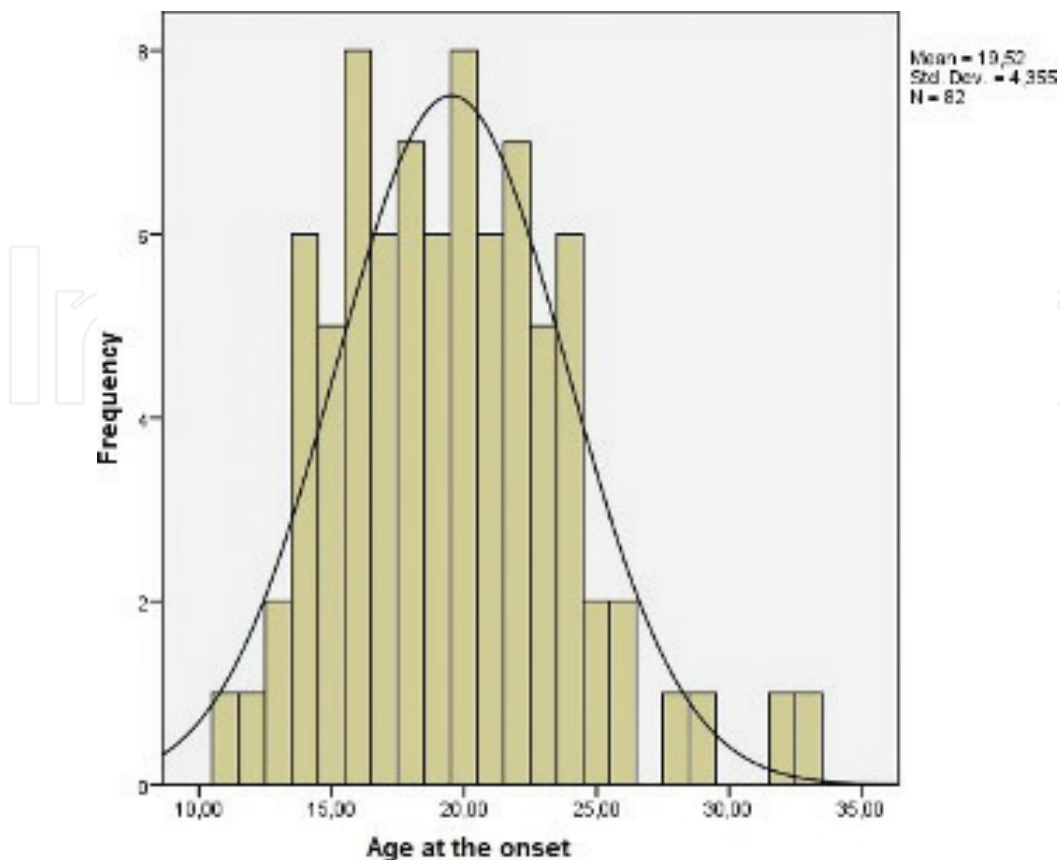**Figure 1.** Proportion of the patients according to the age.

**Figure 2.** Proportion of the patients according to the age at the beginning of the drug consumption.

less than a year, there is a slight growth of the period of demand of the specialized services: most of the beneficiaries who have never been admitted in the treatment, have required medical assistance after 3 years of drug consumption, comparative to the cases of relapse, in which most of the patients have demanded medical assistance after 2 years of drug consumption [20].

Regarding the category of age, the groups of ages between 26 and 30 years and 31–35 years are pinpointed as follows. We can notice that these groups of ages are distinctly different from the most frequent categories in case of the age at the onset of heroin use (15–20 years and 21–26 years.

### 4.1.3. Indicator: occupation

More than half of the patients (58.83%, 48/82) do not have an occupation, and the others have only a temporary occupation. Only one patient of the group has graduated a private faculty; all the others have graduated high or secondary school. Around 17% of the patients have legal antecedents, respectively detention, because they stole in order to get money for drugs.

Psychologically, the drug addicts have problems because they do not have a permanent job; on the other hand, they are not able to keep a permanent job, because the withdrawal and the relapses prevented them from doing it; it is a vicious circle with no break.
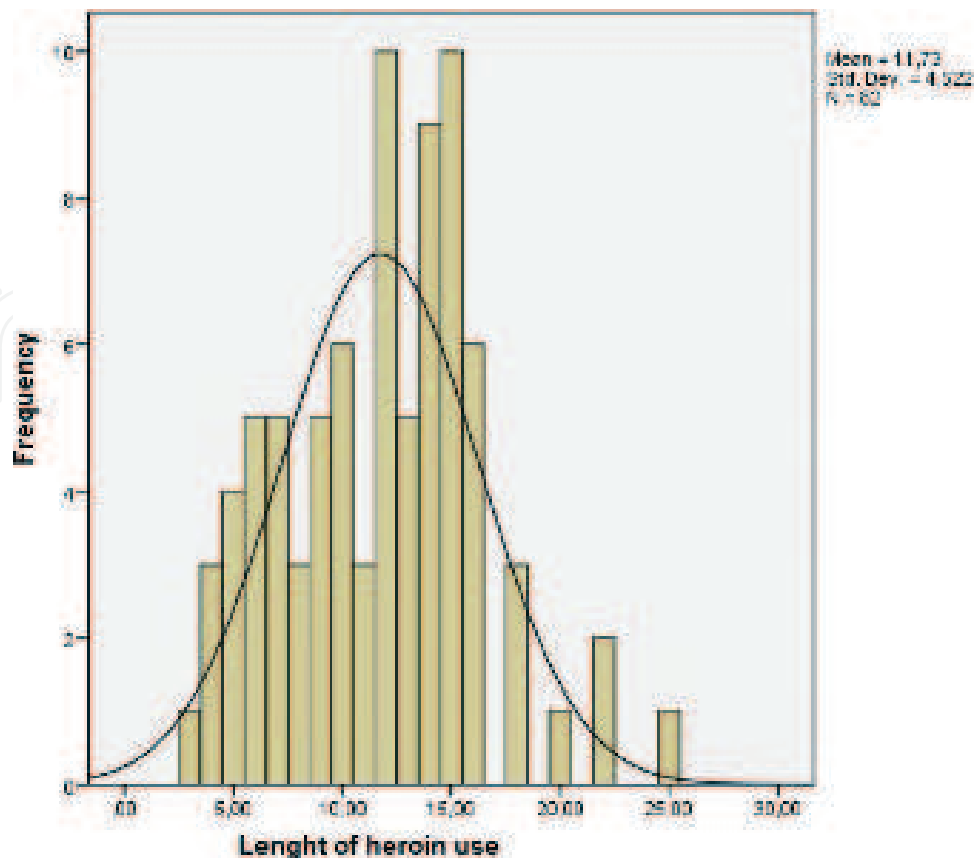
**Figure 3.** Proportion of the patients according to the duration of the consumption.

### 4.1.4. Indicator: comorbidity

A proportion of 70.7% of the target patients are proven to have the virus of the hepatitis C (HCV), hepatitis B (HBV), or HIV. Some of the patients have declared the common use of the syringes, this being the explanation of their infection. Two of the patients have got cardiac arrhythmia and are under adequate treatment. Four of the patients have got post-injection thrombophlebitis. Two of them have received a recommendation of treatment with aceno-coumarole. Some of the patients had different forms of psychic disturbances, ranging from anxious depression to personality disturbance of mixed type; three of these patients were previously hospitalized in Psychiatric Hospitals.

### 4.1.5. Indicator: type of drug addiction

More than half of the patients of the target group are poly-drugaddicts (52.5%, 43/82), because they consume heroin and, occasionally, other types of drugs (frequently NPS, Cannabis or Ecstasy). Thus, the statistics on drug consumption show an important proportion of new psychoactive substances ("ethnobotanicals," like PUR, MAGIC, SPICE), marijuana and hashish in a context of chronic use of heroin. The consumption of ethno-botanicals is the most frequent, being reported by 58% of the patients with poly-drug consumption. It is also noted a relatively high incidence (nearly 20–30%) of psychostimulants use, for example types of
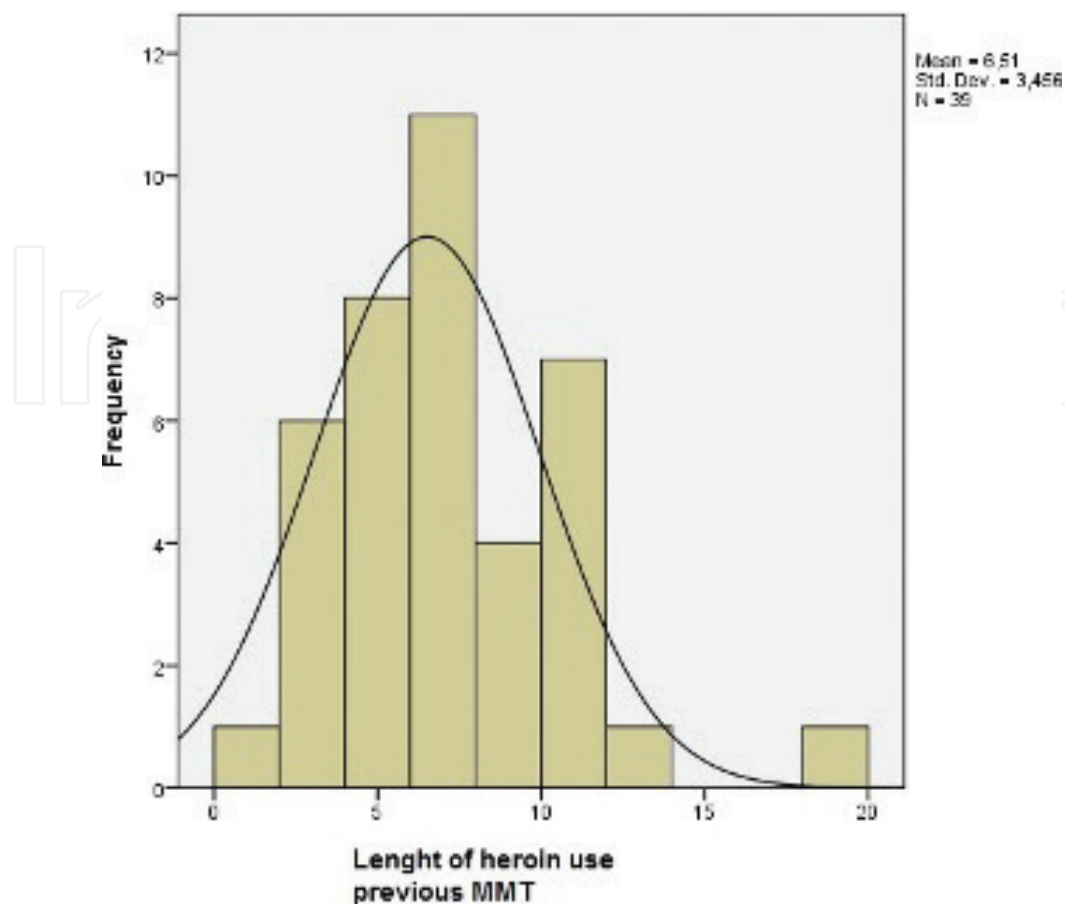
**Figure 4.** Proportion of the patients according to the duration of the consumption, previous to MMT.

cocaine or designer amphetamines with a hallucinogen component (ex. Ecstasy). Other different hallucinogens (ex. L.S.D., ketamine) have occasionally been reported.

### 4.1.6. Indicator: way of administration of the heroin

The most frequent way of the heroin administration is the i.v. (all the patients have declared the intravenous use of the heroin, in most cases, even at the onset use of the heroin (78% of the patients). The other patients have used it differently: smoking or nose sniffing.

The study shows that most of the patients had previous hospitalizations (70.7%, 58/82), an average number of 8.31 periods and previous periods of MMT (48.78%, 40/82 patients), an average number of 5.45 treatments, previous to the presented study. Also, 40.24% of the patients (33/82) have benefited from psychological counseling, an average of 9.48 meetings. Referring to the abstinence length, only a little percentage (24.4%, 20/82) had abstinence on relatively short length of time, up to 1 year.

These results show that, among the confirmed drugaddicts, the opiates consumers present the most invalidating, with the longest duration and frequency of drug consumption, with a lower compliance to treatment and high resistance as regards the initiation and the maintenance of the abstinence. These present a high frequency of relapses as well as long term and high intensity of drug consumption.

The data in terms of demographic characteristics, addiction, and comorbidity are in accordance with the official statistics and reports. Thus according to the annual report with respect to the situation of drugs in Europe, in 2012, the number of the male patients, consumers of opiates, exceeds three times the number of female consumers. Most of the opiates consumers report that they have first started using the drug before the age of 30, and nearly half (46%) of all the opiates consumers confess that they started before the age of 20. Generally, the opiates consumers frequently report their lack of a dwelling, unemployment, as well as a more reduced level of education than the primary consumers of other drugs [21].

The national report as regards the situation of drugs [20] shows that, at national level, the profile of the consumers of injection drugs, no matter the provided assistance (program of changing the syringes, admission to treatment, and emergency assistance), reveals a 30 year old man, who lives in Bucharest and has a long period of drug consumption, the main drug used belonging to the opiates category. Out of 1529 persons who received medical assistance in 2013, for illegal drugs consumption and NPS, nearly half of them were consumers of opiates, and among them 328 had previous episodes of substitute treatment with methadone or other opiates.

On the other hand, according to the official data, the heroin (42.7%) and NPS represent the most important types of substances which was the reason why consumers called medical assistance for; however, although heroin is the main drug for which were most treatment demands, significant differences have also been reported among beneficiaries who received previous medical assistance and the new cases, which outlines a possible change in the pattern of drug consumption.

### 4.2. Statistic correlations among the evaluated indicators

Applying some specific statistic methods (the SPSS program, Pearson, Spearman, Kendal correlations), we have evaluated the possible correlations among the analyzed indicators/parameters. Thus, we have obtained positive correlations which are statistically significant among the parameters (**Table 2**): age-length of consumption; age-length of consumption previous to the first MMT; length of the consumption – length of consumption previous to the first MMT; comorbidities – length of consumption previous to the first MMT (suggesting the positive influence of the treatment on the morbidity); the methadone dose - length of consumption previous to the first MMT; MMT number- number of previous hospitalizations. The MMT numbers previous to the presented study has correlated with the number of psychological counseling meetings and this underlines the importance of the psychological intervention, along with the pharmaceutical treatment with methadone.

### 4.3. Toxicological analysis

*4.3.1. Indicator: the urine concentration of heroin and metabolites*

The methodology of the quantitative and qualitative toxicological analysis provides with a support, useful in order to analytically diagnose of the drug abuse and to initiate and supervise the substitution treatment.

In the present study, the quantitative toxicological analysis aimed at determining the levels of the heroin and the metabolites in the urine of the heroin consumers, applying the technique of the fluorescent antibody, and using an automatic analyzer. The heroin and metabolite levels in their urine tests have been placed to a large extent, from approximately 700 to over 30,000 ng/mL (**Figure 5**).

During the treatment, not only the initial one, they do tests (which are marked as follows: negative, slightly positive, positive), no matter the patients' declarations. At the assumption or the declaration of relapses, tests grow in number, especially when we speak about the combinations of opiates and heroin or other medicines. The maximum number of tests along a whole year for a single patient has been 27.

### 4.4. Substitution treatment

All the patients in the group have been administered a substitute treatment with methadone. A single patient with a 15-year drug consumption has been changed on Suboxone instead of Methadone.

The analysis of the group of patients reveals that the average dose of methadone is approximately 56 mg, varying between 15 and 125 mg, enough for the stabilization and avoidance of the abstinence syndrome (**Figure 6**). This is in accordance with the data in the literature, which recommends a test dose of methadone of 20 mg, at the beginning of the substitute treatment. Till the end of the hospitalization, the doses of methadone were generally increased with approximately 10 mg in 2 days; for the outpatients, the level of methadone was increased to 125 mg/methadone/day in some patients.

Some patients have required the reduction or the increase of the doses, but this depended on the symptomatology.

Our study shows that the patients' stabilizing is done with moderate methadone doses (approx. 50–60 mg/zi), compared to those reported in the literature (approx. 90–100 mg); this is an advantage, taking into account the possible interactions with other medicines, under the circumstances of the associations of the necessary medicines during the substitute treatment, as well as the somatic comorbidities of the patients (mainly the liver chronical problems caused by HCV infection).
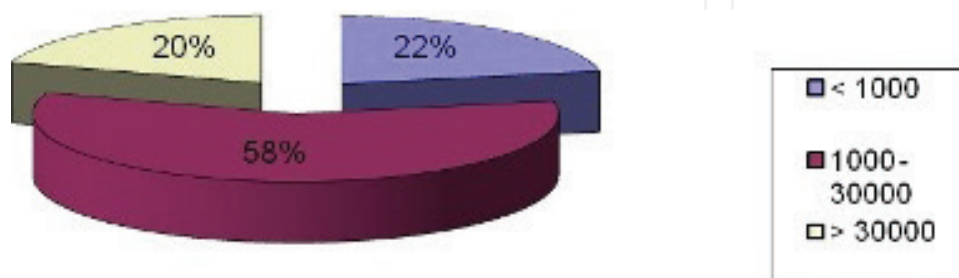


**Figure 5.** Proportions in the patient group according to the concentration of heroin and metabolites (ng/mL) in the urine tests.
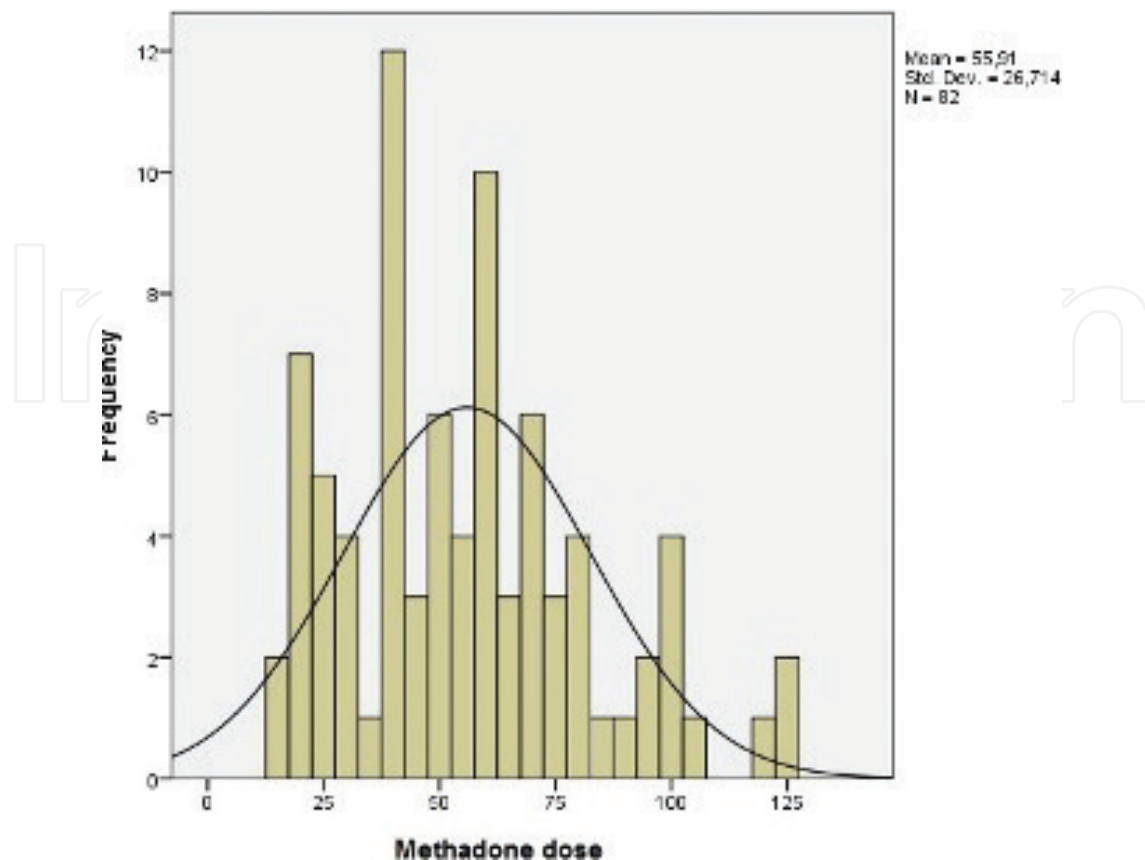
**Figure 6.** Proportion of the patients according to the methadone dose.

During the methadone substitution treatment, they often prescribe different medicines to improve anxiety, agitation, and severe muscular contractions; generally, phenothiazines and benzodiazepines are used to treat agitation, to stabilize the patients' sleep and muscular contractions. They also take into account the somatic and psychic comorbidities of the patients. The co-medication makes possible different medical interactions. Thus, the data in the literature suggest that the benzodiazepines (they themselves being medicines with potential of abuse consumption), especially for the fact that the diazepam interferes with the normal metabolization of the methadone. To be more precised, the individual treatment has a different graphic according to: the test results, symptomatology, and comorbidities. At the beginning of the treatment, patients are informed on the condition to remain under treatment, notably the negative tests of the heroin and combinations. Otherwise, they are removed from the program.

Together with the treatment with methadone, over 80% of the patients have accepted the individual or group psychological therapy. We consider that, without this type of therapy, the situation of the patients would be more dramatic. The study shows that 40% of the patients have confessed their relapses, because of their bad company or some dramatic events in their family. For this reason, the methadone doses have been adjusted and the treatment has been extended. The relapses have been confessed and marked out at the heroin presence in the tests. The rehospitalizations have been done out of the patients own initiatives, because of their syndrome of withdrawal. Their motivation of the relapse was depression, the lack of

a positive emotional support on behalf of the people close to them and inability to prevent from not using drugs. Even if they have not restarted all of a sudden (with heroin) they have used NPS (such as Magic/Supergold, Pure). Three patients who gave up the substitution treatment were hospitalized at Psychiatric Hospitals. The evaluations which maintain or change the methadone doses are made in accordance with the clinical behavior, psychological and paraclinical monitoring. We state that, an important proportion of the patients have confessed self-medication with methadone, before their onset in the program. The methadone was used in order to stop the state of withdrawal with heroin (a short term detoxification), and also, as an agent for long term substitution.

All the patients in the group have been included in the program for years, because of their relapses. Their periods of abstinence have lasted for only several days, months, but not years. For instance, one patient had repeated attempts of abstinence during a year, as follows: four times of 1–7 days, two times of about 1 month, and one time (but interrupted) of approximately 4 months.

In spite of monitoring the treatment carefully, there are relapses which impede the personal and social reintegration. Current literature data indicate that sustained remission occurs in a significant minority of heroin users and the treatment does not cure this addiction, but it can contribute to prevent the heroin use and reduce its adverse effects [22].

The results of the study show that the complex correlative, clinical, laboratory, and psychological evaluation is essential to start and supervise the methadone substitution maintenance. This is in line with the recent data from the literature emphasizing the need for multidisciplinary evaluation of candidates for opioid agonist therapy, including a careful medical history, physical and psychiatric examination, psychosocial evaluation, as well as the determination of the patient's readiness to change [23].

## 5. Conclusions

The study has revealed the following aspects:

- Most of the population using the medical assistance with MMT is represented by male persons, with low level of education, predominantly without any occupation or with a temporary one. The average age of the patients is approximately 30 years; they have a long history of consumption of opiates (approximately 11 years); they predominantly use heroin injections, in most cases associated with other drugs (polyconsumption, i.e., high frequency of association with NPS); most of the patients present somatic co-morbidities (HCV or HIV infections), and have several previous hospitalizations and lengths of treatment. The average age of the patients at the onset of the study is significantly different from the age of the patients at the onset of their drug consumption. The total duration of the consumption is statistically different from the duration of the consumption, previous to the first MMT.

- These aspects, together with the typical profile of the drug addicts, represent essential data, as they contribute to the accurate identification of the target groups who would have to be targeted at the beginning of a prevention or therapeutic program within the phenomenon of drug addiction.

- The methodology of the toxicological analysis provides with a useful support to initiate a substitution treatment as well as to detect the relapses during the treatment.

- The integrated care programs of assistance should involve both therapeutic programs and psychological ones in order to prevent relapses.

- The results of the study contribute to the extension of information area in terms of consumption phenomenon and its breadth; the identification of the onset ages in the case of heroin consumption; establishing the prevalence and types of comorbidities with drug addicts; the identification and description of the multiple facts involved in the consumption (biological, emotional, psychological, familial, interpersonal, educational, social, environmental, and within the community) including the precursors, associated with or favorable to the drug consumption; the identification of the determinant elements to enroll in the treatment program.

- In spite of monitoring the treatment carefully, there are relapses, which impede the personal and social reintegration. They point out the necessity to increase the patients' awareness, in terms of their health, and to enroll them in a substitution program, and they also highlight the complicated situation in case of a dual diagnosis (emotional and personality disturbance).

## Conflict of interest

The authors declare no conflict of interest.

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