182 (2026) 209866

Contents lists available at ScienceDirect

Journal of Substance Use and Addiction Treatment

journal homepage: www.journals.elsevier.com/journal-of-substance-use-and-addiction-treatment

Tailoring opioid substitution therapy: Patient profiles, clinical outcomes, and preferences for new formulations

Federica Ambrosini [a,*], Elisa Zamagni [b], Francesco Iannello [c], Michele Bertini [d], Simona Brusco [e], Ferdinando Cerrato [f], Nadia Marzocchi [g], Teo Vignoli [h], Roberta Biolcati [a]

[a] Department of Education Sciences "G. M. Bertin", University of Bologna, Via Filippo Re, 6, 40126, Bologna, Italy
[b] Department of Mental Health and Pathological Addiction, Local Health Agency of Romagna, Viale Sardegna, 9, 47838, Riccione, Italy
[c] Department of Mental Health and Pathological Addiction, Local Health Agency of Romagna, Via Alberto Missiroli, 16, 48121, Ravenna, Italy
[d] Department of Mental Health and Pathological Addiction, Local Health Agency of Romagna, Via Benigno Zaccagnini, 22, 48018, Faenza, Italy
[e] Department of Mental Health and Pathological Addiction, Local Health Agency of Romagna, Via Bosi, 32, Lugo, 48022, Italy
[f] Department of Mental Health and Pathological Addiction, Local Health Agency of Bologna, Viale Carlo Pepoli, 5, Bologna, 40123, Italy
[g] Department of Mental Health and Pathological Addiction, Local Health Agency of Modena, Via Paradisi, 3, Vignola, 41058, Italy
[h] Department of Mental Health and Pathological Addiction, Local Health Agency of Romagna, Via Publio Ovidio Nasone, 47923, Rimini, Italy

ARTICLE INFO

Keywords:
Opioid substitution therapy
Methadone
Buprenorphine
Recovery capital
Patient perspectives
Stigma
New formulations

ABSTRACT

Introduction: Understanding patient experiences with opioid substitution treatment (OST) is critical to developing more personalized and responsive care strategies. This study employed latent class analysis (LCA) to: (1) identify subgroups of patients based on their perceptions and satisfaction with OST; (2) examine differences across subgroups in clinical outcomes and interest in novel formulations (methadone tablets, weekly/monthly buprenorphine depot, buprenorphine implant); (3) assess associations with individual and treatment-related factors; and (4) explore class-specific risk and protective factors.

Methods: A total of 280 individuals (79 % male; mean age = 46.9 years) receiving OST (methadone syrup = 78 %; sublingual buprenorphine tablets = 22 %) at six public addiction services in Italy completed an anonymous questionnaire. The survey assessed sociodemographics, current OST type and adherence, treatment perceptions and overall satisfaction, treatment duration, recent substance use and OST misuse, interest in novel formulations, motives for switching, and recovery capital (BARC-10).

Results: LCA identified three subgroups: *Satisfied yet burdened*, *Satisfied and engaged*, and *Not experiencing benefit*. The *Not experiencing benefit* class showed low satisfaction and limited perceived effectiveness with OST, high recent heroin and cocaine use, shorter treatment duration, and lowest recovery capital, with living alone emerging as a key risk factor. The *Satisfied yet burdened* class reported high satisfaction with OST but significant stigma and burden; recovery capital was positively linked to age and employment; living alone and higher education were associated with cocaine use; heroin use was higher among those receiving methadone syrup. The *Satisfied and engaged* class showed the highest satisfaction with OST, longer treatment, and appreciation for clinical contact; living alone remained the main risk factor, associated with heroin use. Methadone tablets were preferred by those on methadone syrup across all classes. Interest in monthly buprenorphine depot was highest in the *Satisfied yet burdened* class, especially among women and those on sublingual buprenorphine. The implant was favored in the *Satisfied and engaged* class by men with higher education. Individuals living alone in the *Not experiencing benefit* class showed the lowest interest in long-acting options.

Conclusion: Findings highlight the importance of tailoring OST delivery to distinct patient profiles to enhance engagement, reduce unmet needs, and support long-term recovery.

* Corresponding author.
E-mail address: federica.ambrosini3@unibo.it (F. Ambrosini).

https://doi.org/10.1016/j.josat.2025.209866
Received 18 August 2025; Received in revised form 23 October 2025; Accepted 17 December 2025
Available online 21 December 2025

1. Introduction

Opioid substitution therapy (OST) is a well-established intervention for opioid use disorder (OUD), shown to reduce mortality, morbidity, and infectious disease transmission while supporting psychosocial functioning (Chang et al., 2015). Commonly administered medications include methadone, a full opioid agonist, and buprenorphine, a partial agonist with a favorable safety profile. While methadone carries a higher risk of respiratory depression and overdose during the initial treatment phase (O'Connor et al., 2020), sublingual buprenorphine is more susceptible to diversion and misuse (Lofwall & Walsh, 2014). To address these limitations, long-acting buprenorphine formulations - such as depot injections and subcutaneous implants - were introduced to improve adherence, reduce diversion, and lessen the burden of daily supervision, thereby enhancing treatment satisfaction and integration into daily life (Blair, 2024; Chappuy et al., 2020; Pierlorenzi et al., 2024).

In Italy, depot buprenorphine injections were authorized by AIFA in 2019 and made available to public addiction services (*Ser.D.*) in 2021, while the six-month implant, classified as a hospital-only medicine in 2022, remains largely limited to pilot programs (AIFA, 2019, 2021, 2022a; Pierlorenzi et al., 2024). For the Italian context, another recent innovation is the tablet formulation of methadone, authorized in 2022 and classified as hospital-only in 2023, marking a shift in a treatment system long dominated by methadone syrup and daily supervised dosing (AIFA, 2022b, 2023; Besana et al., 2025; Strepparola et al., 2025). Although tablets may pose higher diversion risks (Dasgupta et al., 2010), their dosing precision and ease of storage and transport (Khazaee-Pool et al., 2018) make them suitable for take-home regimens among stable patients, supporting more flexible, patient-centered care (Gerra et al., 2011; Strepparola et al., 2025). Implementation of these novel formulations across Italian regions, including Emilia-Romagna, is still at an early stage and their introduction is currently under evaluation. Understanding patients' experiences, preferences, and readiness for change is therefore crucial to ensuring that such innovations are both clinically appropriate and acceptable in everyday treatment practice (SAMHSA, 2023).

Current international evidence on patients' acceptability of OST and readiness to transition to these treatment options remains limited. Qualitative studies suggest that patients may view buprenorphine tablets more favorably than methadone syrup, highlighting advantages such as take-home flexibility and lower perceived stigma (Yarborough et al., 2016). Extended-release formulations are generally welcomed by patients seeking dose stability and greater control over their lives (Neale et al., 2018, 2019). Nevertheless, some patients express concerns regarding perceived challenges related to discontinuation, and the invasiveness of certain modalities, particularly implants. Acceptance also appears to vary across treatment stages, with shorter-acting depots often preferred in early phases and implants in maintenance settings (Neale et al., 2019).

These findings point to the importance of considering both pharmacological features and the broader psychosocial context in which treatment is delivered. Two key constructs potentially linked to how patients perceive and engage with treatment are internalized stigma and recovery capital. Internalized stigma, the process of adopting negative societal beliefs about substance use, has been linked to reduced engagement in care, lower self-esteem, and poorer quality of life (Luoma et al., 2007; Tsai et al., 2019). In the context of OST, treatments offering greater discretion may help mitigate stigma, while those requiring frequent clinic visits can unintentionally reinforce marginalization (Scurti et al., 2023). Recovery capital is defined as the personal and social resources that support sustained recovery (Cloud & Granfield, 2008; Vilsaint et al., 2017). Higher levels of recovery capital have been associated with better clinical outcomes, greater treatment retention, and improved psychosocial functioning (Bormann et al., 2023; Bunaciu et al., 2024). Nonetheless, limited research has investigated how recovery capital is associated with patients' treatment attitudes.

Additional factors – such as ongoing substance use, diversion or misuse of OST, treatment adherence, and duration – may also shape how patients relate to their care. However, few studies have systematically examined how different patient profiles, based on their perceptions of ongoing OST, relate to clinical and behavioral outcomes. A comprehensive understanding of how these multiple dimensions interact is essential to develop flexible, person-centered approaches capable of addressing the diverse needs of individuals in treatment.

Latent Class Analysis (LCA) provides a robust analytical strategy for examining unobserved heterogeneity within populations by uncovering distinct subgroups based on individuals' patterns of responses. In recent years, it has gained increasing prominence in substance use research for its effectiveness in delineating subpopulations characterized by unique behavioral and clinical profiles (e.g., Bray et al., 2023; Lardier et al., 2024; Lister et al., 2022).

This study responds to the growing call for person-centered research and aims: (1) to identify distinct subgroups of patients receiving OST across addiction services in the Emilia-Romagna Region, based on their perceptions and satisfaction with current treatment, using LCA; (2) to examine differences between these subgroups on a range of distal outcomes (i.e., recovery capital, treatment adherence, OST misuse and diversion, ongoing substance use, and interest in alternative OST formulations); (3) to investigate how individual and treatment-related characteristics (i.e., sex, age, educational attainment, occupational status, living situation, current OST formulation, and treatment duration) are associated with class membership; and (4) to explore how these same characteristics relate to clinical outcomes within each latent class, in order to identify class-specific patterns of risk and protective factors. Findings may inform the development of more acceptable and effective treatment strategies, with the potential to enhance patient engagement, retention, and recovery outcomes in OST settings.

2. Methods

2.1. Study design and procedures

This study employed a cross-sectional, multicenter design and was conducted across six addiction service units in the Emilia-Romagna region of Italy, specifically located in Rimini, Ravenna, Faenza, Lugo, Bologna, and Vignola.

Eligible participants were identified by clinical staff through a review of patient records at each participating center. Eligible individuals were adults (≥18 years) receiving methadone syrup or sublingual buprenorphine tablets for at least three months, with adequate written comprehension of Italian. Exclusion criteria included cognitive or intellectual impairments, as assessed by clinicians. Recruitment took place in outpatient clinics, where nursing staff approached eligible individuals during scheduled OST visits, provided a standardized explanation of the study, and invited voluntary, uncompensated participation. Written informed consent was obtained, including authorization to access clinical and personal data from medical records. Following consent, an anonymous online questionnaire, developed using the Qualtrics platform, was administered in the clinic using a tablet. The nurse initiated the survey by completing the first five items – pertaining to the type and dosage of OST, adherence to treatment and toxicological screenings, and take-home dosing days – based on information extracted from the patient's clinical records. The tablet was then handed to the participant, who completed the remainder of the questionnaire independently in a private setting. The online form was designed to restrict backward navigation, ensuring that participants could not review or modify the responses entered by the staff. Questionnaire responses were collected anonymously via Qualtrics. Clinical staff had no access to the response database, and the research team at the University of Bologna had no access to personal identifiers or recruitment logs, which were securely managed by local staff and deleted after recruitment ended.

The study received ethical approval from the local ethics committee, namely Comitato Etico della Romagna (Approval number: 3702, Prot. 1557/2024 I.5/226), and was conducted in accordance with the ethical outlined in the 1964 Declaration of Helsinki and its later amendments. Data collection was conducted from the 15th of April 2024 to the 27th of January 2025. The final sample of respondents was composed of 280 individuals undergoing OST.

2.2. Measures

The survey was jointly developed by addiction medicine professionals and academic researchers and was designed to collect the following data.

2.2.1. Sociodemographic characteristics

Data on sex at birth, age, highest educational attainment, employment status, student status, marital status, and living arrangement were collected.

2.2.2. Information on current OST and compliance

The following data were obtained from medical records: (1) regular completion of toxicology screenings in the past three months (Yes/No; defined as missing no more than one per month); (2) adherence to OST during the same period (Yes/No, defined as missing no more than one dose per month); (3) current OST formulation (Methadone syrup or Sublingual buprenorphine tablets); and (4) number of take-home doses authorized (number of days the patient could self-administer treatment at home). Duration of the current OST was collected as an open-ended numeric entry in months or years, as reported by participants, and subsequently transformed in years for the purposes of data analysis.

2.2.3. Perceptions of current OST

To assess participants' perceptions of their current OST, 14 ad hoc items were developed, drawing on prior qualitative research on patient experiences (e.g., Crapanzano et al., 2019; Neale et al., 2018, 2019; Woo et al., 2017; Yarborough et al., 2016). The items were designed to capture the following dimensions: (1) the perceived adequacy and utility of the treatment; (2) the extent to which the treatment is perceived as supporting personal goals and recovery processes; (3) perceived limitations and restrictions associated with treatment logistics; (4) the quality of therapeutic engagement; and (5) internalized and anticipated stigma. Each statement was rated using a 5-point Likert scale, with the following response options explicitly presented to participants: 1 = Strongly disagree, 2 = Disagree, 3 = Neither agree nor disagree, 4 = Agree, and 5 = Strongly agree.

2.2.4. Overall satisfaction with current OST

To assess overall satisfaction with the OST currently received, participants were asked: "*Overall, how satisfied are you with the opioid substitution treatment you are currently receiving?*" Responses were recorded on a 5-point Likert scale, ranging from 1 = Very dissatisfied to 5 = Very satisfied.

2.2.5. Recent substance use behaviors

Participants self-reported substance use and medication-related behaviors over the past three months. They were asked whether they had: (a) injected methadone; (b) used buprenorphine intranasally or intravenously; (c) diverted methadone or buprenorphine to others; (d) used heroin; and (e) used cocaine. Each behavior was assessed with a Yes/No response format.

2.2.6. Interest toward novel formulations of opioid substitution treatment

Participants' openness to switching to alternative OST formulations was assessed through a series of items, introduced by a standardized, accessible description of three treatment options (oral methadone tablets, weekly or monthly buprenorphine depot injection, and subcutaneous buprenorphine implant). The descriptions of the depot injection and implant were adapted from Neale et al. (2018), whereas the description of the oral methadone tablets was developed by clinicians. The full text of all treatment option descriptions is provided in the Supplementary Materials. Participants were explicitly informed that these treatments were under evaluation and not yet routinely offered at their clinic, and that their responses would not influence current or future clinical decisions. After reading the descriptions, participants were asked whether they would hypothetically be interested in switching to each formulation if it became available and was recommended by their healthcare provider (response options: Yes, No, Unsure), with responses collected separately for each option. They were then presented with a forced-choice item asking them to select their preferred formulation if all options were available.

2.2.7. Motives for switching to novel OST formulations

Participants' reasons for considering a switch to methadone tablets, prolonged-release buprenorphine depot injections, or subcutaneous buprenorphine implants were assessed through three dedicated sections of the questionnaire, each targeting a specific formulation. Based on their preference indicated in a preceding forced-choice item, participants completed only the corresponding section. Each section included 17 ad hoc statements evaluating expectations and concerns regarding the selected formulation, rated on a 5-point Likert scale (1 = Strongly disagree, 2 = Disagree, 3 = Neither agree nor disagree, 4 = Agree, 5 = Strongly agree). Items were conceptually informed by prior qualitative research on patient experiences and treatment priorities (e.g., Neale et al., 2018, 2019), and addressed a broad range of domains, including perceived clinical utility, treatment flexibility, personal autonomy, impact on daily life and social functioning, and stigma.

2.2.8. Recovery capital

Recovery capital was assessed using the Brief Assessment of Recovery Capital (BARC-10; Vilsaint et al., 2017), a validated 10-item self-report measure designed to capture the personal, social, and community resources that support recovery from substance use disorders. Participants rated each statement using a 6-point Likert scale, ranging from 1 = Strongly disagree to 6 = Strongly agree. Total scores range from 10 to 60, with higher scores indicating greater levels of recovery capital (cut-off $\geq$47, Vilsaint et al., 2017). In the present study the measure showed good internal consistency (Cronbach's $\alpha = 0.88$).

2.3. Data analyses

Preliminary descriptive analyses were conducted using SPSS version 25.0 (IBM Corp., 2017). There were no missing data on the variables included in the analyses. Latent class analysis (LCA) was performed in Mplus v.8 (Muthén & Muthén, 1998–2017) to identify subgroups based on 15 items assessing perceptions and satisfaction with OST. To avoid estimation issues due to sparse categories, all items were dichotomized: responses of 4 or 5 on the 5-point scale (indicating agreement or satisfaction) were coded as 1, all others as 0. Models ranging from one to six classes were estimated. Replication of the highest log-likelihood value was verified for each model to ensure convergence on a global maximum. Model fit was evaluated using Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and sample-size adjusted BIC (SABIC), with lower values indicating better fit. When indices disagreed, the BIC was prioritized, following Nylund et al. (2007). Classification quality was assessed using entropy, with values $\geq$0.80 indicating high classification precision. The Vuong-Lo-Mendell-Rubin likelihood ratio test (VLMR-LRT) and the bootstrap likelihood ratio test (BLRT) were used to compare adjacent class solutions.

To examine how class membership relates to individual characteristics and clinically relevant outcomes, two auxiliary models were estimated using the manual BCH procedure (Asparouhov & Muthén, 2021; Bakk & Vermunt, 2016; Bolck et al., 2004), which accounts for

classification error and provides unbiased estimates of class-specific means or probabilities. The first BCH model assessed differences between latent classes in multiple distal outcomes, including recovery capital, recent toxicology testing, heroin use, and cocaine use, and interest in novel OST formulations (methadone tablets, weekly depot, monthly depot, implant). The second BCH model examined associations between covariates and class membership, as well as class-specific effects of covariates on clinical outcomes. Statistical significance was evaluated using 95 % confidence intervals (CIs). Effects were considered statistically significant when the CI did not include zero (for continuous outcomes) or one (for binary outcomes). Direct associations between covariates and outcomes, independent of class membership, were also tested and are reported in the Supplementary Material (Table S2). Categorical covariates were dummy coded and included sex (female vs. male), educational attainment (≥ upper secondary vs. lower), employment status (in work or training vs. not), living situation (living alone vs. not), and current OST type (sublingual buprenorphine tablets vs. methadone syrup). Age and treatment duration were included as continuous covariates; the latter was log-transformed to correct for positive skew. Three hypothesized outcomes – regular OST intake, OST misuse, and diversion – were excluded from the second BCH model. These variables exhibited highly skewed distributions, which likely contributed to estimation instability and non-convergence.

3. Results

3.1. Preliminary descriptive analyses

Among the 280 respondents, 78.6 % were male and 21.4 % female. Participants' ages ranged from 20 to 76 years, with a mean of 46.9 years (SD = 11.1). The majority of participants (78.2 %) were receiving methadone syrup, while 21.8 % were receiving sublingual buprenorphine tablets as their OST. Additional sociodemographic and clinical characteristics of the sample, along with endorsement rates for each item assessing patients' perceptions and satisfaction with current OST (used as LCA indicators), based on dichotomized Likert-scale responses, are presented in Table 1. Full distributions of responses on the original Likert scale are provided in the Supplementary Material (Figs. S1–S2).

As shown in Fig. 1, percentages indicating interest in alternative OST formulations were highest for methadone tablets, followed by the monthly buprenorphine depot and the buprenorphine implant, and lowest for the weekly depot. Among those on methadone syrup, interest was mainly directed toward methadone tablets, whereas participants on sublingual buprenorphine preferred the monthly depot or implant, with low interest in methadone tablets. Similar results were obtained when patients were asked to indicate their preferred OST formulation in a forced-choice format (see Supplementary Material, Fig. S3).

Among patients currently receiving methadone syrup who expressed interest in switching to tablets (N = 175), perceived benefits included greater autonomy in self-administration (56 %), improved dosing precision (51 %), and reduced burden on daily routines (50 %). One-third (33 %) felt that tablets would lessen the sense of being “hostage” to treatment. However, it is worth noting that a substantial proportion of patients selected the “neither agree nor disagree” option for several statements about the perceived greater potential of methadone tablets, compared with syrup, to: relieve withdrawal symptoms (60 %), be effective (56 %), reduce cravings and relapse risk (51 %), help achieve personally important goals (49 %), increase one's sense of responsibility for treatment (48 %), and make tapering off treatment easier (43 %). Such responses indicate a degree of uncertainty about what to expect from the tablet formulation. Among buprenorphine patients willing to switch to the depot formulation (N = 41), key advantages included reduced treatment burden (59 %), lessened feelings of captivity (61 %), improved dosing precision (54 %), and better alignment with individual needs (49 %). Most did not report concerns about reduced clinical contact. However, 42 % of patients selected the “neither agree nor

Table 1
Sociodemographic characteristics, OST type and dosage, duration of OST, compliance, take-home doses, and recent substance use behaviors.

Characteristics	N = 280
Age (Years) *mean (SD) [range]*	46.9 (11.1) [20–76]
Sex *N (%)*	
Females	60 (21.4)
Males	220 (78.6)
Level of educational attainment *N (%)*	
Primary school	4 (1.4)
Lower secondary school	151 (53.9)
Upper secondary school	108 (38.6)
Bachelor's degree	6 (2.1)
Master's degree	9 (3.2)
Doctorate / Medical specialization school	2 (0.7)
Employed *Yes N (%)*	196 (70.0)
In a training *Yes N (%)*	12 (4.3)
Marital status *N (%)*	
Single	193 (68.9)
Married	49 (17.5)
Separated	15 (5.4)
Divorced	17 (6.1)
Widowed	6 (2.1)
Living status *N (%)*	
Living alone	110 (39.3)
Living with the family of origin	66 (23.6)
Living with partner and/or sons/daughters	95 (33.9)
Living with housemates	9 (3.2)
Current OST *N (%)*	
Methadone syrup	219 (78.2)
Sublingual buprenorphine tablets	61 (21.8)
Dosage in mg of methadone syrup *mean (SD) [range]*	59.3 (39.2) [3.0–200.0]
Dosage in mg of sublingual buprenorphine tablets *mean (SD) [range]*	9.3 (7.2) [1.0–32.0]
Duration of OST (Years) *mean (SD) [range]*	12.7 (9.5) [0.08–40]
Toxicology screening adherence (≤1 missed/month in the past 3 months) *Yes N (%)*	199 (71.1)
OST adherence (≤1 missed dose/month in the past 3 months) *Yes N (%)*	260 (92.9)
Take-home doses (in days) *mean (SD)[range]*	11.2 (8.7) [0.0–30.0]
Injected methadone in the previous 3 months *Yes N (%)*	8 (2.9)
Used buprenorphine intranasally or intravenously in the previous 3 months *Yes N (%)*	10 (3.6)
Diverted methadone or buprenorphine to friends or acquaintances in the previous 3 months *Yes N (%)*	27 (9.6)
Used heroin in the previous 3 months *Yes N (%)*	93 (33.2)
Used cocaine in the previous 3 months *Yes N (%)*	118 (42.1)
Recovery capital *mean (SD)[range]*	43.6 (9.7) [19.0–60.0]
Patients' perceptions and satisfaction with OST (LCA indicators) *N (%)*	
I believe that the type and dosage of the OST I am currently receiving are appropriate for me. [a]	222 (79.3)
The OST I am taking helps relieve withdrawal symptoms. [a]	238 (85.0)
The OST I am taking helps reduce craving and the risk of relapse. [a]	183 (65.4)
I feel that the OST I am taking helps me achieve important personal goals. [a]	169 (60.4)
The tapering modalities that have been proposed to me are acceptable. [a]	152 (54.3)
I consider the OST I am currently taking to be effective. [a]	228 (81.4)
The OST makes me feel responsible for my treatment journey. [a]	196 (70.0)
When I take the therapy, I immediately feel better and would not want to be without it. [a]	161 (57.5)
The way I take the OST limits my ability to engage in activities that could improve my wellbeing (e.g., traveling, maintaining daily work commitments, being more present for my children…). [a]	124 (44.3)
Coming to the clinic to take the OST takes time away from meeting and spending time with other people. [a]	90 (32.1)

(*continued on next page*)

Table 1 (*continued*)

Characteristics	N = 280
I like coming to the clinic to take my therapy because it allows me to maintain regular contact with the professionals who are following me. [a]	167 (59.6)
I tend to hide the fact that I am receiving OST because I fear what others might think of me. [a]	161 (57.5)
Receiving this therapy makes me feel like a "dirty" person. [a]	70 (25.0)
Having to take this therapy prevents me from feeling like others. [a]	98 (35.0)
Overall, how satisfied are you with the OST you are currently receiving? [b]	223 (79.6)

Note.
[a] *N* (%) refer to dichotomized items, with endorsement defined as selecting "agree" or "strongly agree.".
[b] *N* (%) refer to dichotomized items, with endorsement defined as selecting "somewhat satisfied" or "satisfied." OST = opioid substitution therapy.

disagree" option regarding whether depot buprenorphine would be more effective than their current formulation (see Supplementary Fig. S4-S5).

3.2. LCA results

3.2.1. LCA model specification

Latent class models with one to six classes were estimated and compared using multiple fit indices (see Supplementary Material, Table S1). The three-class model demonstrated a clear improvement in fit over the two-class model, with lower AIC, BIC, and SABIC values, and higher entropy, indicating better classification precision. Both the VLMR-LRT and BLRT were statistically significant in favor of the three-class solution. Although incremental improvements in fit were observed in models with four or more classes, the VLMR-LRT became non-significant, and additional classes tended to be small (e.g., <10 % of the sample), raising concerns about overfitting and interpretability. Based on statistical fit, classification quality, and parsimony, the three-class model was selected as the most appropriate solution.

3.2.2. Interpretation of the latent classes

As shown in Fig. 2, Class 1 (28 %), labeled "*Satisfied yet burdened*", comprised individuals who generally endorsed positive perceptions of their OST: high proportions considered the treatment appropriate (0.82), effective (0.94), and beneficial for managing withdrawal (0.92), craving and relapse risk (0.87), as well as for supporting the achievement of personal goals (0.64). Overall satisfaction was also high (0.89). However, this group simultaneously reported substantial internalized stigma – frequently concealing treatment (0.93), feeling ashamed or "dirty" (0.60), and perceiving themselves as different from others (0.79) – alongside moderate functional burden (e.g., interference with daily activities: 0.67).

Class 2 (44 %), labeled "*Satisfied and engaged*", exhibited uniformly favorable treatment experiences. Most participants endorsed the appropriateness (0.96) and effectiveness (0.98) of OST, its efficacy in reducing withdrawal (0.94) and craving (0.82), and felt responsible for their recovery (0.90). Satisfaction with treatment was very high (0.96), and many valued routine contact with providers (0.74). Perceived stigma and burden were minimal (e.g., feeling "dirty": 0.01; hiding treatment: 0.37; treatment limiting activities: 0.24).

Class 3 (27 %), labeled "*Not experiencing benefit*", was characterized by low overall satisfaction (0.43), limited perceived effectiveness (0.40), and minimal endorsement of OST's impact on craving (0.16), or support for personal goals (0.25). While a moderate proportion reported relief from withdrawal (0.64), stigma and burden remained prominent (e.g., concealing treatment: 0.54; interference with daily activities: 0.54), suggesting a subgroup that perceives limited therapeutic benefit and continues to experience significant psychosocial and practical challenges related to treatment.

3.2.3. Latent class differences in adherence, substance use, OST misuse, diversion, recovery capital and interest toward novel formulations

The first manual BCH model examined latent class differences in compliance, substance use, OST misuse, diversion, recovery capital and interest toward novel formulations, identifying significant differences across multiple distal outcomes (see Table 2). Participants in the *Satisfied and engaged* class reported the highest levels of recovery capital, followed by the *Satisfied yet burdened* class and the *Not experiencing benefit* class. All pairwise differences were statistically significant.

Regarding toxicology monitoring, the *Not experiencing benefit* class showed a significantly lower probability of regular testing in the past three months (58 %) compared to both the *Satisfied and engaged* class (78 %) and the *Satisfied yet burdened* class (73 %). No significant class differences were observed in regular OST intake or OST misuse.

The *Not experiencing benefit* class exhibited elevated risk for several negative outcomes. Compared to the *Satisfied and engaged* class, participants in this group had 4.6 times the odds of diverting OST, 6.5 times the odds of recent heroin use, and 3.0 times the odds of cocaine use. Similar patterns were observed in comparison with the *Satisfied yet burdened* class: odds of OST diversion were 3.1 times higher, heroin use 6.5 times higher, and cocaine use 2.4 times higher. However, OST diversion was reported by only 27 participants (9.6 %), with cases markedly concentrated in the *Not experiencing benefit* class (20 % vs. 5–7 % in other classes). These results should be interpreted with caution due to potential sparse data bias and reduced reliability of the OR estimates. Similarly, the lack of statistically meaningful differences in regular OST intake and misuse may reflect distributional limitations. Regular intake was reported by 93 % of participants, with minimal variation across classes (89–97 %), while OST misuse was reported by only 16 individuals (5.7 %). These low base rates constrain inferential power and may compromise estimate stability.

As for treatment preferences, oral methadone tablets were the most frequently endorsed formulation across all classes. Interest was highest among the *Not experiencing benefit* class (56 %), followed by the *Satisfied yet burdened* (54 %) and *Satisfied and engaged* (48 %) classes, although no significant pairwise differences emerged. For the monthly buprenorphine depot, the *Satisfied yet burdened* class expressed significantly greater interest compared to the *Satisfied and engaged* class (38 % vs. 23 %). No significant differences emerged for the weekly buprenorphine depot or the implant formulation, both of which were endorsed at modest rates (19–24 % and 20–31 %, respectively) across all classes.

3.2.4. Associations between patients' characteristics, latent class membership and clinical outcomes

The second auxiliary BCH model first examined the association between individual characteristics and class membership. Results indicated that shorter treatment duration was associated with greater odds of being in the *Not experiencing benefit* class compared to either of the other two classes. Additionally, individuals receiving methadone syrup (as opposed to sublingual buprenorphine tablets) were more likely to belong to the *Not experiencing benefit* class compared to the *Satisfied and engaged* class (see Table 3).

Class-specific associations between covariates and distal outcomes revealed distinct patterns (see Table 4). In the *Satisfied yet burdened* class, higher recovery capital was associated with older age and being in work or training, while regular toxicology testing was more likely among older and more educated individuals. In the *Not experiencing benefit* class, recovery capital was negatively associated with living alone, and regular testing was predicted only by longer treatment duration. Heroin use was less likely among those receiving sublingual buprenorphine in the *Satisfied yet burdened* class, and more likely among individuals living alone in both the *Satisfied and engaged* and *Not experiencing benefit* classes, though estimates in the former may be unstable due to sparse data. Longer treatment duration appeared protective

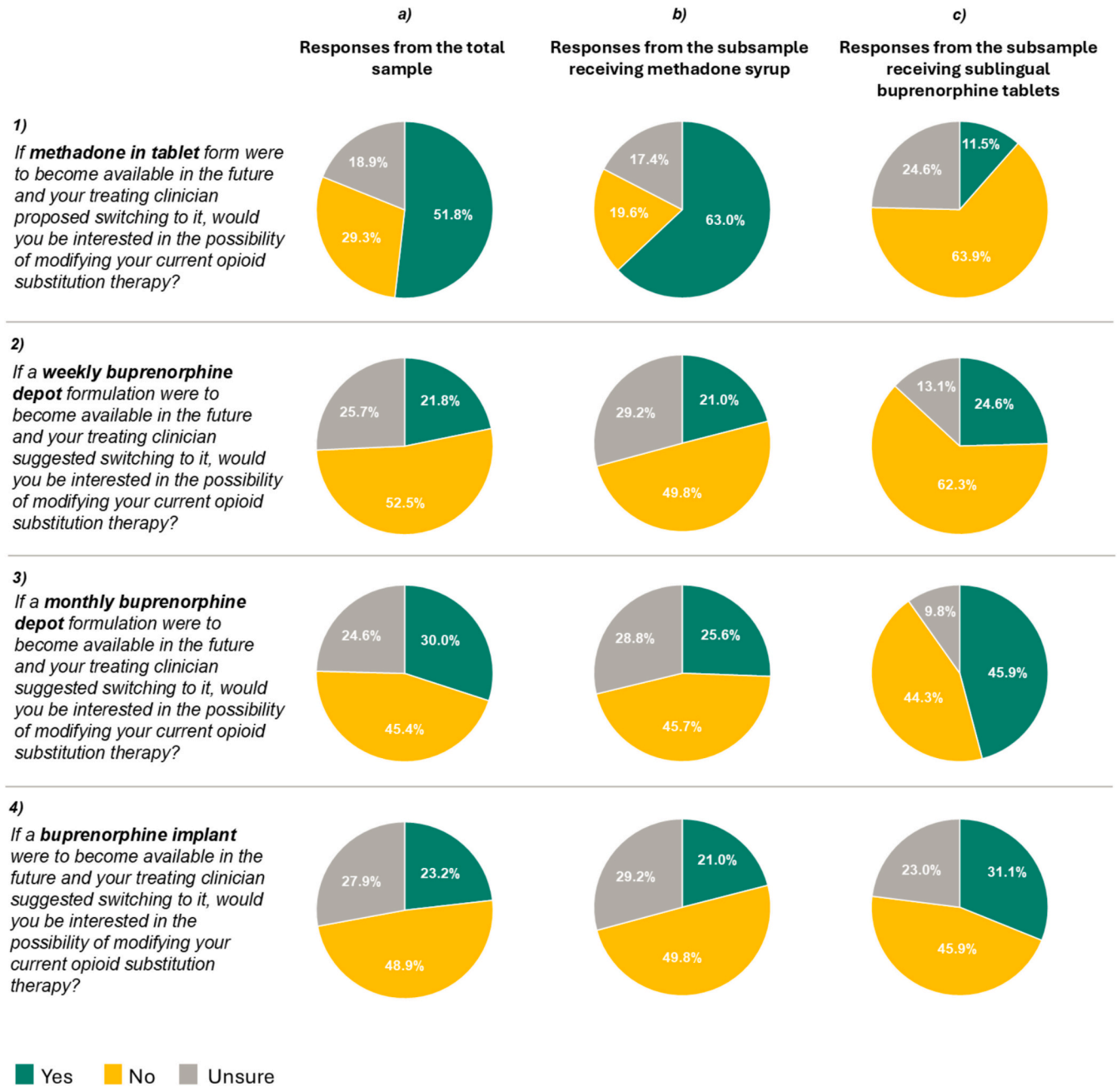

Fig. 1. Participants' interest in switching to alternative formulations of opioid substitution therapy (OST), if proposed by their treating clinician and available in the future. Panel (a) shows responses from the total sample ($N = 280$), panel (b) from participants currently receiving methadone syrup ($n = 219$), and panel (c) from those receiving sublingual buprenorphine tablets ($n = 61$). For each group, interest was assessed with regard to (1) methadone in tablet form, (2) weekly buprenorphine depot, (3) monthly buprenorphine depot, and (4) buprenorphine implant. Response options were: Yes (green), No (yellow), and Unsure (gray). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

against heroin use in the *Not experiencing benefit* class. Cocaine use in the *Satisfied yet burdened* class was associated with living alone and higher education, while sublingual buprenorphine was linked to lower odds of use in the *Not experiencing benefit* class.

Interest in methadone tablets was consistently higher among those on methadone syrup across all classes. Interest in monthly buprenorphine depot was higher among women and individuals on sublingual buprenorphine in the *Satisfied yet burdened* class, but lower among those living alone in the *Not experiencing benefit* class. Interest in the buprenorphine implant was positively associated with sublingual buprenorphine treatment in the *Satisfied yet burdened* class. In the *Satisfied and engaged* class, interest was higher among participants with upper secondary education and lower among women. Living alone remained a negative predictor of interest in the *Not experiencing benefit* class.

4. Discussion

This study adopted a person-centered approach to understanding patient experiences with OST, identifying three distinct subgroups based on treatment perceptions and satisfaction: *Satisfied yet burdened*, *Satisfied and engaged*, and *Not experiencing benefit*. These subgroups were differentially associated with sociodemographic and treatment-related characteristics, substance use behaviors, adherence indicators, and interest in novel OST formulations. Taken together, these findings have

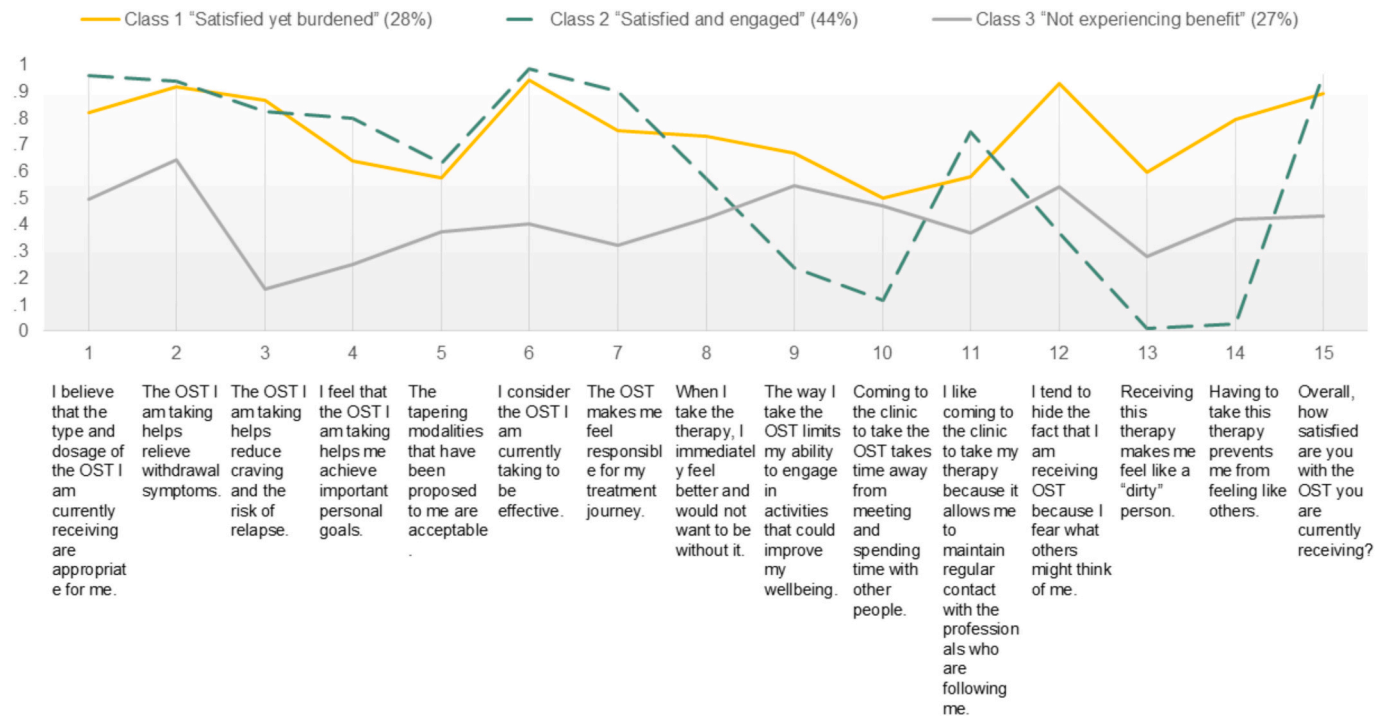

Fig. 2. Item-response probabilities by latent class for each OST-related indicator. Line graph displaying the probability of endorsement (i.e., agreeing or being satisfied) for each of the 15 dichotomized items regarding perceptions and satisfaction with opioid substitution therapy (OST), across the three latent classes identified.

Table 2
Distal outcomes across latent classes.

				Pairwise comparisons		
	Class 1 "Satisfied yet burdened"	Class 2 "Satisfied and engaged"	Class 3 "Not experiencing benefit"	Class 1 "Satisfied yet burdened" [a]	Class 3 "Not experiencing benefit" [b]	Class 3 "Not experiencing benefit" [a]
	Mean / % SE	*Mean / % SE*	*Mean / % SE*	*ΔM / OR [95 %CI]*	*ΔM / OR [95 %CI]*	*ΔM / OR [95 %CI]*
Recovery capital	43.84 (1.09)	47.42 (0.82)	37.05 (1.24)	**−3.58 [−5.90, −1.25]**	**−6.79 [−9.64, −3.94]**	**−10.36 [−12.86, −7.38]**
Regular toxicology testing in the past 3 months	73 % (0.06)	78 % (0.04)	58 % (0.06)	0.76 [0.40, 1.43]	**0.51 [0.26, 0.98]**	**0.38 [0.22, 0.69]**
Regular OST intake in the past 3 months	97 % (0.03)	93 % (0.02)	89 % (0.04)	2.16 [0.53, 8.84]	0.29 [0.07, 1.22]	0.62 [0.25, 1.54]]
OST misuse in the past 3 months	7 % (0.03)	5 % (0.02)	5 % (0.3)	1.26 [0.41, 3.87]	0.76 [0.20, 2.83]	0.96 [0.29, 3.17]
Diversion of OST in the past 3 months	7 % (0.03)	5 % (0.02)	20 % (0.05)	1.50 [0.47, 4.80]	**3.06 [1.11, 8.49]**	**4.59 [1.80, 11.67]**
Heroin use in the past 3 months	22 % (0.05)	22 % (0.04)	64 % (0.06)	0.99 [0.50, 1.95]	**6.54 [3.18, 13.42]**	**6.45 [3.53, 11.78]**
Cocaine use in the past 3 months	39 % (0.06)	34 % (0.05)	60 % (0.06)	1.24 [0.71, 2.19]	**2.38 [1.26, 4.49]**	**2.96 [1.70, 5.15]**
Interest in oral methadone tablets	54 % (0.06)	48 % (0.05)	56 % (0.06)	1.28 [0.74, 2.20]	1.06 [0.57, 1.98]	1.36 [0.80, 2.32]
Interest in weekly buprenorphine depot	24 % (0.05)	22 % (0.04)	19 % (0.05)	1.13 [0.60, 2.15]	0.76 [0.36, 1.62]	0.86 [0.44, 1.68]
Interest in monthly buprenorphine depot	38 % (0.06)	23 % (0.04)	35 % (0.06)	**2.07 [1.14, 3.77]**	0.88 [0.46, 1.67]	1.82 [1.00, 3.29]
Interest in buprenorphine implant	31 % (0.06)	20 % (0.04)	21 % (0.05)	1.84 [0.99, 3.44]	0.57 [0.28, 1.17]	1.05 [0.54, 2.05]

Note.
SE = standard error; ΔM = mean difference; OR = odds ratio; CI = 95 % confidence interval; OST = opioid substitution therapy. Values in bold indicate statistically significant differences.
[a] Reference class: Class 2 "Satisfied and engaged".
[b] Reference class: Class 1 "Satisfied yet burdened".

Table 3
Associations between covariates and latent classes.

Class	Class 1 "Satisfied yet burdened" [a]	Class 3 "Not experiencing benefit" [b]	Class 3 "Not experiencing benefit" [a]
	OR [95 %CI]	OR [95 %CI]	OR [95 %CI]
Female	1.08 [0.56, 2.10]	1.11 [0.51, 2.43]	1.20 [0.59, 2.47]
Age	0.99 [0.96, 1.01]	1.00 [0.97, 1.03]	0.99 [0.96, 1.02]
≥ Upper secondary education	1.03 [0.58, 1.82]	0.61 [0.31, 1.18]	0.63 [0.35, 1.12]
In work or training	1.21 [0.63, 2.33]	0.81 [0.39, 1.68]	0.98 [0.53, 1.81]
Living alone	1.08 [0.60, 2.33]	1.22 [0.63, 2.36]	1.32 [0.75, 2.33]
On sublingual buprenorphine tablets	0.51 [0.25, 1.04]	0.91 [0.39, 2.14]	**0.47 [0.23, 0.95]**
Treatment duration	1.07 [0.44, 2.58]	**0.29 [0.11, 0.77]**	**0.31 [0.14, 0.70]**

Note.
OR = odds ratio; CI = 95 % confidence interval. Values in bold indicate statistically significant differences.
[a] Reference class: Class 2 "Satisfied and engaged".
[b] Reference class: Class 1 "Satisfied yet burdened".

important implications for the development of more tailored and responsive care strategies that align with the needs, resources, and preferences of diverse patient groups.

4.1. Distinct subgroups of OST patients: Characteristics and implications

The *Not experiencing benefit* class represents a clinically vulnerable subgroup characterized by low satisfaction with OST and limited perceived therapeutic benefit, despite reporting only moderate levels of internalized stigma. Shorter treatment duration, lower likelihood of undergoing regular toxicology testing, and higher odds of recent heroin use likely reflect earlier phases of treatment, during which stabilization and therapeutic engagement have not yet been fully established (O'Connor et al., 2020; Tran et al., 2012). The predominance of methadone syrup in this class may further indicate a more intensive phase of clinical supervision, as liquid formulations allow for flexible dose titration and are commonly used in contexts requiring careful monitoring (Dematteis et al., 2017). Taken together, these findings underscore the need for targeted interventions in this subgroup, aimed at strengthening therapeutic engagement and support early stabilization. Such strategies may improve treatment receptivity and create the conditions necessary for considering alternative OST formulations.

The *Satisfied yet burdened* class included individuals who reported high satisfaction with their current OST and perceived clear benefits in terms of craving relief and relapse prevention. A defining feature of this profile was the coexistence of internalized stigma (e.g., feelings of shame or dirtiness, concealment of treatment, feeling unlike others) and functional constraints (e.g., limitations on travel, employment, or family engagement). Clinically, this pattern may reflect individuals who have achieved clinical stabilization but continue to struggle with the long-term psychosocial demands of the treatment. Within this class, higher recovery capital was significantly associated with older age and being engaged in work or training. Employment is a well-established protective factor in the recovery process, linked to increased structure, purpose, and social integration (Lin et al., 2024). In contrast, the association with older age diverges from prior research that highlight age-related barriers to recovery (Cloud & Granfield, 2008; Sánchez et al., 2020). An interpretative hypothesis for this result is that older participants may reflect greater life stability and lower engagement in high-risk environments. Having attained upper secondary education was associated with increased odds of cocaine use. This result may reflect broader socioeconomic trends, given that cocaine use tends to be more prevalent among individuals from higher socioeconomic strata, typically characterized by greater financial resources and higher levels of education (da Silva Junior et al., 2024). Individuals on sublingual buprenorphine within this class showed lower odds of heroin use, in line with prior research indicating that this formulation may be associated with improved treatment retention and lower likelihood of illicit opioid consumption (O'Connor et al., 2020). Taken together, these findings suggest that individuals in this class may represent a relatively stable segment of the OST population who nonetheless remain at risk of stagnation or disengagement unless treatment approaches evolve to better align with patients' aspirations for autonomy, social integration, and broader recovery goals.

The *Satisfied and engaged* class included individuals reporting high satisfaction across all treatment domains, including craving relief, relapse prevention, and support for meaningful personal goals. This profile likely reflects a well-stabilized segment of the OST population in which both pharmacological and psychosocial needs are being met. Compared to the *Not experiencing benefit* class, these individuals had longer treatment duration – a pattern that may reflect a greater treatment stability (Saloner et al., 2018) – and were more likely to receive sublingual buprenorphine. Notably, individuals in this class expressed the strongest appreciation for regular clinic-based contact with care providers, suggesting a positive and supportive therapeutic alliance. While such engagement can be an important protective factor, it may also reflect an ongoing reliance on external structure as a source of stability. Should this be the case, developing care pathways that gradually foster self-management and autonomy, while maintaining a sense of support, may be key to promoting long-term recovery (Bjornestad et al., 2019; SAMHSA, 2012).

It is noteworthy that living alone emerged as a consistent risk factor across all three classes. This condition remained a potent vulnerability even among patients reporting high engagement and satisfaction. Specifically, living alone was associated with higher odds of heroin use and lower recovery capital in the *Not experiencing benefit* class, higher odds of cocaine use in the *Satisfied yet burdened* class, and higher odds of heroin use in the *Satisfied and engaged* class. These findings underscore the importance of social connectedness in sustaining long-term recovery, consistent with the Social Model Identity of Recovery (SIMOR, Best et al., 2016).

4.2. Interest in novel OST options across identified subgroups of patients and clinical implications

Across the total sample, interest in novel OST formulations varied considerably, reflecting both treatment history and patients' psychosocial positioning within the care process. Individuals currently treated with methadone syrup expressed greater interest in these alternatives across all classes. In contrast, extended-release buprenorphine formulations elicited more selective patterns of interest, which varied both across latent classes and according to individual characteristics. Interest in the monthly depot was highest among individuals in the *Satisfied yet burdened* class and lowest among those in the *Satisfied and engaged* class. Within the *Satisfied yet burdened* class, female participants were more likely to express interest in the monthly depot, particularly among those receiving sublingual buprenorphine. For women in particular, the depot may be more acceptable than the implant due to its lower perceived

Table 4
Associations between covariates and distal outcomes within each latent class.

Outcome	Covariate	Satisfied yet burdened	Satisfied and engaged	Not experiencing benefit
		b / OR [95 %CI]	b / OR [95 %CI]	b / OR [95 % CI]
Recovery capital	Female	−1.55 [−5.05, 1.95]	−0.13 [−5.20, 4.93]	−3.40 [−8.28, 1.49]
	Age	**0.19 [0.06, 0.33]**	−0.05 [−0.27, 0.17]	−0.02 [−0.23, 0.19]
	≥ Upper secondary education	0.21 [−2.48, 2.90]	−2.16 [−5.73, 1.41]	−2.03 [−5.97, 1.90]
	In work or training	**3.63 [0.56, 6.71]**	2.35 [−1.49, 6.20]	1.67 [−3.55, 6.89]
	Living alone	−0.45 [−3.21, 2.31]	0.74 [−2.92, 4.40]	**−6.96 [−11.35, −2.58]**
	On sublingual buprenorphine tablets	0.87 [−2.18, 3.92]	−1.05 [−5.30, 3.20]	3.32 [−2.12, 8.76]
	Treatment duration	1.51 [−3.27, 6.28]	1.01 [−4.99, 7.01]	1.51 [−4.04, 7.06]
Regular toxicology testing in the past 3 months	Female	0.44 [0.17, 1.16]	0.49 [0.13, 1.81]	0.46 [0.12, 1.74]
	Age	**0.94 [0.90, 0.99]**	0.98 [0.92, 1.04]	1.04 [0.99, 1.08]
	≥ Upper secondary education	**2.84 [1.14, 7.04]**	1.32 [0.51, 3.44]	1.36 [0.47, 3.98]
	In work or training	0.81 [0.33, 1.98]	1.29 [0.39, 4.27]	2.62 [0.81, 8.40]
	Living alone	1.65 [0.67, 4.05]	0.87 [0.33, 2.28]	0.52 [0.17, 1.57]
	On sublingual buprenorphine tablets	1.92 [0.77, 4.79]	1.33 [0.34, 5.15]	0.81 [0.24, 2.79]
	Treatment duration	1.23 [0.30, 4.99]	1.15 [0.23, 5.86]	**4.10 [1.15, 14.69]**
Heroin use in the past 3 months	Female	0.34 [0.10, 1.17]	0.01 [0.00, 1.06]	1.54 [0.41, 5.83]
	Age	0.97 [0.93, 1.01]	0.95 [0.85, 1.06]	0.98 [0.93, 1.02]
	≥ Upper secondary education	1.79 [0.67, 4.77]	2.63 [0.35, 19.89]	0.91 [0.28, 2.93]
	In work or training	0.53 [0.18, 1.60]	5.11 [0.67, 39.27]	3.28 [0.84, 12.74]
	Living alone	1.36 [0.54, 3.40]	**53.13 [3.10, 911.34]**	**3.62 [1.00, 13.12]**
	On sublingual buprenorphine tablets	**0.04 [0.00, 0.56]**	0.46 [0.05, 4.77]	0.57 [0.14, 2.38]
	Treatment duration	0.40 [0.08, 1.88]	0.22 [0.02, 2.39]	**0.12 [0.03, 0.48]**
Cocaine use in the past 3 months	Female	1.27 [0.55, 2.97]	0.51 [0.15, 1.70]	0.79 [0.24, 2.56]
	Age	0.97 [0.93, 1.01]	0.96 [0.91, 1.02]	1.00 [0.95, 1.06]
	≥ Upper secondary education	**2.17 [1.02, 4.61]**	0.52 [0.20, 1.40]	0.40 [0.13, 1.23]
	In work or training	0.69 [0.28, 1.72]	3.04 [0.88, 1.50]	0.81 [0.21, 3.04]
	Living alone	**2.70 [1.27, 5.72]**	2.37 [0.87, 6.47]	2.29 [0.75, 6.96]
	On sublingual buprenorphine tablets	0.93 [0.42, 2.07]	0.76 [0.20, 2.89]	**0.10 [0.02, 0.50]**
	Treatment duration	0.47 [0.12, 1.81]	0.91 [0.19, 4.32]	0.29 [0.07, 1.16]
Interest in methadone tablets	Female	2.00 [0.69, 5.84]	1.05 [0.34, 3.27]	0.56 [0.18, 1.76]
	Age	1.02 [0.98, 1.06]	1.00 [0.94, 1.07]	1.00 [0.96, 1.05]
	≥ Upper secondary education	1.12 [0.50, 2.50]	0.93 [0.33, 2.59]	0.65 [0.25, 1.72]
	In work or training	1.63 [0.61, 4.33]	0.82 [0.24, 2.79]	1.70 [0.53, 5.45]
	Living alone	1.15 [0.51, 2.59]	0.65 [0.24, 1.81]	1.23 [0.46, 3.30]
	On sublingual buprenorphine tablets	**0.06 [0.02, 0.20]**	**0.04 [0.00, 0.43]**	**0.14 [0.04, 0.59]**
	Treatment duration	0.60 [0.16, 2.18]	0.91 [0.16, 5.29]	3.51 [0.93, 13.18]
Interest in weekly buprenorphine depot	Female	1.81 [0.76, 4.36]	0.36 [0.08, 1.70]	0.95 [0.25, 3.56]
	Age	0.97 [0.93, 1.01]	0.92 [0.85, 1.00]	1.02 [0.96, 1.09]
	≥ Upper secondary education	1.43 [0.63, 3.27]	2.67 [0.96, 7.45]	0.82 [0.24, 2.76]
	In work or training	0.87 [0.36, 2.12]	0.30 [0.08, 1.13]	2.61 [0.61, 11.21]
	Living alone	0.63 [0.27, 1.48]	1.12 [0.35, 3.63]	1.12 [0.31, 3.97]
	On sublingual buprenorphine tablets	2.08 [0.86, 5.01]	0.70 [0.13, 3.68]	0.44 [0.08, 2.40]
	Treatment duration	1.19 [0.29, 4.83]	4.41 [0.34, 7.94]	0.24 [0.05, 1.18]
Interest in monthly buprenorphine depot	Female	**2.73 [1.05, 7.06]**	0.34 [0.09, 1.23]	0.61 [0.17, 2.20]
	Age	0.98 [0.94, 1.02]	0.95 [0.89, 1.01]	1.01 [0.96, 1.06]
	≥ Upper secondary education	1.57 [0.65, 3.81]	2.04 [0.80, 5.20]	2.15 [0.71, 6.53]
	In work or training	1.66 [0.54, 5.08]	0.55 [0.19, 1.63]	1.11 [0.34, 3.61]
	Living alone	0.50 [0.19, 1.32]	0.98 [0.37, 2.62]	**0.25 [0.07, 0.88]**

(*continued on next page*)

Table 4 (*continued*)

Outcome	Covariate	Satisfied yet burdened	Satisfied and engaged	Not experiencing benefit
	On sublingual buprenorphine tablets	**6.79 [2.70, 17.10]**	3.15 [0.82, 2.01]	0.67 [0.16, 2.94]
	Treatment duration	0.60 [0.14, 2.50]	3.68 [0.50, 7.24]	1.57 [0.41, 5.95]
Interest in buprenorphine implant	Female	1.30 [0.49, 3.43]	**0.18 [0.04, 0.84]**	1.09 [0.30, 3.90]
	Age	1.02 [0.97, 1.07]	0.93 [0.86, 1.00]	1.01 [0.95, 1.07]
	≥ Upper secondary education	1.65 [0.66, 4.12]	**2.85 [1.09, 7.48]**	1.80 [0.43, 7.60]
	In work or training	0.95 [0.34, 2.65]	0.86 [0.25, 3.01]	0.27 [0.05, 1.46]
	Living alone	0.45 [0.16, 1.23]	1.09 [0.37, 3.21]	**0.13 [0.02, 0.78]**
	On sublingual buprenorphine tablets	**2.69 [1.14, 6.33]**	0.60 [0.12, 2.92]	2.08 [0.44, 9.83]
	Treatment duration	0.29 [0.07, 1.31]	1.46 [0.92, 9.10]	1.29 [0.24, 7.00]

Note. OR = odds ratio; CI = 95 % confidence interval. Values in bold indicate statistically significant differences.

invasiveness. Indeed, prior research has shown that women are more likely than men to prioritize concerns related to bodily control, discomfort, and procedural burden when considering invasive medical interventions (Ziefle & Schaar, 2011).

While overall interest in the buprenorphine implant was slightly higher in the *Satisfied yet burdened* class than in the *Satisfied yet burdened class*, the correlates differed between groups. In the *Satisfied and engaged* group, interest was linked to being male and having upper secondary education. Greater health literacy may favor openness to long-acting, low-maintenance treatments requiring sustained commitment (Neale et al., 2019). Conversely, in the *Satisfied yet burdened* class, interest was mainly associated with ongoing sublingual buprenorphine use, possibly reflecting a wish to ease the daily demands of treatment. Notably, in the *Not experiencing benefit* class, interest in the monthly depot and implant was significantly lower among individuals living alone. Our results are consistent with the literature highlighting that readiness for long-acting treatments requires advance planning, trust in continuity of care, and a supportive home environment to manage reduced clinical contact (Neale et al., 2018, 2023). Rather than reflecting a lack of interest per se, this pattern may indicate underlying psychosocial barriers that limit the acceptability of extended-release options among more vulnerable segments of the OST population.

Taken together, these findings may help inform the clinical use of novel OST formulations. Methadone tablets may benefit those on methadone syrup, while long-acting buprenorphine options appear more suitable for clinically and psychosocially stable individuals. The monthly depot may be especially appropriate for patients experiencing stigma or daily treatment burden – particularly women on sublingual buprenorphine – while the implant may align with profiles marked by high engagement, autonomy, and health literacy. For patients with greater instability, reduced social support, or ongoing substance use, priority should be given to strengthening engagement and support before transitioning to less containing treatments.

4.3. Limitations

This study has several limitations. The cross-sectional design precludes causal inference regarding the observed associations between latent class membership, covariates, and outcomes. Future longitudinal research is needed to examine how patient perceptions and OST preferences evolve throughout the course of treatment and in response to clinical progression. Importantly, individuals may move between profiles over time. Future studies could investigate the extent to which individuals shift between profiles over time and identify possible patterns of transition. Although conducted across six addiction services, all were located in a single Italian region, which may limit generalizability to other contexts with differing service structures or patient populations. The LCA relied on items developed specifically for this study rather than on validated scales. While this limits comparability with other research, item development was informed by a targeted literature review and clinical consultation to ensure relevance to the Italian public treatment system. In addition, the overrepresentation of methadone syrup recipients may have shaped the class structure, potentially underrepresenting experiences specific to buprenorphine treatment, despite its inclusion as a covariate in auxiliary models. Skewed distributions in several outcome indicators – particularly those related to misuse and diversion – restricted their inclusion in the multivariate analysis. The use of dichotomized items, though necessary for estimation, may have limited the sensitivity of the LCA to subtle variations in patient perceptions. The questionnaire was not tested with patients prior to data collection, which may limit its psychometric robustness. However, its content was conceptually grounded in previous qualitative research on patients' experiences with different OST formulations, from which key themes and items were derived, and it was further refined in consultation with addiction medicine professionals to ensure clinical relevance and clarity. Finally, preferences for novel formulations were based on self-reported interest following brief standardized descriptions. As such, responses reflect perceived acceptability rather than actual experience and may have been influenced by limited familiarity with these options.

5. Conclusions

By integrating patient-reported perceptions, satisfaction, and treatment-related burdens, this study offers a novel, person-centered typology of individuals receiving OST within the Italian public health system. The identification of clinically meaningful subgroups – each with distinct needs, risks, and levels of receptivity to alternative formulations – provides a critical foundation for more responsive and individualized care strategies. These findings underscore the value of going beyond clinical stabilization alone, promoting treatment models that acknowledge the broader dimensions of patient engagement and satisfaction within the care experience.

CRediT authorship contribution statement

Federica Ambrosini: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **Elisa Zamagni:** Writing – review & editing, Resources, Project administration, Methodology, Investigation, Conceptualization. **Francesco Iannello:** Resources, Investigation. **Michele Bertini:** Resources, Investigation. **Simona Brusco:** Resources, Investigation. **Ferdinando Cerrato:** Resources, Investigation. **Nadia Marzocchi:** Resources, Investigation. **Teo Vignoli:** Writing – review & editing, Resources, Project administration, Methodology, Investigation, Conceptualization. **Roberta Biolcati:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Funding acquisition, Data curation, Conceptualization.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used ChatGPT in order to improve the readability and language of the manuscript. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

Sources of funding

This study was funded through a consultancy agreement between the Department of Education Sciences "G. M. Bertin" University of Bologna, and Local Health Agency of Romagna (Contract No. 104/2023; Protocol No. 1183, 29 June 2023), under the responsibility of Prof. Roberta Biolcati.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Roberta Biolcati reports financial support was provided by Azienda USL della Romagna. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors would like to thank the clinical staff of the participating addiction services in Emilia-Romagna for their valuable support with participant recruitment and data collection.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.josat.2025.209866.

References

AIFA. (2019, February 18). Classificazione, ai sensi dell'articolo 12, comma 5, della legge 8 novembre 2012, n. 189, dei medicinali per uso umano «Apealea» e «Buvidal», approvati con procedura centralizzata. (Determina n. 18197/2019). Gazzetta Ufficiale della Repubblica Italiana, Serie Generale No. 53 (March 4, 2019). https://www.gazzettaufficiale.it/eli/id/2019/03/04/19A01359/sg.

AIFA. (2021, July 26). Classificazione di medicinali per uso umano ai sensi dell'art. 12 comma 5 del decreto-legge 13 settembre 2012 n. 158 convertito nella legge 8 novembre 2012 n. 189 (Determina n. 102/2021). Gazzetta Ufficiale della Repubblica Italiana, Serie Generale No. 186 (August 6, 2021). https://www.gazzettaufficiale.it/eli/id/2021/08/06/21A04642/sg.

AIFA. (2022, January 12). Riclassificazione del medicinale per uso umano «Sixmo», ai sensi dell'articolo 8, comma 10, della legge 24 dicembre 1993, n. 537 (Determina n. 36/2022). Gazzetta Ufficiale della Repubblica Italiana, Serie Generale No. 21 (January 27, 2022). https://www.gazzettaufficiale.it/eli/id/2022/01/27/22A00402/sg.

AIFA. (2022, May 12). Autorizzazione all'immissione in commercio del medicinale per uso umano, a base di Metadone cloridrato, «Metadone Cloridrato G.L.». Gazzetta Ufficiale della Repubblica Italiana, Serie Generale No. 110 (May 12, 2022). https://www.gazzettaufficiale.it/eli/id/2022/05/12/22A02834/sg.

AIFA. (2023, August 9). Riclassificazione del medicinale per uso umano «Omtisa», ai sensi dell'art. 8, comma 10, della legge 24 dicembre 1993, n. 537. (Determina n. 516/2023). Gazzetta Ufficiale della Repubblica Italiana, Serie Generale No. 185 (August 9, 2023). https://www.gazzettaufficiale.it/eli/id/2023/08/09/23A04408/sg.

Asparouhov, T., & Muthén, B. O. (2021). *Auxiliary variables in mixture modeling: Using the BCH method in Mplus to estimate a distal outcome model and an arbitrary secondary model (Mplus Web Note No. 21)*. Muthén & Muthén. https://www.statmodel.com/examples/webnote.shtml.

Bakk, Z., & Vermunt, J. K. (2016). Robustness of stepwise latent class modeling with continuous distal outcomes. *Structural Equation Modeling, 23*(1), 20–31. https://doi.org/10.1080/10705511.2014.955104

Besana, F., Pasquariello, S., Costa, V., & Negri, A. (2025). The history of addiction clinics and treatment in Italy: An overview and future directions. *Histories, 5*(1), 15. https://doi.org/10.3390/histories5010015

Best, D., Beckwith, M., Haslam, C., Alexander Haslam, S., Jetten, J., Mawson, E., & Lubman, D. I. (2016). Overcoming alcohol and other drug addiction as a process of social identity transition: The social identity model of recovery (SIMOR). *Addiction Research & Theory, 24*(2), 111–123. https://doi.org/10.3109/16066359.2015.1075980

Bjornestad, J., Svendsen, T. S., Slyngstad, T. E., Erga, A. H., McKay, J. R., Nesvåg, S., … Moltu, C. (2019). "A life more ordinary" processes of 5-year recovery from substance abuse. Experiences of 30 recovered service users. *Frontiers in Psychiatry, 10*, Article 689. https://doi.org/10.3389/fpsyt.2019.00689

Blair, H. A. (2024). Buprenorphine extended-release injection (Brixadi®) in the management of opioid use disorder: A profile of its use in the USA. *Drugs & Therapy Perspectives, 40*(2), 61–71. https://doi.org/10.1007/s40267-024-01055-y

Bolck, A., Croon, M., & Hagenaars, J. (2004). Estimating latent structure models with categorical variables: One-step versus three-step estimators. *Political Analysis, 12*(1), 3–27. https://doi.org/10.1093/pan/mph001

Bormann, N. L., Weber, A. N., Miskle, B., Arndt, S., & Lynch, A. C. (2023). Recovery capital correlates with less methamphetamine use and crime in the community. *Journal of Addiction Medicine, 17*(6), e361–e366. https://doi.org/10.1097/ADM.0000000000001200

Bray, B. C., Watson, D. P., Salisbury-Afshar, E., Taylor, L., & McGuire, A. (2023). Patterns of opioid use behaviors among patients seen in the emergency department: Latent class analysis of baseline data from the POINT pragmatic trial. *Journal of Substance Use and Addiction Treatment, 146*, Article 208979. https://doi.org/10.1016/j.josat.2023.208979

Bunaciu, A., Bliuc, A.-M., Best, D., Hennessy, E. A., Belanger, M. J., & Benwell, C. S. Y. (2024). Measuring recovery capital for people recovering from alcohol and drug addiction: A systematic review. *Addiction Research & Theory, 32*(3), 225–236. https://doi.org/10.1080/16066359.2023.2245323

Chang, K.-C., Lu, T.-H., Lee, K.-Y., Hwang, J.-S., Cheng, C.-M., & Wang, J.-D. (2015). Estimation of life expectancy and the expected years of life lost among heroin users in the era of opioid substitution treatment (OST) in Taiwan. *Drug and Alcohol Dependence, 153*, 152–158. https://doi.org/10.1016/j.drugalcdep.2015.05.033

Chappuy, M., Trojak, B., Nubukpo, P., Bachellier, J., Bendimerad, P., Brousse, G., & Rolland, B. (2020). Prolonged-release buprenorphine formulations: Perspectives for clinical practice. *Therapies, 75*(5), 397–406. https://doi.org/10.1016/j.therap.2020.05.007

Cloud, W., & Granfield, R. (2008). Conceptualizing recovery capital: Expansion of a theoretical construct. *Substance Use & Misuse, 43*(12−13), 1971–1986. https://doi.org/10.1080/10826080802289762

Crapanzano, K. A., Hammarlund, R., Ahmad, B., Hunsinger, N., & Kullar, R. (2019). The association between perceived stigma and substance use disorder treatment outcomes: A review. *Substance Abuse and Rehabilitation, 10*, 1–12. https://doi.org/10.2147/SAR.S183252

Dasgupta, N., Bailey, E. J., Cicero, T., Inciardi, J., Parrino, M., Rosenblum, A., & Dart, R. C. (2010). Post-marketing surveillance of methadone and buprenorphine in the United States. *Pain Medicine, 11*(7), 1078–1091. https://doi.org/10.1111/j.1526-4637.2010.00877.x

Dematteis, M., Auriacombe, M., D'Agnone, O., Somaini, L., Szerman, N., Littlewood, R., … Soyka, M. (2017). Recommendations for buprenorphine and methadone therapy in opioid use disorder: A European consensus. *Expert Opinion on Pharmacotherapy, 18*(18), 1987–1999. https://doi.org/10.1080/14656566.2017.1409722

Gerra, G., Saenz, E., Busse, A., Maremmani, I., Ciccocioppo, R., Zaimovic, A., … Somaini, L. (2011). Supervised daily consumption, contingent take-home incentive and non-contingent take-home in methadone maintenance. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 35*(2), 483–489. https://doi.org/10.1016/j.pnpbp.2010.12.002

IBM Corp.. (2017). *IBM SPSS Statistics for Windows (Version 25.0) [Computer software]*.

Khazaee-Pool, M., Moeeni, M., Ponnet, K., Fallahi, A., Jahangiri, L., & Pashaei, T. (2018). Perceived barriers to methadone maintenance treatment among Iranian opioid users. *International Journal for Equity in Health, 17*(1), 75. https://doi.org/10.1186/s12939-018-0787-z

Lardier, D. T., Davis, A. N., Verdezoto, C. S., Cruz, L., Magliulo, S., Herrera, A., … Reid, R. J. (2024). Latent class groups of concurrent substance use among adolescents in an Urban Community: Correlates with mental health, access to drugs and alcohol, and risk perception. *Substance Use & Addiction Journal, 45*(1), 124–135. https://doi.org/10.1177/29767342231207192

Lin, C., Cousins, S. J., Zhu, Y., Clingan, S. E., Mooney, L. J., Kan, E., … Hser, Y.-I. (2024). A scoping review of social determinants of health's impact on substance use disorders over the life course. *Journal of Substance Use and Addiction Treatment, 166*, Article 209484. https://doi.org/10.1016/j.josat.2024.209484

Lister, J. J., Yoon, M., Nower, L., Ellis, J. D., & Ledgerwood, D. M. (2022). Subtypes of patients with opioid use disorder in methadone maintenance treatment: A pathways model analysis. *International Gambling Studies, 22*(2), 300–316. https://doi.org/10.1080/14459795.2022.2044502

Lofwall, M. R., & Walsh, S. L. (2014). A review of buprenorphine diversion and misuse: The current evidence base and experiences from around the world. *Journal of Addiction Medicine, 8*(5), 315–326. https://doi.org/10.1097/ADM.0000000000000045

Luoma, J. B., Twohig, M. P., Waltz, T., Hayes, S. C., Roget, N., Padilla, M., & Fisher, G. (2007). An investigation of stigma in individuals receiving treatment for substance abuse. *Addictive Behaviors, 32*(7), 1331–1346. https://doi.org/10.1016/j.addbeh.2006.09.008

Muthén, L. K., & Muthén, B. O. (1998–2017). *Mplus (Version 8)*. [Computer software]. Muthén & Muthén.

Neale, J., Parkin, S., & Strang, J. (2023). Patients' goals when initiating long-acting injectable buprenorphine treatment for opioid use disorder: Findings from a

longitudinal qualitative study. *Substance Abuse Treatment, Prevention, and Policy, 18* (1), 37. https://doi.org/10.1186/s13011-023-00551-0

Neale, J., Tompkins, C. N. E., McDonald, R., & Strang, J. (2018). Implants and depot injections for treating opioid dependence: Qualitative study of people who use or have used heroin. *Drug and Alcohol Dependence, 189*, 1–7. https://doi.org/10.1016/j.drugalcdep.2018.03.057

Neale, J., Tompkins, C. N. E., & Strang, J. (2019). Prolonged-release opioid agonist therapy: Qualitative study exploring patients' views of 1-week, 1-month, and 6-month buprenorphine formulations. *Harm Reduction Journal, 16*(1), 25. https://doi.org/10.1186/s12954-019-0296-4

Nylund, K. L., Asparouhov, T., & Muthén, B. O. (2007). Deciding on the number of classes in latent class analysis and growth mixture modeling: A Monte Carlo simulation study. *Structural Equation Modeling, 14*(4), 535–569. https://doi.org/10.1080/10705510701575396

O'Connor, A. M., Cousins, G., Durand, L., Barry, J., & Boland, F. (2020). Retention of patients in opioid substitution treatment: A systematic review. *PLoS One, 15*(5), Article e0232086. https://doi.org/10.1371/journal.pone.0232086

Pierlorenzi, C., Nunzi, M., Cirulli, S., Direnzo, G. F. M., Curatella, L., Liberatori, S., … Leonardi, C. (2024). Patients' perspectives on buprenorphine subcutaneous implant: A case series. *Journal of Medical Case Reports, 18*(1), 202. https://doi.org/10.1186/s13256-024-04483-6

Saloner, B., Stoller, K. B., & Alexander, G. C. (2018). Moving addiction care to the mainstream—Improving the quality of buprenorphine treatment. *New England Journal of Medicine, 379*(1), 4–6. https://doi.org/10.1056/NEJMp1804059

SAMHSA. (2012). SAMHSA'S working definition of recovery. SAMHSA https://library.samhsa.gov/sites/default/files/pep12-recdef.pdf.

SAMHSA. (2023). *Medications for substance use disorders*. Department of Health and Human Services: U.S. https://www.samhsa.gov/medications-substance-use-disorders.

Sánchez, J., Sahker, E., & Arndt, S. (2020). The assessment of recovery capital (ARC) predicts substance abuse treatment completion. *Addictive Behaviors, 102*, Article 106189. https://doi.org/10.1016/j.addbeh.2019.106189

Scurti, P., Nunzi, M., Leonardi, C., Pierlorenzi, C., Marenzi, R., & Lamartora, V. (2023). The experience of buprenorphine implant in patients with opioid use disorder: A series of narrative interviews. *Frontiers in Psychiatry, 14*. https://doi.org/10.3389/fpsyt.2023.1205285

da Silva Junior, A. L. S., Santana, G. M., Nascimento, M. M., Cunha, R. L., Mesquita, P. R. R., & de Jesus, R. M. (2024). Illicit drugs in Brazil: Environmental consequences and consumption patterns. *Environmental Science and Pollution Research, 31*(35), 47530–47551. https://doi.org/10.1007/s11356-024-34183-z

Strepparola, G., Caminiti, C., Marvulli, V., Epifani, A., & Manfrè, S. (2025). Analisi di Questionari preliminari e di gradimento rivolti ai pazienti sull'utilizzo di formulazioni solide di Metadone nel Trattamento del Disturbo da Uso di Oppioidi. *Mission, 69*, 50–53. https://doi.org/10.3280/mis69-2025oa19923

Tran, B. X., Ohinmaa, A., Mills, S., Duong, A. T., Nguyen, L. T., Jacobs, P., & Houston, S. (2012). Multilevel predictors of concurrent opioid use during methadone maintenance treatment among drug users with HIV/AIDS. *PLoS One, 7*(12), Article e51569. https://doi.org/10.1371/journal.pone.0051569

Tsai, A. C., Kiang, M. V., Barnett, M. L., Beletsky, L., Keyes, K. M., McGinty, E. E., … Venkataramani, A. S. (2019). Stigma as a fundamental hindrance to the United States opioid overdose crisis response. *PLoS Medicine, 16*(11), Article e1002969. https://doi.org/10.1371/journal.pmed.1002969

Vilsaint, C. L., Kelly, J. F., Bergman, B. G., Groshkova, T., Best, D., & White, W. (2017). Development and validation of a brief assessment of recovery capital (BARC-10) for alcohol and drug use disorder. *Drug and Alcohol Dependence, 177*, 71–76. https://doi.org/10.1016/j.drugalcdep.2017.03.022

Woo, J., Bhalerao, A., Bawor, M., Bhatt, M., Dennis, B., Mouravska, N., … Samaan, Z. (2017). "Don't judge a book by its cover": A qualitative study of methadone patients' experiences of stigma. *Substance Abuse: Research and Treatment, 11*, Article 1178221816685087. https://doi.org/10.1177/1178221816685087

Yarborough, B. J. H., Stumbo, S. P., McCarty, D., Mertens, J., Weisner, C., & Green, C. A. (2016). Methadone, buprenorphine and preferences for opioid agonist treatment: A qualitative analysis. *Drug and Alcohol Dependence, 160*, 112–118. https://doi.org/10.1016/j.drugalcdep.2015.12.031

Ziefle, M., & Schaar, A. K. (2011). Gender differences in acceptance and attitudes towards an invasive medical stent. *Electronic Journal of Health Informatics, 6*(2), 13.