Evaluation of Functional Status Among Patients Undergoing Maintenance Treatments for Opioid use Disorders

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Research

Keywords: Opioid Use Disorders, Methadone, Buprenorphine, Functional status, Sexual dysfunction

DOI: https://doi.org/10.21203/rs.3.rs-47994/v1

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Abstract

Objective Methadone and buprenorphine are the most prevalent types of opioid maintenance programs in Andalusia. The main objective is comparing the functional and health status of patients with pharmacological opioid maintenance treatments according to different socio-demographic characteristic, disabilities and sexual functioning difficulties.

Methods A total of 593 patients from the Andalusia community, 329 were undergoing methadone treatment and 264 were undergoing buprenorphine treatment. The patients were interviewed by socio-demographic and opioid-related variables, assessed by functional disability and health variables (WHODAS 2.0.) and for sexual dysfunction (PRSexDQ-SALSEX).

Results We found significant differences in the socio-demographic and the opioid-related variables as the onset of opioid use, being on previous maintenance programs, opioid intravenous use, the length of previous maintenance programs, polydrug use and elevated seroprevalence rates (HCV and HIV) between the methadone group and the buprenorphine group. There were differences in the Understanding and communication domain, Getting around domain, Participation in society domain and in the WHODAS 2.0. simple and complex score, favoring buprenorphine-treated patients. The methadone group had elevated sexual dysfunction than the buprenorphine group. Opioid-related variables as seroprevalence rates, other previous lifetime maintenance program, the daily opioid dosage and the daily alcohol use are the most discriminative variables between both groups. Participation in society variables and sexual problems were the most important clinical variables in distinguishing the methadone group from the buprenorphine group.

Conclusions The methadone group showed higher prevalence in opioid dependence-related variables, elevated disabilities in participation in society activities and sexual problems compared with the buprenorphine group.

Introduction

Opioid dependence is a chronic and relapsing substance use disorder that causes a significant burden on the global community, leading to 9.2 million disabilities per year [1]. In 2016, in Europe, there were 1.3 million opioid users at high risk, of whom only 628,000 were in opioid substitution programs (63% with methadone treatment) [2]. In Spain, the number of admissions for treatment for opioid use disorders showed a decreasing trend since 2010 but remained stable since 2013-2014 [3]. Particularly, in Andalusia (Southern Spain), there were 2,842 new cases of treatment requests for opioid dependence in 2017, and only 329 of them were made by women [4]. Currently, the most common pharmacological treatment for these patients is based on methadone or buprenorphine controlled administration to achieve recovery and normalization. Thus, 13,456 patients and 1,252 patients benefited from maintenance programs involving methadone and buprenorphine, respectively, in Andalusia [5].

Methadone has been used as the first-line therapy for opioid dependence and has reduced the risk for heroin use and associated damage for more than fifty years [6, 7]. Is an orally active synthetic full μ-receptor agonist with an inhibitory effect on the NMDA receptor, and it produces a better analgesic effect and has a longer half-life than does
morphine [8]. Additionally, tolerance and physical dependence are commonly observed, so methadone treatment should not be stopped abruptly. Buprenorphine is a partial agonist at the µ-opioid receptors, and its administration results in a lower risk of toxicity [9]. It is used during opioid detoxification for managing withdrawal and reducing cravings with less potential for opioid use than nonprescription full opioid agonists do [10]. The most common side effects of buprenorphine are constipation and nonspecific headache [11].

The maintenance treatments using methadone or buprenorphine have better adherence to treatment for opioid dependence compared with other therapeutic options, such as opioid tapering or psychological therapies alone [12]. These substitution treatments have been shown to be safe in physical and mental health [13, 14] and they have been reported to decrease criminal activity and improvements in social functioning [13]. Moreover, maintenance pharmacological treatments were effective in preventing the spread of infectious diseases [15, 16] and decreasing violence and the overdose mortality [17, 18], especially when opioids are used with other depressants drugs, such as alcohol and benzodiazepines [19].

Usually, the length of pharmacological maintenance treatment depends on the patients needs, considering his or her past instability (dysfunction related to work, social relations and behavior) and chronicity (duration of opioid dependence) [11]. The effectiveness of the treatment is sensitive and related with other factors as the use of other drugs, the doses of the opioid and the quality of the therapeutic supporting services [13]. Moreover, has been reported a deterioration in the quality of life of patients in opioid maintenance treatments [16, 20]. Because prolonged opioid use can be associated with clinical debilitating side-effects [21], these patients are likely to suffer from cognitive and physical disabilities and comorbid mood, anxiety and sleep disorders [22, 23], other substance use disorders [24] and a higher risk for death caused by respiratory depression [17].

In addition to cognitive and physical disabilities, sexual dysfunction are associated with opioid use disorders [25]. Age, the presence of comorbid depressive disorders and the long-term use of opioids are other factors related to sexual dysfunctions [26, 27]. Disability and sexual dysfunction are important factors to consider in achieving a good adherence to maintenance programs, which maximizes the likelihood a long-term recovery [28].

Because opioid maintenance treatments tend to last over time, the main objective of this cross-sectional and descriptive study was to compare patients in methadone and buprenorphine maintenance programs in Andalusia according to their socio-demographic characteristics, level of functioning (positive aspects of the interaction between an individual's health condition and contextual factors) and sexual dysfunctions to assess the functional status of opioid patients, offer guidance based on the evaluation of the disease and supporting the identification of the needs, treatment adjustments, and measurements of effectiveness for these patients, establishing priorities and allocating resources.

**Methods**

**Study Design and Treatment**

The present cross-sectional descriptive study involved a data collection of patients undergoing pharmacological maintenance treatments for opioid use disorders from an intra-community Andalusia multicenter called *Servicios Provinciales de Drogodependencias* over a 3-month period from February to April 2017. Most of the patients were recruited from Malaga 214 (33.2%), and the remaining patients were recruited from other Andalusian provinces: 88 (13.7%) patients were recruited from Cadiz, 82 (12.7%) from Seville, 65 (10.1%) from Granada, 63 (9.8%) from
Almería, 46 (7.1%) from Jaen, 55 (8.5%) from Córdoba and 31 (4.8%) from Huelva. We compared both groups using a consecutive sampling technique.

Based on the attendance indicators, approximately 14,000 patients were in opioid maintenance treatment programs in Andalusia during 2016 [5]. Using a bilateral asymptotic 95% confidence interval to determine the sample size and to achieve an accuracy of 0.4%, we determined that we needed at least 576 participants. To compare the effect of the two main pharmacological maintenance treatments in opioid use disorders, we selected patients with opioids use disorders in active pharmacological treatments with methadone or buprenorphine. Therefore, 644 patients were informed to participate in the study and 631 were recruited and signed for consent. Finally, 593 volunteers were selected due to the inclusion criteria, 329 patients undergoing methadone treatment and 264 patients undergoing buprenorphine treatment. The inclusion criteria were being older than 18 years old and undergoing treatment with maintenance medication with methadone or buprenorphine for opioid use disorders with a stable dose for at least 90 days. The exclusion were the presence of cognitive impairment and pregnancy.

Clinical Assessments

Study participants were evaluated by trained interviewers and dependence on opioids was confirmed according to the DSM-IV-TR criteria [29]. The participants were assessed using three parameters: 1) *Ficha de Información Básica de Admisión al Tratamiento* (FIBAT), a standardized database of socio-demographic and opioid-related characteristics; 2) *The World Health Disability Assessment Schedule* (WHODAS 2.0) collecting symptoms experienced indicating health problems; and 3) *The Psychotropic-related Sexual Dysfunction Questionnaire* (PRSexDQ-SALSEX) to evaluate sexual problems during the opioid maintenance treatment programs.

The FIBAT database is a computerized record composed by a basic information sheet used for admission to substance treatment programs, including previous medical treatment, education level, employment, lifetime opioid use and variables related to opioid historical records, the frequency and quantity of drug consumption, and information about previous treatments.

The WHODAS 2.0. is an instrument developed by the World Health Organization [30] according to the International Classification of Functioning, Disability and Health (ICF) [31] used to quantify disability domains. According to this, disability is a comprehensive term that includes deficiencies, limitations in activity and restrictions in participation [30], used in epidemiological studies to measure the impact of a given intervention in different populations in clinical contexts [32]. This instrument displayed good metric properties in clinic and rehabilitation samples [33] and the Spanish version was validated [34]. In the present study, the scores were categorized as follow: none, mild/moderate, or severe/extreme.

The PRSexDQ-SALSEX [34] is a brief sexual dysfunction questionnaire that includes seven questions, with scores range from 0 to 15. The Cronbach's alpha for the questionnaire was 0.68 in a schizophrenia population and 0.98 in depressive patients [35].

Statistical Analysis

All data in the tables are expressed as percentage of subjects (%) or the mean and standard deviation [mean (SD)] and the differences that had a p value of less than 0.05 were considered significant. The statistical significance of the differences in the categorical and normally distributed continuous variables was determined using Fisher's exact test (chi-squared test).
Finally, a binary logistic regression model was employed to distinguish between methadone- and buprenorphine-treated patients, and the model included all the relevant and significant health and physiological variables related with the opioid maintenance treatments. The goodness of fit for the model was tested with the Hosmer-Lemeshow test. The statistical analyses were carried out with IBM SPSS Statistical version 22 (IBM, Armonk, NY, USA).

Results

Socio-demographic characteristics and opioid dependence-related variables

The average opioid-dependent patient was a 47-year-old man (84.3%) with an elementary education (65.7%) who lived with his family (75.4%). The 66.1% of the participants were employed and the 63% had a driving license. The average of opioid onset was 22.6 years and the 57.6% had participated in other maintenance programs or had previously received health services before the last year.

Table 1 describes the socio-demographic and opioid-related variables for participants of the study. There were significant differences in socio-demographic and opioid-related variables between the methadone group and the buprenorphine group. The mean age of the buprenorphine group was younger than methadone group (45.7 years vs. 47.8) and they started opioid dependence later than patients with methadone (21.6 years vs. 23.9 years). The buprenorphine group had a higher educational attainment, elevated employment rates (73.9%), and more prevalence of driving license (71.6%). Regarding the abuse of other substances, there were significant differences found in the daily use in smoked heroin with cocaine (3.6% methadone vs. 0.8% buprenorphine), alcohol (23.4% methadone vs. 17.0% buprenorphine) and non-prescribed benzodiazepines (22.8% methadone vs. 14.4% buprenorphine). Moreover, we found elevated rates of seroprevalences with higher daily opioid dosage in the methadone group.

Functioning, disabilities and health

The differences between both maintenance treatments in degrees of intensity on disabilities are described in Table 2. Regarding disabilities, it should be noted that for the different items the most prevalent answer was none difficulty although the methadone group is the one that turns out to have more mild/moderate difficulties in the different responses.

Respect the Understanding and communication domain (UAC), the methadone group responses with higher difficulty than the buprenorphine group in most of the items. In the Getting around domain (GAR) and in Participation in society domain (PSO), the methadone group responses with higher difficulties than the buprenorphine group. Moreover, we did not found differences between the groups in Self-care domain, in Getting along with people domain neither in Life activities domain.

Overall, the methadone group showed higher WHODAS 2.0. simple and complex score than the buprenorphine group (p<0.010 and p<0.05, respectively). Despite occupation was a differential socio-demographic variable between both groups; we did not found significant differences between employed and unemployed patients in the pharmacological maintenance groups.

Sexual dysfunction

The PRSexDQ-SALSEX was used to explore sexual dysfunction in the sample. There were significant differences in the predicted responses between the methadone and the buprenorphine groups: a) the presence of sexual
dysfunction after pharmacological treatment (41.8% vs. 27.2%, respectively) and b) a sexual alteration spontaneously mentioned to the clinician (43.9% vs. 33.4%, respectively).

Table 4 shows the results obtained by the PRSexDQ-SALSEX regarding the differences between the methadone and buprenorphine groups. The proportion of patients suffering any dysfunction was significantly higher in the methadone group with special attention on those answers showing moderate or severe/extreme difficulties.

Variables related to the functional status

In order to investigate the most relevant variables and to discriminate patients between the methadone and the buprenorphine group related with functioning, disability and health characteristics and the sexual dysfunction, a logistic regression analysis was performed including those variables that were different between both groups in the previous evaluation. The logistic regression model is described in Table 4.

The most explanatory variables were PSO domain ($p<0.034$), sexual dysfunction ($p<0.003$), HCV ($p<0.003$), VIH ($p<0.006$), previous lifetime maintenance program ($p<0.001$), daily opioid dosage ($p<0.019$), and alcohol use every day ($p<0.048$). Regarding the odds ratio in the logistic model, the probability of belonging to the buprenorphine group: decreased by 1.3% when PSO domain increases one unit; increases 1.9% when the sexual dysfunction variable increases one unit, increases 2.1% when HCV seroprevalence increases one unit, increases 3.4% when HIV seroprevalence increases one unit; decreased 63% when the previous maintenance treatment variable increases one unit, decreases 56% when the daily doses increased one unit and finally, decreased 1.7% when alcohol use every day increases one unit. PSO domain and sexual dysfunction are the clinical variables most discriminative and regarding the opioid related variables: HCV, HIV, previous opioid maintenance programs, the daily opioid use and the daily alcohol use provide the differential information between the methadone and buprenorphine groups. The Hosmer-Lemeshow test revealed a good fit for the model ($\chi^2=13.669; p=0.091$) and the ROC curve showed a good discriminative power (AUC=0.757) with an optimal cut-point value of 0.1502 (sensitivity of 98% and specificity of 82%).

Discussion

The preservation of the functional status during the opioid maintenance treatments has to be considered as an important criterion in the selection of pharmacological maintenance programs. The main findings were as follows: (a) There were significant differences in variables related to the opioid use between both groups, suggesting a better social competence for buprenorphine-treated patients; (b) We found differences between both groups in variables related to functioning, disability and health favoring buprenorphine-treated patients; (c) The methadone group had an elevated prevalence on sexual dysfunction than the buprenorphine group; (d) Opioid-related variables as HCV and VIH seroprevalence, previous maintenance program, the daily opioid dosage and the alcohol use were the most discriminative variables between both groups; (e) Participation in society and the sexual dysfunction are the most relevant functional variables in distinguishing the methadone group from the buprenorphine group. Our findings suggest a better level of functioning of buprenorphine patients compared with methadone patients, however it is possible that other differences underlie these results rather than directly due the opioid medication treatment. Randomized controlled trials are required to explore these differences.

The opioid patient profile in this study is a middle-aged individual employed that uses chronically opioids through smoked administration, older than the samples of young adults described in Spanish studies [36, 37]. However, other characteristics are similar to studies previously reported, including the higher percentage of men (84%) with
an elementary education (66%), with family support (the 75.4% lives with family), driving daily (55%) and with other substance use disorders (e.g., nicotine, cannabis and alcohol) [22, 38]. Concerning the substance use, the pattern was similar in both groups with the exception of the daily use of benzodiazepines which was more common in the methadone group, accordingly with the elevated prevalence of benzodiazepine use found among patients in methadone maintenance programs [39].

Evidence revealed a general health and disability impairment described in patients undergoing maintenance treatment [1, 21]. We found higher levels of difficulty in methadone group than the buprenorphine group in those related with cognitive variables (i.e., concentration, problem solving, learning and communication); and in those related with movement activities, (i.e., standing, moving inside the home, leaving home and walking long distances) and in variables involving social activities. Moreover, neuropsychological studies reported that patients with methadone treatment showed mental impulsivity, less flexibility and difficulties related to verbal working memory tasks [40, 41]. Regarding physical impairment, methadone maintenance patients showed greater difficulty and impaired psychomotor skills in compared with buprenorphine[9]. However, it is important to stress that methadone remains as a safe profile for its use in opiate-addicted patients [7, 42].

Due to the positive correlation found between every health disability domain and sexual dysfunction, problems in this area have an impact on the quality of life of opioid patients with undergoing maintenance treatment. According, literature reported that opioid patients could experience orgasm dysfunction, a lack of intercourse satisfaction, less sexual desire and a diminished satisfaction after the initiation of methadone treatment [43, 44]. Methadone doses have been related to decreasing orgasms and greater sexual problems compared with buprenorphine treatment [45, 46]. Otherwise, literature is not clear in this regard because some studies justified the existence of comorbid psychiatric problems related with the opioid use affecting to sexual problems [47-49]. Based on their pharmacological action the methadone is likely to produce an intense inhibition of the sexual performance than buprenorphine [50]. Finally, the testosterone replacement therapy could be interesting for those patients with sexual dysfunction [51], although there are described important side effects [52].

Although our findings, we are aware of the limitations. First, the participants were not randomized to the different treatment groups and these differences could be related to observed or unobserved confounders. Second, it is conceivable that additional social, comorbid clinical diagnoses and addiction-related variables can influence disability and functioning. Third, we could not exclude the impact of the social desirability bias from the measurements used in this study based on the scores taken from the self-report responses. Finally, the impact of the differences between men and women in the variation of disability and functioning must be studied in a larger sample size. The strengths of the study are as follows: the sample size is larger in opioid-dependent patients under maintenance treatment and performed with patients from all the provinces of the Andalusian autonomous community in Spain, a representative region of Southern Europe; and the good metric properties of the clinical questionnaires used.

This study shows the importance of carry out a constant clinical and global health evaluation of patients in long medical treatments. In conclusion, there is a clinical difference in health disabilities and sexual dysfunction between patients undergoing methadone and buprenorphine maintenance treatments. The sexual dysfunction evaluation is an important criterion to considered when the health functioning is evaluated, because its impact on the treatment adherence.

**Declarations**
Ethics approval and consent to participate and for publication

This study, the privacy and confidentially of the protocols and recruitment were approved by the plenary of the Research Ethics Committee of our institution (Comité de Ética de la Investigación Provincial de Málaga del 27 de abril de 2017) and conducted according to the guidelines instated by the Ethical Principles for Medical Research Involving Human Subjects adopted in the Declaration of Helsinki by the World Medical Association (64th WMA General Assembly, Fortaleza, Brazil, October 2013), Recommendation No. R (97) 5 of the Committee of Ministers to Member States on the Protection of Medical Data (1997), and European data protection act (Ley Orgánica del Parlamento Europeo y del Consejo de 27 de abril de 2016 de Protección de Datos, RGDP). All collected data were assigned numerical codes for privacy and confidentiality. Written informed consent was obtained from all patients in this study.

Availability of data and material

Not applicable

Competing interest

None

Fundings

This work has been funded by Sociedad Médica Andaluza de Adicciones y Patologías Médicas Asociadas (SOMAPA) and supported by Research Project funded by Consejería de Salud y Bienestar Social, Junta de Andalucía-Fundación Progreso y Salud (PI-0140-2018). NGM holds a Sara Borrell research contract (CD19/00019) funded by Instituto de Salud Carlos III (ISC-III) and European Regional Development Funds-European Union (ERDF-EU).

Author’s contributions

JJR and JMM were responsible for the study concept and design. NGM performed statistical analysis and interpretation of findings and drafted the manuscript. JJR and JMM coordinated the recruitment of participants. The ASG contributed to the acquisition of socio-demographic and psychiatric data by means of interviews and generated the database. All authors critically reviewed content and approved final version for publication.

Acknowledgements

The authors are grateful to The ANDOPIO Study Group for their valuable assistance throughout the clinical part of the study. All authors critically reviewed the content and approved final version for publication:

Aguilera Peralta G.1, Alaminos l.1, Cáceres Jerez C.1, Navarro González J.L.1, Rodríguez Rodríguez A.1, Suárez Márquez. C.1, Bernal Jimenez L.2, Corbalán Guerrero C.2, Crespo Jimenez Y.2, Diosdado Fernández J.2, Girón García S.2, Gómez Tortosa R.2, Jiménez Barea F.J.2, Lobo Lara M.J.2, Luque Pérez F.2, Rodríguez Melgar M. J.2, Roquete Castro J.L.2, Sánchez Pérez J.A.2, Seijo Ceballos P.2, Valdayo Boza M.J.2, Alcántara López F.C.3, Castro Granados M.G.3, Chacón Villafranca R.3, De la Fuente Darder B.3, Lizaur Barbudo M.3, Manchado López L.3, Moreno López R.3, Moya Mejías A.3, Castillo Fernández G.M.4, Joya Redondo J.4, Jurado De Flores Yepez G.4, López Callejas C.4, Orozco Carreras L.4, Ruiz Martinez M.4, Sánchez Viñas A.M.4, Álvarez García M.5, Bozquez Gómez I.5, Conseguier...
Ponce C.\textsuperscript{5}, De Mula Duran M.D.\textsuperscript{5}, Gegundez Arias E.\textsuperscript{5}, González Regalado J.\textsuperscript{5}, Morales Rojas D.\textsuperscript{5}, Ramírez López J.F.\textsuperscript{5}, Gil Martínez A.\textsuperscript{6}, Herrera Benítez F.\textsuperscript{6}, Montanet Fernández E.\textsuperscript{6}, Navarro Cabrera H.\textsuperscript{6}, Rodríguez Rus S.\textsuperscript{6}, Andújar Pérez C.\textsuperscript{7}, Bravo López F.\textsuperscript{7}, Burgos Bravo I.\textsuperscript{7}, Campos Cloute R.\textsuperscript{7}, Campos Gómez R.\textsuperscript{7}, Fournier López R.\textsuperscript{7}, Galán Ruiz de la Herranz A.\textsuperscript{7}, Gardeta Sabater P.\textsuperscript{7}, Gómez Villaespesa Mará F.\textsuperscript{7}, Guerrero Florido A.\textsuperscript{7}, Luque García F.\textsuperscript{7}, Martín de la Hinojosa J.M.\textsuperscript{7}, Moreno Arrebola A.\textsuperscript{7}, Pretel Pretel J.\textsuperscript{7}, Torroba Molina J.\textsuperscript{7}, Vázquez García F.\textsuperscript{7}, Segura Zamudio J.A.\textsuperscript{7}, Baena B.\textsuperscript{8}, Cartagena E.\textsuperscript{8}, Claro E.\textsuperscript{8}, Iglesias Azcue C.\textsuperscript{8}, López A.\textsuperscript{8}, Morera A.\textsuperscript{8}, Osuna P.\textsuperscript{8}, Rodríguez A.\textsuperscript{8}, Sánchez C.\textsuperscript{8}, Torres I.\textsuperscript{8}, Velo L.\textsuperscript{8}, Villafuerte V.\textsuperscript{8}, Vázquez M.M.\textsuperscript{8}

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**Tables**

**Table 1.** Socio-demographic characteristics between the sample groups.
| Variables                                | Methadone (N=329) | Buprenorphine (N=264) | p-value |
|------------------------------------------|-------------------|------------------------|---------|
| Sex (%)                                  | 86.3              | 81.8                   | 0.083   |
| Age [Mean ± SD]                          | 47.8 ± 7.9        | 45.7 ± 8.4             | 0.002\(^a\) |
| Educational attainment (%)               |                   |                        |         |
| None                                     | 1.50              | 0.4                    | 0.019   |
| Elementary                               | 68.3              | 62.4                   |         |
| Secondary                                | 27.4              | 29.7                   |         |
| University                               | 2.7               | 7.6                    |         |
| Occupation (%)                           | Employed          | 59.9                   | <0.001  |
| Driving license (%)                      | 56.1              | 71.6                   | <0.001  |
| Cohabiting (%)                           |                   |                        |         |
| Alone                                    | 17.9              | 17.4                   | 0.157   |
| With family                              | 74.5              | 76.5                   |         |
| With friends                             | 2.1               | 3.8                    |         |
| Other                                    | 5.5               | 2.3                    |         |
| Age onset opioid use [Mean ± SD]         |                   |                        |         |
| Years                                    | 21.6 ± 7.0        | 23.9 ± 9.6             | 0.001\(^a\) |
| I.v. opioid* (%)                         | 5.2               | 6.8                    | <0.001  |
| Seroprevalence (%)                       |                   |                        |         |
| HBV                                      | 18.6              | 9.8                    | 0.005   |
| HCV                                      | 43.3              | 25.1                   | <0.001  |
| VIH                                      | 13.9              | 3.9                    | <0.001  |
| TB                                       | 2.2               | 2.0                    | 0.629   |
| Syphilis                                 | 0.6               | -                      |         |
| Previous maintenance program (%)         | 59.3              | 74.2                   | <0.001  |
| Length maintenance program (%)           |                   |                        |         |
| Less than a year                         | 14.7              | 32.0                   | <0.001  |
| Between 1 and 3 years                    | 25.0              | 45.3                   |         |
| More than 3 years                        | 60.3              | 22.7                   |         |
| Daily opioid dosage (mg)                 |                   |                        |         |
| Low †                                    | 37.5              | 24.6                   | 0.002   |
| Moderate ‡                               | 48.4              | 63.4                   |         |
| High ‖                                   | 14.2              | 12.1                   |         |
| Substances (in the last 30 days) (%)     |                   |                        |         |
| Heroin                                   | 2.5               | 3.5                    | 0.308   |
| Heroin + Cocaine                         | 14.8              | 13.0                   | 0.313   |
| Cocaine                                  | 12.9              | 10.3                   | 0.207   |
| Nicotine                                 | 83.5              | 81.8                   | 0.277   |
| Substances (every day) (%) | Heroin | Heroin + Cocaine | Cocaine | Nicotine | Cannabis | Alcohol | Benzodiazepines |
|---------------------------|--------|------------------|---------|----------|----------|---------|-----------------|
| Cannabis                  | 33.5   | 30.4             | 0.238   |          |          |         |                 |
| Alcohol                   | 42.1   | 35.5             | 0.064   |          |          |         |                 |
| Benzodiazepines           | 28.3   | 19               | 0.006   |          |          |         |                 |
| Heroin                    | 0.3    | 0.4              | 0.693   |          |          |         |                 |
| Heroin + Cocaine          | 3.6    | 0.8              | 0.017   |          |          |         |                 |
| Cocaine                   | 3.0    | 1.9              | 0.270   |          |          |         |                 |
| Nicotine                  | 76.9   | 75               | 0.329   |          |          |         |                 |
| Cannabis                  | 16.7   | 19.7             | 0.203   |          |          |         |                 |
| Alcohol                   | 23.4   | 17.0             | 0.035   |          |          |         |                 |
| Benzodiazepines           | 22.8   | 14.4             | 0.006   |          |          |         |                 |

| Current psychiatric medication (%) | Benzodiazepines | Antidepressants | Antipsychotics | Anticonvulsants | Others |
|-----------------------------------|-----------------|-----------------|----------------|-----------------|--------|
|                                   | 41.6            | 21.3            | 6.4            | 7.9             | 5.8    |
|                                   | 36.4            | 22.0            | 9.5            | 6.4             | 4.5    |
|                                   | 0.111           | 0.458           | 0.107          | 0.302           | 0.317  |

Abbreviations: *I.v.*=Intravenous administration of opioids; HIV=human immunodeficiency virus; HBV=hepatitis B virus; HCV=hepatitis C virus; TB=tuberculosis; † low doses: methadone (2.5-27.50mg), buprenorphine (1-3mg); ‡ moderate doses: methadone (30-75mg), buprenorphine (4-8mg), ‖ high doses: methadone (80-160mg), buprenorphine (10-24mg). p-values were calculated with Fisher’s exact test or chi-squared test; a p-value from Student’s t-test.

**Table 2.** Differences in functioning, disabilities and health between the sample groups.
| WHODAS 2.0 variables | Methadone (N=329) | Buprenorphine (N=264) | p-value |
|----------------------|-------------------|-----------------------|---------|
|                      | None | Mild/ | Severe/ | None | Mild/ | Severe/ |
| D1.1 Concentrating on performing a task for 10 minutes (%) | 56.4 | 35.4 | 8.2 | 65.7 | 30.2 | 4.2 | 0.029 |
| D1.2 Remembering to do important things (%) | 43.3 | 48.5 | 8.2 | 53.2 | 41.1 | 5.7 | 0.046 |
| D1.3 Analyzing and finding solutions to problems in day-to-day life (%) | 47.6 | 44.8 | 7.6 | 55.5 | 39.6 | 4.9 | 0.110 |
| D1.4 Learning a new task (%) | 65.9 | 30.5 | 3.7 | 76.2 | 21.1 | 2.6 | 0.023 |
| D1.5 Generally understanding what people say (%) | 70.1 | 28.4 | 1.5 | 84.5 | 13.6 | 1.9 | <0.001 |
| D1.6 Starting and maintaining a conversation (%) | 72.0 | 25.3 | 2.7 | 77.7 | 20.0 | 2.3 | 0.274 |
| **Understanding and communication (UAC) (Mean ± SD)** | 18.6 ± 18.9 | 13.5 ± 16.3 | <0.001 |
| D2.1 Standing for long periods, such 30 minutes (%) | 72.9 | 21.6 | 5.5 | 80.4 | 17.7 | 1.9 | 0.029 |
| D2.2 Standing up from a sitting position (%) | 75.9 | 22.3 | 1.8 | 80.8 | 17.7 | 1.5 | 0.366 |
| D2.3 Moving around inside your home (%) | 83.2 | 15.2 | 1.5 | 88.7 | 11.3 | - | 0.045 |
| D2.4 Getting out of your home (%) | 77.4 | 19.5 | 3.0 | 81.9 | 15.8 | 2.3 | 0.407 |
| D2.5 Walking a long distance, such as a kilometer (%) | 76.5 | 18.9 | 4.6 | 80.8 | 15.8 | 3.4 | 0.446 |
| **Getting around (GAR) (Mean ± SD)** | 10.7 ± 16.9 | 7.9 ± 16.0 | 0.030 |
| D3.1 Washing your whole body (%) | 83.2 | 16.2 | 0.6 | 87.9 | 10.2 | 1.9 | 0.043 |
| D3.2 Getting dressed (%) | 87.8 | 11.9 | 0.3 | 90.9 | 7.5 | 1.5 | 0.065 |
| D3.3 Eating (%) | 84.1 | 14.0 | 1.8 | 86.4 | 12.1 | 1.5 | 0.741 |
| D3.4 Staying by yourself for a few days (%) | 80.8 | 17.7 | 1.5 | 85.7 | 11.3 | 3.0 | 0.052 |
| **Self-care (SCA) (Mean ± SD)** | 7.2 ± 13.3 | 6.0 ± 14.1 | 0.309 |
| D4.1 Dealing with people you do not know (%) | 62.8 | 32.6 | 4.6 | 69.8 | 26.4 | 3.8 | 0.201 |
| D4.2 Maintaining a friendship (%) | 70.1 | 25.3 | 4.6 | 75.8 | 20.4 | 3.8 | 0.298 |
| D4.3 Getting along with people who are closet to you (%) | 82.6 | 15.9 | 1.5 | 83.0 | 16.6 | 0.4 | 0.375 |

* Significant difference.
| Variable                                                      | Mean ± SD | Mean ± SD | Mean ± SD | Mean ± SD | Mean ± SD | t-value |
|---------------------------------------------------------------|-----------|-----------|-----------|-----------|-----------|---------|
| D4.4 Making new friends (%)                                   | 59.5 ± 33.8 | 6.7 ± 6.7 | 66.8 ± 25.7 | 7.5 ± 7.5 | 0.098 |
| D4.5 Sexual activities (%)                                    | 64.6 ± 28.7 | 6.7 ± 6.7 | 70.6 ± 21.1 | 8.3 ± 8.3 | 0.103 |
| **Getting along with people (GAP) (Mean ± SD)**               | 17.3 ± 20.3 | 14.8 ± 20.4 |             |           | 0.152 |
| D5.1 Taking care of your household responsibilities (%)       | 75.0 ± 21.6 | 3.4 ± 3.4 | 72.7 ± 24.2 | 3.0 ± 3.0 | 0.747 |
| D5.2 Doing the most important household task well (%)         | 79.6 ± 17.7 | 2.7 ± 2.7 | 76.9 ± 21.2 | 1.9 ± 1.9 | 0.466 |
| D5.3 Getting all of the household work done that you needed to do [%] | 70.4 ± 26.5 | 3.0 ± 3.0 | 71.2 ± 26.1 | 2.7 ± 2.7 | 0.951 |
| D5.4 Getting your household work done as quickly as needed [%] | 64.0 ± 33.5 | 2.4 ± 2.4 | 69.7 ± 26.9 | 3.4 ± 3.4 | 0.192 |
| D5.5 Your day-to-day work/school (%)                          | 77.0 ± 22.4 | 0.5 ± 0.5 | 76.0 ± 19.9 | 4.1 ± 4.1 | 0.056 |
| D5.6 Doing your most important work/school tasks well (%)     | 82.1 ± 16.3 | 1.5 ± 1.5 | 77.6 ± 19.4 | 3.1 ± 3.1 | 0.412 |
| D5.7 Getting all of the work done that you need to do (%)     | 78.6 ± 20.4 | 1.0 ± 1.0 | 78.6 ± 18.4 | 3.1 ± 3.1 | 0.331 |
| D5.8 Getting your work done as quickly as needed (%)          | 73.0 ± 25.5 | 1.5 ± 1.5 | 73.0 ± 24.0 | 3.1 ± 3.1 | 0.579 |
| **Life activities (LAC) (Mean ± SD)**                         | 13.1 ± 20.1 | 13.2 ± 21.0 |             |           | 0.981 |
| D6.1 Problems joining community activities (%)                | 56.4 ± 34.8 | 8.8 ± 8.8 | 66.3 ± 23.5 | 10.2 ± 10.2 | 0.012 |
| D6.2 Problems because of barriers or hindrances around you (%) | 51.2 ± 40.5 | 8.2 ± 8.2 | 66.3 ± 26.9 | 6.8 ± 6.8 | 0.001 |
| D6.3 Problems living with dignity because of the attitudes/actions of others (%) | 53.0 ± 34.8 | 12.2 ± 12.2 | 62.9 ± 30.3 | 6.8 ± 6.8 | 0.022 |
| D6.4 Time spent on one's health condition or its consequences (%) | 39.9 ± 52.4 | 7.6 ± 7.6 | 50.4 ± 45.1 | 4.5 ± 4.5 | 0.025 |
| D6.5 Emotionally affected by your health condition (%)        | 36.0 ± 44.7 | 18.3 ± 18.3 | 43.9 ± 43.6 | 12.5 ± 12.5 | 0.060 |
| D6.6 Your health is a drain on your financial resources (%)   | 44.8 ± 34.5 | 20.7 ± 20.7 | 53.4 ± 31.1 | 15.5 ± 15.5 | 0.087 |
| D6.7 Family problems because of your health problems (%)      | 43.0 ± 36.3 | 20.7 ± 20.7 | 54.5 ± 32.2 | 13.3 ± 13.3 | 0.009 |
| D6.8 Problems performing activities by yourself for relaxation or pleasure (%) | 52.7 ± 41.5 | 5.8 ± 5.8 | 57.2 ± 35.2 | 7.6 ± 7.6 | 0.258 |
| **Participation in society (PSO) (Mean ± SD)**                 | 28.0 ± 22.3 | 22.1 ± 21.5 |             |           | 0.001 |

*a* indicates a significant difference.
**Table 3.** Differences in sexual dysfunction between the sample groups.

| PRSexDQ-SALSEX variables                                                                 | Methadone (N=329) | Buprenorphine (N=264) | p-value |
|------------------------------------------------------------------------------------------|-------------------|------------------------|---------|
| 1. Decrease in desire for sexual activity (%)                                            | 51.5              | 23.8                   | 14.6    | 10.1    | 64.2 |
|                                                                                         | 23.8              | 14.6                   | 21.9    | 6.4     | 7.5  | 0.002 |
| 2. Delay in ejaculation/orgasm (%)                                                       | 56.4              | 21.3                   | 13.4    | 8.8     | 69.8 |
|                                                                                         | 21.3              | 13.4                   | 15.8    | 7.9     | 6.4  | 0.008 |
| 3. Unable to ejaculate/to have an orgasm once you begin sexual relation (%)              | 61.6              | 26.2                   | 7.6     | 4.6     | 76.6 |
|                                                                                         | 26.2              | 7.6                    | 14.3    | 4.5     | 4.5  | 0.001 |
| 4. Experienced difficulties obtaining an erection/vaginal lubrication once the sexual activity is initiated (%) | 60.4              | 23.8                   | 9.5     | 6.4     | 69.4 |
|                                                                                         | 23.8              | 9.5                    | 22.1    | 5.3     | 3.0  | 0.032 |
| 5. Tolerated changes in sexual relations (%)                                              | 39.3              | 31.4                   | 23.5    | 5.8     | 53.2 |
|                                                                                         | 31.4              | 23.5                   | 31.7    | 12.5    | 2.6  | <0.001 |

Abbreviations: PRSexDQ-SALSEX = Psychotropic-related Sexual Dysfunction Questionnaire. p-values were calculated with ANOVA test.

**Table 4.** Binary logistic regression analysis for distinguishing the sample groups.
### Variables introduced in the model

Variables introduced in the model: UAC domain, GAR domain, SCA domain, GAP domain, LA domain, PSO domain, sexual dysfunction, age, i.v. opioid, HBV, HCV, VIH, previous maintenance program, daily opioid dosage, heroin + cocaine use every day, alcohol use every day and benzodiazepines use every day. Abbreviation: i.v.=intravenous administration of opioid; CI=confidence interval.

| Variables                                           | Odd Ratio | 95% CI       | p-value |
|-----------------------------------------------------|-----------|--------------|---------|
| Understanding and communication domain (UAC)         | 0.990     | 0.974 - 1.007 | 0.242   |
| Getting around domain (GAR)                         | 0.999     | 0.982 - 1.017 | 0.935   |
| Self-care domain (SCA)                              | 1.009     | 0.990 - 1.030 | 0.353   |
| Getting along with people domain (GAP)              | 1.006     | 0.993 - 1.019 | 0.369   |
| Life activities domain (LA)                         | 1.010     | 0.996 - 1.024 | 0.159   |
| Participation in society domain (PAR)               | 0.987     | 0.975 - 0.999 | 0.034   |
| Sexual dysfunction                                  | 1.915     | 1.247 - 2.940 | 0.003   |
| Age                                                 | 0.984     | 0.959 - 1.009 | 0.209   |
| I.v. opioid                                         | 1.126     | 0.542 - 2.339 | 0.750   |
| HBV                                                 | 1.316     | 0.704 - 2.462 | 0.390   |
| HCV                                                 | 2.056     | 1.268 - 3.332 | 0.003   |
| VIH                                                 | 3.359     | 1.405 - 8.033 | 0.006   |
| Previous maintenance program                        | 0.366     | 0.237 - 0.565 | <0.001  |
| Daily opioid dosage                                 | 0.438     | 0.220 - 0.872 | 0.019   |
| Heroin + Cocaine use every day                      | 6.670     | 0.742 - 59.958 | 0.090  |
| Alcohol use every day                               | 1.682     | 1.004 - 2.819 | 0.048   |
| Benzodiazepines use every day                       | 1.298     | 0.743 - 2.265 | 0.359   |
| Constant                                            | 0.034     |              | 0.019   |