Factors Influencing Sexual Dysfunction in Men Receiving Opioid Substitution Therapy in a Portuguese Center

Fatores que Influenciam a Disfunção Sexual em Homens Submetidos a Terapêutica de Substituição com Opioides num Centro Português

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DOI: https://doi.org/10.29315/gm.1049

ABSTRACT

Introduction: We intended to assess the prevalence of sexual dysfunction in men receiving opioid substitution therapy in a Portuguese center, which domains of sexual function are affected, and which factors influence sexual dysfunction.

Methods: We conducted a self-administered form, including: sociodemographic and clinical characterization; maintenance treatment with methadone or buprenorphine; presence of anxiety/depression, assessed with Hospital Anxiety and Depression Scale; sexual dysfunction, assessed with Massachusetts General Hospital – Sexual Functioning Questionnaire; erectile dysfunction, assessed with International Index of Erectile Function.

Results: A total of eighty-two patients participated in the study. Of these, 80.5% were receiving methadone treatment, with a mean current dose of 53.5 mg, a mean duration of treatment of 12.6 years, and a mean maximum dose of 86.2 mg. Buprenorphine was used by 19.5% of participants, with a mean current dose of 5.74 mg, a mean duration of treatment of 10.4 years, and a mean maximum dose of 8.07 mg. Antidepressants and antipsychotics were taken by 23.8% and 14.8% of participants, respectively. Anxiety and depression were present in 43.5% and 46.2% of cases, respectively. The Massachusetts General Hospital – Sexual Functioning Questionnaire revealed that 42.1% had sexual dysfunction and the item with the lowest score was general satisfaction. The International Index of Erectile Function revealed that 67.9% had erectile dysfunction and the item with the lowest score was achieving and maintaining an erection.

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Recebido/Received: 2025-05-05 Aceite/Accepted: 2025-11-24. Publicado online/Published: 2026-04-10.

There were no statistically significant differences between patients treated with methadone or buprenorphine, regarding the presence of sexual dysfunction and erectile dysfunction.
The factors significantly correlated with sexual dysfunction were: age, professional status, maximum methadone dose used by the patient, anxiety, and depression. The factors significantly correlated with erectile dysfunction, e não; maximum methadone dose used by the patient, tobacco, anxiety and depression.

Conclusion: We did not find evidence to switch from methadone to buprenorphine, if sexual dysfunction arises. Anxiety and depression seem to be the factors most correlated with sexual dysfunction and erectile dysfunction.

KEYWORDS: Buprenorphine; Methadone; Opiate Substitution Treatment; Sexual Dysfunction, Physiological; Sexual Dysfunctions, Psychological.

RESUMO

Introdução: Pretendemos avaliar a prevalência de disfunção sexual em homens a realizar terapia de substituição opiácea num centro português; quais os domínios da função sexual afetados; quais os fatores que influenciam a disfunção sexual.

Métodos: Foi aplicado um formulário de autopreenchimento, incluindo: caracterização sociodemográfica e clínica; tratamento de manutenção com metadona ou buprenorfina; presença de ansiedade/depressão, avaliada pela *Hospital Anxiety and Depression Scale*; disfunção sexual, avaliada pelo *Massachusetts General Hospital – Sexual Functioning Questionnaire*; disfunção erétil, avaliada pelo *International Index of Erectile Function*.

Resultados: Participaram 82 pacientes. Encontravam-se em tratamento com metadona, 80,5%, com dose atual média de 53,5 mg, por um tempo médio de 12,6 anos e com dose máxima média de 86,2 mg. Encontravam-se em tratamento com buprenorfina, 19,5%, com dose atual média de 5,74 mg, por um tempo médio de 10,4 anos e dose máxima média de 8,07 mg. Relativamente ao tratamento psicofarmacológico, 23,8% tomavam antidepressivos e 14,8% tomavam antipsicóticos. Para além disso, 43,5% apresentavam ansiedade e 46,2% depressão. O *Massachusetts General Hospital – Sexual Functioning Questionnaire* revelou que 42,1% apresentavam disfunção sexual e o item com menor pontuação foi a satisfação geral. O *International Index of Erectile Function* revelou que 67,9% apresentavam disfunção erétil e o item com menor pontuação foi alcançar e manter uma ereção.
Não houve diferenças estatisticamente significativas entre os pacientes a tomar metadona e buprenorfina, quanto à presença de disfunção sexual e disfunção erétil.
Os fatores significativamente correlacionados com a disfunção sexual foram: idade, *status* profissional, maior dose de metadona que o paciente tomou, tem; a mais. Os fatores significativamente correlacionados com a disfunção erétil foram: idade, estado civil, maior dose de metadona que o paciente tomou, tabaco, ansiedade, depressão.

Conclusão: Não encontramos evidências que justifiquem a substituição de metadona por buprenorfina em casos de disfunção sexual. A ansiedade e a depressão parecem ser os fatores mais correlacionados com a disfunção sexual e a disfunção erétil.

PALAVRAS-CHAVE: Buprenorfina; Disfunção Sexual, Fisiológica; Disfunções Sexuais, Psicológicas; Metadona; Tratamento de Substituição Opiácea.

INTRODUCTION

Sexual dysfunctions (SD) are frequently present in patients receiving opioid substitution therapy (OST). A meta-analysis by Yee *et al*[1] revealed that the prevalence of SD in men receiving methadone maintenance treatment (MMT) varied from 14% to 97% in individual studies, with a pooled prevalence of 52%. In the same study, the prevalence of SD in men receiving buprenorphine maintenance treatment (BMT) varied from 10% to 36% in individual studies, with a pooled prevalence of 24%.

Regarding the effect of OST on sexual function, men on MMT have difficulties with sexual function in all IIEF-15 domains[2] (erectile function, sexual desire, orgasm, intercourse satisfaction, overall satisfaction) and the most frequently reported SD is hypoactive sexual desire dysfunction. When comparing men on MMT with men on BMT, SD reported in several studies is significantly greater in the population on MMT. The work of Yee *et al*[3] showed that patients with sexual partners on MMT had lower scores for sexual desire and overall satisfaction than patients with sexual

partners on BMT. Patients on MMT without a sexual partner also scored lower in orgasmic function than patients on BMT. However, there are not sufficient studies to draw definitive conclusions about sexual function in patients on BMT.

About the potential factors implicated with SD, eight risk factors were identified among the MMT population[4]: age, lower testosterone level, duration of MMT, dose of methadone, medical status, psychiatric illness, other current substance use and familial status (such as a stable sexual partner). The work of Ghosh *et al*[5] showed no significant effect of age, current dose of buprenorphine, and duration of therapy on the prevalence or degree of SD in men with BMT. However, there is great heterogeneity among the results of the different studies, and, for this reason, more studies are needed to assess the relevance of these factors.

As far as we know, there are no studies concerning SD in men receiving OST in Portugal. Additionally, previous studies from other countries are scarce and have contradictory results. Therefore, our study aims to assess the prevalence of SD in men receiving MMT or BMT in a Portuguese center; to assess which domains of sexual function are affected in this population; and to identify which factors influence SD in these individuals.

MATERIAL AND METHODS

PARTICIPANTS

This work was performed at Centro de Respostas Integradas (CRI) Porto Central – Polo de Cedofeita (Porto, Portugal), a specialized center for the treatment of addictions related to the use of licit or illicit drugs and behavioral addictions.

We defined the inclusion criteria as follows: people of the masculine gender; receiving maintenance treatment for opioid dependence with methadone or buprenorphine, at the time of the study; and being followed at this center. We defined the following exclusion criteria: people under 18 years of age; people who could not fill in the questionnaire; people who did not live in Portugal.

We obtained approval from the ethics committee on March 31, 2022. The study began in April 2022 and finished by the end of September 2022. At that time, a total of 522 male patients were receiving OST, of whom 394 were on MMT, 120 were on BMT, and 8 patients were taking the buprenorphine + naloxone combination.

MEASURES AND INSTRUMENTS

We developed an anonymous self-administered form. The first part of this form included questions related to the sociodemographic and clinical characterization: age, marital status, romantic relationship status, children, scholarity, professional status, MMT or BMT (current dose, for how long the patient is taking the drug, the highest dose the patient has received), comorbid consumption of recreational drugs and frequency of its use, comorbid medical conditions and treatment with antidepressants or antipsychotics.

The second part included a screening for depression or anxiety, and for that purpose, the Hospital Anxiety and Depression scale (HADS) was applied. The HADS[6] is a self-report rating scale of 14 items on a 4-point Likert scale (ranging from 0–3). It is designed to measure anxiety and depression and for each subscale, the score is the sum of the respective seven items (ranging from 0 to 21). This scale is validated for the Portuguese population.[7]

The third part of the form consisted of the evaluation of sexual function. We included the Massachusetts General Hospital – Sexual Functioning Questionnaire (MGH-SFQ),[8] also validated for the Portuguese population.[9] It is a self-report questionnaire, composed of 5 items on a 7-point Likert scale (1-7) that assesses the following domains: desire, arousal, orgasm, erection, and general sexual satisfaction. We calculated a total sexual functioning variable corresponding to the sum of the five items comprising the scale, in relation to which we determined that the value 20 would be the normal theoretical cut-off point for SD, according to previous studies.[10]

Finally, in the third part, we also included the International Index of Erectile Function-5 (IIEF-5),[11] that is currently validated for the Portuguese population.[12] The IIEF-5 consists of five items on a 5-point Likert scale (1-5) and is used for screening and diagnostic severity assessment of erectile dysfunction (ED). Four of its five items were taken from the erectile function domain of the original IIEF and the fifth item concerns intercourse satisfaction. The responses are summed, resulting in a total IIEF-5 score ranging from 1 to 25, with lower values representing poorer erectile function. ED can be classified into five severity grades: absence (score 22–25), mild (17–21), mild to moderate (12–16), moderate (8–11), and severe (1–7).

DATA COLLECTION

All eligible patients were invited to participate voluntarily and without any counterparts. Informed consent was obtained from every patient who agreed to par-

ticipate in this study. The self-administered form was applied in person and placed inside a box to guarantee anonymity.

STATISTICAL ANALYSIS

Statistical analysis was performed using Microsoft Excel® and IBM® SPSS® version 27. The analysis included descriptive statistical measures (absolute and relative frequencies, means and corresponding standard deviations and coefficients of variation) and inferential statistics.

About the inferential statistics, the chi-square test was used to study the relationship between two categorical variables (such as comparison between men on MMT and BMT, regarding MGH-SFQ qualitative results, IIEF qualitative results and HADS qualitative results); the t-test was used to compare the means of two quantitative variables (such as comparison between men on MMT and BMT, regarding MGH-SFQ total score, IIEF total score and HADS scores for anxiety and depression); ANOVA test, an extension of the t-test, was used to compare the means of three or more independent groups (such as the MHG-SFQ total score for age categories, marital status, etc.).

For these parametric tests, we also calculated the effect size, determined by Cohen´s d. The effect size can be interpreted as follows: d>0.20 indicates a small effect, d>0.50 indicates a medium effect, and d>0.80 indicates a large effect.

For the ANOVA test, when significant relationships were found, Tukey's post-hoc test was used when homogeneity of variances was verified, and Tamhane's T2 post-hoc test was used when homogeneity of variances was not verified, to determine between which categories the differences are significant.

The association analysis, through the Pearson coefficient, was used to determine the relationship between quantitative variables or on a Likert scale, being a measure of the linear association between variables that varies between -1 and 1 (such as the relationship between the total score of MGH-SFQ and current dose of buprenorphine or methadone, etc.). The correlation coefficient values can be interpreted according to Table 1.

TABLE 1. Interpretation of the correlation coefficient values.

Correlation	Interpretation
0.90 a 1.00 (−0.90 a -1.00)	Very strong correlation (positive or negative)
0.75 a 0.90 (−0.90 a - 0.75)	Strong correlation (positive or negative)
0.60 a 0.75 (−0.75 a - 0.60)	Moderate-strong correlation (positive or negative)
0.40 a 0.60 (−0.60 a - 0.40)	Moderate correlation (positive or negative)
0.25 a 0.40 (−0.40 a - 0.25)	Weak correlation (positive or negative)
0.00 a 0.25 (−0.25 a 0.00)	Very weak correlation (positive or negative)

When comparing small samples, the Kolmogorov-Smirnov (K-S) test was used to verify the normality assumption. The significance level for rejecting the null hypothesis was set at $\alpha \leq .05$.

RESULTS

SOCIODEMOGRAPHIC AND CLINICAL CHARACTERIZATION

We obtained a total of 82 participants, corresponding to 15.71% of the male patients receiving OST at the time of this study in CRI Porto Central – Polo de Cedofeita. From these patients, 64 were on MMT and 16 were on BMT, which corresponds to 16.24% of the patients on MMT and 13.33% of the patients on BMT followed at this center. We did not have patients in our study taking the combination of buprenorphine + naloxone.

The sociodemographic characterization of the sample is presented in Table 2. The most frequent age category was 46-55 years (46.8%) and most were single (61.0%) despite having a current romantic relationship (56.1%). Most of these patients did not have children (51.9%). Regarding professional status, a minority were employed with a working contract (34.1%). When it comes to scholarship, the most frequent response was 7 to 9 years.

About the clinical characterization (Table 2), 80.5% were on MMT, with a mean current dose of 53.5 mg, for an average time of 12.6 years and with a mean maximum dose of 86.2 mg. Regarding the patients on BMT (19.5%), the study revealed a mean current dose of 5.74 mg, for an average time of 10.4 years and a mean maximum dose of 8.07 mg. The most frequently reported recreational drug was tobacco (69.1%), followed by cocaine (37.0%) and alcohol (33.3%). When there is polydrug use, the most frequently used is tobacco, being consumed every day or almost every day. Regarding comorbid health conditions, 16.0% reported a history of HCV infection and 13.3% reported status of HIV positive. A percentage of 23.8% were taking antidepressants and 14.8% were taking antipsychotics.

The results encountered for HADS can be found in Table 3. According to the results, 43.5% of the re-

TABLE 2. Sociodemographic and clinical characterization of the sample.

Item of the questionnaire	Response categories	N	%
1. **Age** M= 50.8 years; SD= 8.29 years; VC= 16%; Min=23 years; Max=65 years (5 missing answers)	23 to 45 years 46 to 55 years 56 to 65 years	17 36 24	22.1 46.8 31.2
2. **Marital status**	Single Married or in common-law marriage Widowed Divorced Separated despite being married	50 12 3 14 3	61.0 14.6 3.7 17.1 3.7
3. **Do you have a current romantic relationship?**	No Yes	36 46	43.9 56.1
4. **For how long do you have that relationship?** (1 missing answer)	Less than one year Between 1 and 3 years Between 3 and 5 years More than 5 years Does not have a romantic relationship	8 11 6 20 36	9.9 13.6 7.4 24.7 44.4
5. **Do you have children?** (1 missing answer)	No One Two Three More than three	42 25 10 2 2	51.9 30.9 12.3 2.5 2.5
6. **Professional status** (1 missing answer)	Employed Unemployed Unpaid activity Non-tax declared activity Retired Receiving social pension	28 28 1 6 9 10	34.1 34.1 1.2 7.3 11.0 12.2
7. **Scholarity**	Until 4 years 5 or 6 years 7 to 9 years 10 to 12 years Bachelor´s degree or Master´s degree	11 19 25 23 4	13.4 23.2 30.5 28.0 4.9
8. **Currently, are you being treated with any of these drugs?**	Methadone Buprenorphine Buprenorphine + Naloxone	66 16 0	80.5 19.5 0.0
9. **Which dose of this drug do you take currently?** (mg) (2 missing answers for methadone)	Methadone M=53.5 SD= 31.0 Min=7.0 Max= 150.0	Buprenorphine M= 5.74 SD= 4.3 Min= 0.4 Max= 16.0	
10. **For how long do you take this drug? (years)** (5 missing answers for methadone; 2 missing answers for buprenorphine)	Methadone M= 12.6 SD= 7.91 Min= 0.0 Max= 35.0	Buprenorphine M= 10.4 SD= 5.45 Min= 0.6 Max= 20.0	
11. **Which is the highest dose you have taken of this drug?** (mg) (8 missing answers for methadone and 1 missing answer for buprenorphine)	Methadone M= 86.2 SD= 45.3 Min= 30.0 Max= 300.0	Buprenorphine M= 8.07 SD= 3.61 Min= 2.0 Max= 16.0	
12. **Do you use any of these drugs currently?** (1 missing answer)	Heroin Other opiates excluding heroin Cocaine Cannabis Hallucinogens Amphetamines Tobacco Alcohol Does not take any of these drugs	11 3 30 15 0 0 56 27 6	13.6 3.7 37.0 18.5 0 0 69.1 33.3 7.4
13. **If you selected more than one drug in the previous question, indicate the substance that you use more frequently".** (1 missing answer)	Does not take any of these drugs Heroin Cocaine Cannabis Tobacco Alcohol Cocaine and other Tobacco and alcohol	6 3 7 6 45 3 5 6	7.4 3.7 8.6 7.4 55.6 3.7 6.2 7.4

Item of the questionnaire	Response categories	N	%
14. **If you selected any of the options in the previous answer, indicate how often you consume the most frequent substance?** (1 missing answer)	Does not take any of these drugs Every day or almost every day 1 to 3 times per week 1-3 times per month Sporadically (not every month)	6 58 7 4 6	7.4 71.6 8.6 4.9 7.4
15. **Do you have any of these health conditions?** (7 missing answers)	No Arterial hypertension HCV infection HIV positive or HIV positive and other Other medical condition	33 6 12 10 14	44.0 8.0 16.0 13.3 18.7
16. **Do you take antidepressant medication?** (2 missing responses)	No Yes	61 19	76.3 23.8
17. **Do you take any antipsychotic medication?** (1 missing response)	No Yes	69 12	85.2 14.8

N – absolute number of respondents; % - percentage; M- mean; SD- standard deviation; VC – variation coefficient; Min – minimum number; Max – maximum number.

TABLE 3. Description of the results encountered in the scales applied in this study.

Scale	Item in analysis	N	%	M	SD	VC %	Min	Max
HADS score (4 missing answers)	Total score - anxiety subscale Total score - depression subscale	78 78	100.0 100.0	7.44 6.81	4.06 4.13	55 61	1 0	20 17
HADS qualitative results (4 missing answers)	**Anxiety subscale** Normal Mild Moderate Severe **Total**	 44 20 9 5 **78**	 56.4 25.6 11.5 6.4 **100.0**					
	Depression subscale Normal Mild Moderate Severe **Total**	 42 21 13 2 **78**	 53.8 26.9 16.7 2.6 **100.0**					
MGH-SFQ score 7-point Likert scale (6 missing answers)	**Total score MGH-SFQ** Item 1 (desire) Item 2 (arousal) Item 3 (orgasm) Item 4 (erection) Item 5 (general satisfaction)	**76** 77 76 76 76 76	**100.0**	**20.17** 4.12 4.14 4.05 4.09 3.80	**6.71** 1.41 1.36 1.52 1.52 1.59	**33** 34 33 38 37 42	**5** 1 1 1 1 1	**35** 7 7 7 7 7
MGH-SFQ qualitative results (6 missing answers)	Without sexual dysfunction (>=20 points) Sexual dysfunction (< 20 points)	44 32	57.9 42.1					
IIEF score 5-point Likert scale (4 missing answers; 8 not eligible respondents)	**Total score IIEF** Item 1 (achieving and maintaining an erection) Item 2 (achieving penetration) Item 3 (maintaining erection after penetration) Item 4 (maintaining erection until the end of the sexual relation) Item 5 (satisfaction with sexual relation)	**70** 70 70 70 70 70	**100.0**	**18.36** 3.19 3.47 3.60 4.24 3.86	**4.61** 0.92 1.40 1.29 1.16 1.16	**25** 29 40 36 27 30	**5** 1 1 1 1 1	**24** 5 5 5 5 5
IIEF qualitative results (4 missing answers)	Without ED (> 22 points) Mild ED (17-22 points) Mild to moderate ED (12-17 points) Moderate ED (8-11 points) Severe ED (< 11 points) Does not have a recent sexual partner (in the last 6 months) **Total**	17 34 12 4 3 8 **78**	21.8 43.6 15.4 5.1 3.8 10.3 **100.0**					

HADS – Hospital Anxiety and Depression Scale; MGH-SFQ – Massachusetts General Hospital - Sexual Functioning Questionnaire; IIEF – International Index of Erectile Function; ED – erectile dysfunction; N – absolute number of respondents; % - percentage; M- mean; SD- standard deviation; VC – variation coefficient; Min – minimum number; Max – maximum number.

spondents had anxiety, with most of them having mild anxiety. On the other hand, 46.2% had a positive screening for depression, with the majority scoring for mild depression.

Regarding sexual problems (Table 3), the MGH-SFQ revealed that 42.1% had a score compatible with SD and the item with the lowest median score was general satisfaction. The IIEF revealed that 67.9% of respondents had ED, with the most frequent response being mild ED (43.6%). The IIEF item that had the lowest score was achieving and maintaining an erection.

COMPARISONS BETWEEN THE METHADONE AND BUPRENORPHINE GROUPS

Regarding the results of MGH-SFQ and IIEF (Table 4), both the total scores and the qualitative results of these scales revealed that patients on MMT generally had poorer sexual function and poorer erectile function than patients on BMT. However, the differences observed between the two groups were not statistically significant.

Concerning the anxiety subscale of HADS (Table 5), we can observe that for the methadone group, both the mean total score and the percentage of patients

TABLE 4. Comparison between the groups treated with methadone and buprenorphine regarding sexual dysfunction (measured with MGH-SFQ) and erectile dysfunction (measured with IIEF).

	Treatment		t	*p*	*Cohen's d*
	Methadone	Buprenorphine			
MGH-SFQ total score	**Total N=60 (100%)** M= 19.72 SD=6.39	**Total N=16 (100%)** M= 21.88 SD= 7.79	-1.145	0.256	0.322
IIEF total score	(N=56) M=18.09 SD=4.99	(N=14) M=19.43 SD= 2.44	-0.971	0.335	0.290
	Methadone	Buprenorphine	χ^2	p	
MGH-SFQ qualitative results Without sexual dysfunction Sexual dysfunction	**Total N=60 (100%)** N=33 (55.0%) N=27 (45.05%)	**Total N=16 (100%)** N=11 (68.8%) N=5 (31.3%)	**0.980**	**0.322**	
IIEF qualitative results Without ED Mild ED Mild to moderate ED Moderate ED Severe ED Does not have a recent sexual partner (in the last 6 months)	**Total N=62 (100%)** N=14 (22.6%) N= 25 (40.3%) N= 10 (16.1%) N= 4 (6.5%) N= 3 (4.8%) N= 6 (9.7%)	**Total N=16 (100%)** N= 3 (18.8%) N= 9 (56.3%) N= 2(12.5%) N= 0 (0%) N= 0 (0%) N=2 (12.5%)	**2.840**	**0.725**	

MGH-SFQ – Massachusetts General Hospital - Sexual Functioning Questionnaire; IIEF – International Index of Erectile Function; ED – erectile dysfunction; N – absolute number of respondents; % - percentage; M- mean; SD- standard deviation; t – t-test; χ^2 – chi-square test; *$p \leq 0.05$; **$p \leq 0.01$; ***$p \leq 0.001$.

TABLE 5. Comparisons between the groups treated with methadone and buprenorphine regarding the presence of anxiety and depression (measured with HADS).

	Treatment		t	*p*	*Cohen's d*
	Methadone	Buprenorphine			
HADS score Anxiety subscale Depression subscale	**Total N= 62 (100%)** M= 7.85 SD= 4.18 M= 7.24 SD= 4.39	**Total N= 16 (100%)** M= 5.81 SD= 3.17 M= 5.13 SD= 2.39	 1.819 1.855	 0.073 0.068	 0.510 0.520
	Methadone	Buprenorphine	χ^2	p	
HADS qualitative results – anxiety Normal Mild Moderate Severe	**Total N= 62 (100%)** N= 34 (54.8%) N= 15 (24.2%) N= 8 (12.9%) N= 5 (8.1%)	**Total N= 62 (100%)** N= 10 (62.5%) N= 5 (31.3%) N= 1 (6.3%) N= 0 (0%)	**2.158**	**0.540**	
HADS qualitative results – depression Normal Mild Moderate Severe	**Total N= 62 (100%)** N= 30 (48.4%) N= 17 (27.4%) N= 13 (21.0%) N= 2 (3.2%)	**Total N= 16 (100%)** N=12 (75.0%) N=4 (25.0%) N=0 (0%) N=0 (0%)	**5.571**	**0.134**	

HADS – Hospital Anxiety and Depression Scale; N – absolute number of respondents; % - percentage; M- mean; SD- standard deviation; t- t-test; χ2 – chi-square test; *$p \leq 0.05$; **$p \leq 0.01$; ***$p \leq 0.001$.

with anxiety (45.2%) were higher than the mean total score and the percentage of patients having anxiety (37.6%) in the buprenorphine group. However, these differences were not statistically significant.

About the depression subscale, we also verified a higher mean score and a higher percentage of depression for the methadone group (51.6%) than for the buprenorphine group (25%). However, these differences were not statistically significant.

FACTORS THAT INFLUENCE SEXUAL DYSFUNCTION

We also studied the variables possibly associated with SD and ED. In Table 6, we can observe that considering the MGH-SFQ total score, the variables age, professional status, the highest dose of methadone used by the patient, and the anxiety and depression subscales present statistically significant differences. For the remaining variables, we found no significant differences.

The MGH-SFQ total score showed significant differences between the categories 46 to 55 years and 56 to 65 years. This score was lower for 56 to 65 years old, which means that older patients had higher levels of SD. However, the effect size was very small (0.093). Regarding professional status, the MGH-SFQ total score showed significant differences between the categories employed or active and unemployed. The score was higher for the employed or active. In other words, those who were employed or active had less SD. For this variable, the effect size was also very small (0.119). For methadone, an increase in the highest dose of the drug used by the patient corresponded

TABLE 6. Relation between total score of MGH-SFQ and the sociodemographic and clinical variables obtained in this study.

		MGH-SFQ Total Score							*Cohen's d*	Tukey or T2 post-hoc
Item of the questionnaire	Response categories	N	M	SD	t	F	r	*p*		
1. **Age**	23 to 45 years	17	19.24	5.07		3.576		*0.033	0.093	46 to 55 years > 56 to 65 years (Tukey)
	46 to 55 years	34	22.35	6.10						
	56 to 65 years	22	17.82	7.79						
2. **Marital status**	Single	46	20.57	6.48		2.566		0.061	0.097	
	Married or in common-law marriage	12	23.33	6.14						
	Widowed	3	19.67	2.52						
	Divorced or separated	15	16.53	7.25						
3. **Do you have a current romantic relationship?**	No	32	20.41	6.59	0.259			0.796	0.060	
	Yes	44	20.00	6.87						
4. **For how long do you have that relationship**?	Less than one year	7	17.29	2.93		1.005		0.411	0.054	
	Between 1 and 3 years	11	17.82	8.29						
	Between 3 and 5 years	6	20.83	5.08						
	More than 5 years	19	21.95	7.38						
	Does not have a romantic relationship	32	20.41	6.59						
5. **Do you have children?**	No	38	20.26	5.85		0.941		0.425	0.038	
	One	23	20.78	7.82						
	Two	10	17.20	7.38						
	More than two	4	23.00	6.98						
6. **Professional status**	Employed or in activity	33	22.79	6.46		3.244		*0.027	0.119	Employed or in activity > Unemployed
	Unemployed	26	18.27	6.55						
	Retired	9	17.67	6.42						
	Receiving social pension	4	18.38	5.85						

Item of the questionnaire	Response categories	MGH-SFQ Total Score N	M	SD	t	F	r	p	*Cohen's d*	Tukey or T2 post-hoc
7. **Scholarity**	Until 4 years	9	15.56	7.04		1.753		0.148	0.090	
	5 or 6 years	18	21.89	7.01						
	7 to 9 years	23	19.30	6.59						
	10 to 12 years	22	21.55	5.13						
	Bachelor´s degree or Master´s degree	4	20.25	10.56						
9. **Which dose of this drug do you take currently?**	Methadone	59					-0.144	0.276		
	Buprenorphine	16					0.064	0.815		
10. **For how long do you take this drug?**	Methadone	56					-0.093	0.498		
	Buprenorphine	14					-0.023	0.937		
11. **Which is the highest dose you have taken of this drug?**	Methadone	53					-0.330	*0.016		
	Buprenorphine	15					0.173	0.538		
12. **Do you use any of these drugs currently?**	Heroin									
	No	65	19.97	6.27	-0.979			0.331	0.333	
	Yes	10	22.20	9.21						
	Other opiates									
	No	72	20.31	6.83	0.245			0.808	0.144	
	Yes	3	19.33	2.31						
	Cocaine									
	No	45	20.51	6.65	0.384			0.702	0.091	
	Yes	30	19.90	6.88						
	Cannabis									
	No	60	19.95	6.79	-0.816			0.417	0.263	
	Yes	15	21.53	6.42						
	Tobacco									
	No	22	21.77	8.12	1.258			0.212	0.319	
	Yes	53	19.64	6.00						
	Alcohol									
	No	51	20.22	7.15	-0.095			0.924	0.024	
	Yes	24	20.38	5.80						
	Does not take any of these drugs				-0.147			0.883	0.076	
	No	71	20.24	6.40						
	Yes	4	20.75	12.34						
13. **If you selected more than one drug in the previous question, indicate the substance that you use more frequently**	Does not take any of these drugs	4	20.75	12.34		0.465		0.857	0.046	
	Heroin	3	23.00	15.87						
	Cocaine	7	20.86	3.67						
	Cannabis	6	22.83	5.49						
	Tobacco	44	19.25	6.18						
	Alcohol	2	24.00	5.66						
	Cocaine and other	5	22.00	8.15						
	Tobacco and alcohol	4	20.00	3.56						
14. **If you selected any of the options in the previous answer, indicate how often you consume the most frequent substance?**	Does not take any of these drugs	4	20.75	12.34		0.514		0.674	0.021	
	Every day or almost every day	56	19.77	6.24						
	1 to 3 times per week	5	20.80	10.33						
	1-3 times per month or sporadically	10	22.60	5.04						

		MGH-SFQ Total Score							Cohen's d	Tukey or T2 post-hoc
Item of the questionnaire	Response categories	N	M	SD	t	F	r	p		
15. **Do you have any of these health conditions?**	No	28	20.21	7.25		0.518		0.722	0.031	
	Arterial hypertension	6	20.00	9.67						
	HCV infection	12	22.50	6.78						
	HIV positive or HIV positive and other	10	18.40	2.76						
	Other medical condition	13	19.77	6.92						
16. **Do you take 6ntidepressant medication?**	No	56	20.02	6.57	-0.021			0.984	0.006	
	Yes	18	20.06	7.41						
17. **Do you take any antipsychotic medication?**	No	63	20.06	6.95	-0.204			0.839	0.064	
	Yes	12	20.50	5.84						
HADS	Anxiety subscale	76					-0.306	**0.007		
	Depression subscale	76					-0.473	***0.000		

MGH-SFQ – Massachusetts General Hospital - Sexual Functioning Questionnaire; HADS – Hospital Anxiety and Depression Scale; N – absolute number of respondents; % - percentage; M- mean; SD- standard deviation; t- t-test; F- ANOVA test; r – Pearson correlation coefficient; * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$.
Note: The item 8 of the questionnaire ("Currently, are you being treated with any of these drugs?") is already analyzed in table 3.

to a significant decrease in the total MGH-SFQ score, which corresponded to a significant decrease in sexual function. For this variable, the correlation was weak (-0.330). An increase in the anxiety and depression subscales scores corresponded to a significant decrease in the MGH-SFQ total score, meaning that an increase in anxiety and depression corresponded to a significant decrease in sexual function. We verified a weak correlation for anxiety (-0.306) and a moderate correlation for depression (-0.473).

In Table 7, we can observe that for the IIEF total score, the variables age, marital status, the highest dose of methadone or buprenorphine used by the patient, the consumption of tobacco, and the anxiety and depression subscales presented with statistically significant differences. For the remaining variables, we found no significant differences.

The total IIEF score showed significant differences observed between the categories 46 to 55 years and 56 to 65 years. The score was lower for 56 to 65 years old, that is, older men had higher rates of ED. For this variable, we found a very small effect size (0.101). Regarding marital status, the IIEF was lower for single, divorced or separated, with significant differences in comparison to the married participants. For this variable, we found a very small effect size (0.127). An increase in the highest dose of methadone used by the patient corresponded to a significant decrease in IIEF, which corresponded to a significant increase in ED (with a weak correlation (-0.293)); an increase in the highest dose of buprenorphine used by the patient corresponded to a significant increase in IIEF, which corresponded to a significant decrease in ED (with a moderate correlation (0.578)). The consumption of tobacco was also associated with a significant decrease in IIEF, with higher levels of ED. For this variable, we found a medium effect size (0.634). An increase in anxiety and depression subscales scores corresponded to a significant decrease in the total IIEF score, which corresponded to a significant increase in ED. We found a moderate correlation for these variables (-0.469 for anxiety and -0.568 for depression).

DISCUSSION

The typical profile of the male participant in this study was: age between 46-55 years, single, with a current romantic relationship, without children, without a current declared professional activity, with 7-9 years of scholarity, receiving MMT, taking recreational drugs and not taking antidepressants or antipsychotics. The work of Maina *et al*[13] in Canada, with people on MMT of both genders, revealed some similarities to our center in terms of sociodemographic characteristics, since in their study most people were single (61%, similarly to our study), had incomplete secondary education, and had similar rates of unemployment (36.6% *vs* 34.1% in our study). The main difference is that in their center, most of the patients were under 40 years of age, unlike in our center, which included mostly older patients. On the other hand, the work of Gutiér-

TABLE 7. Relation between total score of IIEF and the sociodemographic and clinical variables obtained in this study.

		IIEF Total Score							Cohen's d	Tukey or T2 post-hoc
Item of the questionnaire	Response categories	N	M	SD	t	F	r	*p*		
1. **Age**	23 to 45 years	17	19.06	3.93		3.631		*0.032	0.101	46 to 55 years > 56 to 65 years (T2)
	46 to 55 years	32	19.38	3.66						
	56 to 65 years	19	16.00	6.03						
2. **Marital status**	Single	43	18.70	4.69		3.190		*0.029	0.127	Married or in common-law marriage > Single, Divorced or separated (Tukey)
	Married or in common-law marriage	12	20.17	2.79						
	Widowed	1	23.00							
	Divorced or separated	14	15.53	4.57						
3. **Do you have a current romantic relationship?**	No	26	19.35	3.33	1.388			0.170	0.343	
	Yes	44	17.77	5.17						
4. **For how long do you have that relationship?**	Less than one year	7	15.00	6.81		2.335		0.065	0.127	
	Between 1 and 3 years	11	16.27	5.48						
	Between 3 and 5 years	6	18.00	4.73						
	More than 5 years	19	19.68	4.14						
	Does not have a romantic relationship	26	19.35	3.33						
5. **Do you have children?**	No	35	19.20	3.52		1.208		0.314	0.053	
	One	22	18.05	5.40						
	Two	9	16.00	6.61						
	More than two	3	18.67	0.58						
6. **Professional status**	Employed or in activity	32	19.59	3.85		1.914		0.136	0.080	
	Unemployed	25	17.36	5.31						
	Retired	5	15.40	2.51						
	Receiving social pension	8	18.38	5.18						
7. **Scholarity**	Until 4 years	7	14.57	6.55		2.027		0.101	0.111	
	5 or 6 years	17	19.29	3.67						
	7 to 9 years	22	17.64	5.22						
	10 to 12 years	20	19.70	3.26						
	Bachelor´s degree or Master´s degree	4	18.25	4.35						
9. **Which dose of this drug do you take currently?**	Methadone	55					-0.259	0.056		
	Buprenorphine	14					0.385	0.174		
10. **For how long do you take this drug?**	Methadone	53					-0.072	0.611		
	Buprenorphine	13					0.262	0.388		
11. **Which is the highest dose you have taken of this drug?**	Methadone	49					-0.293	*0.041		
	Buprenorphine	13					0.578	*0.039		

Item of the questionnaire	Response categories	IIEF Total Score N	M	SD	t	F	r	p	Cohen's d	Tukey or T2 post-hoc
12. Do you use any of these drugs currently?	Heroin									
	No	60	18.42	4.64	0.183			0.856	0.065	
	Yes	9	18.11	4.94						
	Other opiates									
	No	66	18.53	4.65	1.294			0.200	0.764	
	Yes	3	15.00	3.61						
	Cocaine									
	No	41	19.20	4.14	1.800			0.076	0.441	
	Yes	28	17.18	5.14						
	Cannabis									
	No	54	17.98	4.87	-1.350			0.182	0.394	
	Yes	15	19.80	3.51						
	Tobacco									
	No	20	20.40	2.30	2.391			*0.020	0.634	
	Yes	49	17.55	5.10						
	Alcohol									
	No	47	18.21	4.53	-0.426			0.671	0.110	
	Yes	22	18.73	4.97						
	Does not take any of these drugs							0.321	0.591	
	No	66	18.26	4.67	-1.000					
	Yes	3	21.00	3.61						
13. If you selected more than one drug in the previous question, indicate that it is the substance you use more frequently.	Does not take any of these drugs	3	21.00	3.61		0.954		0.473	0.099	
	Heroin	3	21.00	2.00						
	Cocaine	7	19.71	1.11						
	Cannabis	6	20.67	3.20						
	Tobacco	42	17.33	5.24						
	Alcohol	1	22.00							
	Cocaine and other	3	18.33	2.08						
	Tobacco and alcohol	4	18.75	5.26						
14. If you selected any of the options in the previous answer, indicate how often you consume the most frequent substance?	Does not take any of these drugs	3	21.00	3.61		1.890		0.140	0.080	
	Every day or almost every day	52	17.75	4.92						
	1 to 3 times per week	5	22.20	1.79						
	1-3 times per month or sporadically	9	19.00	3.08						
15. Do you have any of these health conditions?	No	26	19.62	3.84		2.519		0.051	0.148	
	Arterial hypertension	6	17.33	5.20						
	HCV infection	10	18.80	3.88						
	HIV positive or HIV positive and other	9	19.56	3.09						
	Other medical condition	12	15.00	6.19						
16. Do you take antidepressant medication?	No	52	18.50	4.58	0.560			0.577	0.160	
	Yes	16	17.75	5.01						
17. Do you take any antipsychotic medication?	No	58	18.45	4.82	0.292			0.772	0.096	
	Yes	11	18.00	3.71						
HADS	Anxiety subscale	70					-0.469	***0.000		
	Depression subscale	70					-0.568	***0.000		

IIEF – International Index of Erectile Function; HADS – Hospital Anxiety and Depression Scale; N – absolute number of respondents; % - percentage; M- mean; SD- standard deviation; t- t-test; F- ANOVA test; r – Pearson correlation coefficient; * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$.
Note: The item 8 of the questionnaire ("Currently, are you being treated with any of these drugs?") is already analyzed in table 3.

rez-Cáceres *et al*[14] in Spain, with people on MMT of both genders, had a mean age of 48.7 years, which was very similar to the mean of 50.8 years obtained in our study. The average time on MMT of 13.6 years was also very similar to the number obtained in our study (12.6 years). The main differences in relation to our study were a greater prevalence of low literacy, of 4 years or less (50.64% in comparison to 13.4% in our study), and a higher prevalence of a history of HCV infection (64.1% in comparison to 16% in our study). Despite some small regional differences, we can observe that these addiction centers have several sociodemographic and clinical characteristics in common with our study and for that reason, we consider that the results of our center can be considered in other countries.

In our study, according to HADS, 43.5% had anxiety and 46.2% had depression. Maina *et al*[13] in Canada found similar results, with a prevalence of 55.4% for anxiety and 52.5% for depression. Another study,[15] that explored the prevalence of co-occurring mental disorders in patients receiving OST, revealed a prevalence of anxiety of 28.7% in males from Czechia and 31% in males from Norway; on the other hand, it revealed a prevalence of depression of 11.1% in males from Czechia and 19.8% in males from Norway. These figures are lower than the ones obtained in our study. However, this study was derived from a database and not from self-report questionnaires like our study, which could contribute to the differences encountered between the studies.

The meta-analysis conducted by Yee *et al*[1] revealed that SD in men on MMT had a pooled prevalence of 52%, while for men on BMT had a pooled prevalence of 24%. Our study revealed that generally 42.1% of the patients had a score compatible with SD, while it happened for 45.05% of the patients on MMT and 31.3% of the patients on BMT. Therefore, our study confirms the tendency in other studies for poorer sexual function among men on MMT, in comparison to men on BMT. However, the differences encountered in our study were not statistically significant.

Our study also revealed that 67.7% of patients on MMT and 68.8% of patients on BMT had ED, without a statistically significant difference between the groups. The work of Teoh *et al*[16] with male patients on MMT also revealed a prevalence of ED of 67%. The absence of significant differences between the MMT and BMT groups in our study suggests that other factors may be playing a more significant role in SD and ED in these patients, rather than the direct pharmacological effects of methadone or buprenorphine.

In our study, all sexual function domains were affected (Table 3), but especially general satisfaction and erectile function. The study of Zhang *et al*[2] also found a decrease in all domains, but the most affected was hypoactive sexual desire, which was not the case in our study.

Contrary to what was found in the work of Yee *et al*[4] and in accordance with the work of Ghosh *et al*,[5] we did not find in our study a significant correlation between SD or ED and the following factors: current dose of methadone or buprenorphine, duration of treatment with MMT or BMT, medical status, current romantic relationship or recreational drug use (except for tobacco). Older age was found to be significantly correlated both with SD and ED in our study, which is no surprise since age is a well-established risk factor for SD, especially ED.[17] Smoking tobacco is also a proven risk factor for ED[18] and was significantly correlated with ED in our study (presenting with a medium effect size). The factors that were more significantly correlated with SD and ED in our study were anxiety and depression (presenting with the lowest p-value; a weak-moderate correlation for anxiety and a moderate correlation for depression). Our findings are in accordance with the study of Gerra *et al*[19] with men on MMT, which suggests that SD in their patients is more correlated with childhood adversities and comorbid psychiatric symptoms than the direct pharmacological effects of opioid agonist medications. In the work of Teoh *et al*,[16] depression was highly associated with ED, which is also in accordance with our study.

We did not find in our study a correlation between the use of antidepressant medications and sexual dysfunction. However, it is well established that sexual dysfunction is a common side effect of these drugs, particularly of tricyclic antidepressants, selective serotonin reuptake inhibitors and serotonin norepinephrine reuptake inhibitors.[20] Probably, we did not find that correlation due to the low percentage of patients treated with antidepressants (23.8%), despite having symptoms of anxiety and/or depression.

A systematic review and meta-analysis by Ramli *et al*[21] revealed that bupropion, ginseng, *rosa damascena* (damask rose) and trazodone have a promising future as therapy for male SD in patients receiving OST, particularly in the domains of sexual desire, erection, ejaculation, problem assessment, and sexual satisfaction. Considering the results obtained in our study, bupropion could be an interesting antidepressant choice in patients presenting with depressive symptoms and trazodone could be an interesting option in patients

presenting with anxiety or sleep disturbances, given its sedative effect.

LIMITATIONS

This work faced some limitations. First, we encountered a low participation rate (15.71%), since the study was voluntary and there were no counterparts for the patients. Additionally, some patients refused to participate after being informed that they would need to sign an informed consent, even though we explained the anonymity of the responses would be guaranteed. Other patients referred that the form was too long and would take too much time to complete. The low number of participants led to a decrease in statistical power, and for that reason, the generalization of the results of this study to other clinical contexts should be approached with caution.

We also acknowledge that the different methodologies used to assess sexual function in the previous studies limit the comparison with the results obtained in our study.

Another limitation encountered was the fact that the study was anonymous and for that reason, it would not be possible to compare the survey data with the data contained in the patients' clinical files or with data obtained from other studies that might be carried out in the same institution.

Finally, since it was a self-completion questionnaire, some of the information provided might be inaccurate, for example, the presence of medical comorbidities, which we suspect could be underreported in this study.

CONCLUSION

The typical profile of the male participant in this study was: age between 46-55 years, single, currently in a romantic relationship, without children, undergoing methadone treatment, taking recreational drugs and not taking antidepressants or antipsychotics, despite the high prevalence of anxiety and depression. No significant differences were found between patients on methadone and buprenorphine treatment, regarding sexual dysfunction or erectile dysfunction. The factors significantly correlated with sexual dysfunction were: age, professional status, the highest dose of methadone used by the patient, anxiety and depression. The factors significantly correlated with erectile dysfunction were: age, marital status, the highest dose of methadone used by the patient, consumption of tobacco, anxiety, and depression.

According to our study, we did not find evidence to recommend switching from methadone to buprenorphine if complaints related to sexual function arise. Anxiety and depression seem to be the factors most correlated with sexual dysfunction in these patients; therefore, when sexual complaints arise, screening for depressive or anxiety disorders should be prioritized.

PREVIOUS PRESENTATIONS

This work was previously presented as an oral communication at the XVIII National Psychiatry Congress (Albufeira, Portugal), on October 19, 2024.

ACKNOWLEDGEMENTS

The authors would like to thank Equipa de Tratamento de Cedofeita - Centro de Respostas Integradas Porto Central, where the study was conducted.

CONTRIBUTORSHIP STATEMENT/ DECLARAÇÃO DE CONTRIBUIÇÃO

TA: Desenho do estudo, recolha de dados, análise de dados, redação, revisão crítica e aprovação do manuscrito.

PA: Desenho do estudo, recolha de dados, revisão crítica e aprovação do manuscrito.

Todos os autores aprovaram a versão final a ser publicada

TA: Study design, collection of data, data analysis, drafting, critical review and approval of the manuscript.

PA: Study design, collection of data, critical review and approval of the manuscript.

All authors approved the final version to be published

RESPONSABILIDADES ÉTICAS

CONFLITOS DE INTERESSE: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

FONTES DE FINANCIAMENTO: Não existiram fontes externas de financiamento para a realização deste artigo.

CONFIDENCIALIDADE DOS DADOS: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

PROTEÇÃO DE PESSOAS E ANIMAIS: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pela Comissão de

Ética responsável e de acordo com a Declaração de Helsínquia revista em 2024 e da Associação Médica Mundial.

PROVENIÊNCIA E REVISÃO POR PARES: Não comissionado; revisão externa por pares.

ETHICAL DISCLOSURES

CONFLICTS OF INTEREST: The authors have no conflicts of interest to declare.

FINANCING SUPPORT: This work has not received any contribution, grant or scholarship

CONFIDENTIALITY OF DATA: The authors declare that they have followed the protocols of their work center on the publication of patient data.

PROTECTION OF HUMAN AND ANIMAL SUBJECTS: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2024).

PROVENANCE AND PEER REVIEW: Not commissioned; externally peer-reviewed.

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