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ABSTRACT

Aim: To explore the factors determining the interest in extended-release buprenorphine (XR-BUP) injections among patients receiving opioid agonist treatment (OAT) in France.

Methods: 366 patients receiving OAT for opioid use disorder, recruited in 66 French centers, were interviewed from 12/2018 to 05/2019. A structured questionnaire assessed their interest in XR-BUP using a [1−10] Likert scale. 'More' vs. 'less' interested groups were defined using the median score of interest, and their characteristics were explored using adjusted odds ratios (aORs) and 95 % confidence interval (95 %CI). Independent variables were as follows: sociodemographic characteristics, OAT-related features (e.g., type of OAT and prescriber, dosing, or duration of treatment), OAT representations, and personal objectives of treatment.

Results: The median interest in XR-BUP was 7 (interquartile range: 3–9) out of 10. The participants who were 'more interested' (i.e. those scoring ≥7) showed no substantial difference in sociodemographic characteristics, relative to the 'less interested' participants. However, they more frequently reported forgetting to take their OAT (OR = 1.81; CI95 % = 1.06–3.10) or reported experiencing situations where taking their OAT was impractical (aOR = 1.69; CI95 % = 1.05–2.73). Their treatment objective was more focused on stopping illicit drugs (aOR = 1.67; 95 %CI = 1.02–2.70), reducing health risks (aOR = 3.57; 95 %CI = 1.67–7.69) and craving (aOR = 2.38; 95 %CI = 1.39–4.02) or improving family (aOR = 1.81; 95 %CI = 1.03–3.13) or professional (aOR = 2.22; 95 %CI = 1.43–3.85) recovery.

Conclusions: In France, where the access to OAT is relatively unrestricted, the majority of participants were interested in XR-BUP formulations. Being interested was associated with treatment objectives focused on abstinence and recovery, and with experiencing constraints in taking a daily oral OAT.

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1. Introduction

Approximately 27 million people worldwide suffer from opioid use disorder (OUD) (World Health Organization, 2018). The majority of them use heroin, but an increasing proportion of people with OUD also use prescription opioids, in particular in North America (Strang et al., 2020). It is estimated that more than 100,000 people die every year as a result of opioid use, with drug overdose deaths accounting for a significant proportion (World Health Organization, 2018). OUD thus requires a specialized addiction treatment, which comprises using medications, as well as an individualized psychosocial treatment (Strang et al., 2020).

For more than twenty-five years, opioid agonist treatments (OATs), i.e., essentially methadone and buprenorphine, have constituted the pharmacological cornerstone of OUD treatment (Bell and Strang, 2019). OATs support the cessation or reduction of opioid use and related-craving, diminish the likelihood of overdose, and improve psychosocial recovery (Bell and Strang, 2019; Strang et al., 2020). Despite this, the use of the current forms of OATs also has some drawbacks. The induction phase of treatment with the mu-receptor full-agonist methadone is associated with an increased mortality risk (Sordo et al., 2017), and therefore must be carefully managed and supervised (Strang et al., 2020). Furthermore, the mu-receptor partial agonist buprenorphine can be misused, i.e., injected or snorted, which may lead to adverse outcomes or diversion to the illicit market (Lofwall and Walsh, 2014). More practically, being treated with oral OAT can be perceived as a constraint by some patients, because of the need for daily intake and, in some cases, for regular attendance at prescribing or dispensing settings (Neale et al., 2018a).

Recently, new formulations of buprenorphine, named extended-release buprenorphine (XR-BUP), have started to be approved and commercialized (Ling et al., 2019). They comprise either buprenorphine implants or depot formulations, which provide therapeutic effects for periods ranging from one week to six months, depending on the product. These new formulations aim to address the treatment burdens associated with daily oral OATs (Vorspan et al., 2019). However, the interest of people with OUD in these new OAT formulations remains to be more clearly assessed, in particular in the context of national variations in access to different OATs and in treatment delivery models. Both qualitative (Neale et al., 2018b; Tompkins et al., 2019) and quantitative surveys (Larance et al., 2019; Saunders et al., 2020) suggest an interest in XR-BUP in a majority of people with OUD, with some individuals however expressing concerns around such formulations, in particular regarding a risk of coerced treatment.

The different surveys were conducted in England (Neale et al., 2018b; Tompkins et al., 2019), the US (Saunders et al., 2020), and Australia (Larance et al., 2019), respectively. However, these three countries have relatively restrictive conditions of access to sublingual BUP, which sometimes impedes patient engagement with treatment. In France, there is comparatively a less restricted access to buprenorphine, including the ability for any general practitioner (GP), with few limitations, to initiate buprenorphine treatment (Fatseas and Auriacombe, 2007; Vorspan et al., 2019). Moreover, most buprenorphine dispensing is undertaken in community pharmacies, with limited supervision of treatment intake. Buprenorphine dosing is rarely predefined, and is predominantly based on patients' preferences and clinical features such as craving (Fatseas and Auriacombe, 2007; Vorspan et al., 2019). In these aspects, the OAT delivery model in France differ from the treatment delivery models in countries such as the US and Australia (Haffajee et al., 2018; Nielsen and Dietze, 2019; Jin et al., 2020). Consequently, it was not known whether XR-BUP formulations would be of interest to patients, including in individuals willing to seek treatment, in France (Vorspan et al., 2019). In addition to assessing overall interest in these formulations in France, it is also of interest to determine which particular categories of opioid users that might be willing to receive XR-BUP formulations. For example, in Australia, it was found that specific populations of opioid users were more likely to be interested in XR-BUP formulations, such as younger people, females, and those with lower education, or people with a short history of illicit opioid use (Larance et al., 2019). Moreover, until now, personal therapeutic objectives regarding opioid use (e.g., cessation, management, or no particular objective) and individual perceptions of constraints related with taking oral OATs, have not been explored as potential determinants of the interest in XR-BUP, although these features may be crucial to explain the preferences for long-acting OAT formulations.

The 'AMBRE' study was a multicenter French survey conducted in people receiving or initiating an OAT, primarily aiming to determine the interest in XR-BUP in this population, and to explore which features were associated with a significant interest in these new formulations, in terms of: 1) sociodemographic or clinical characteristics, 2) treatment objectives, and 3) individual perceptions of OATs, respectively.

2. Materials and methods

The study is reported according to the 'Strengthening the reporting of observational studies in epidemiology' (STROBE) statement (von Elm et al., 2007). A completed checklist of the STROBE requirements can be consulted in the **Supplemental Materials**.

2.1. Study design and population

The 'AMBRE' study was a cross sectional survey conducted in 366 patients, recruited in 68 OAT settings in France (listed in the **Supplemental Materials**). Among them, 31 were outpatient addiction centers, 31 were GPs prescribing OATs, and 6 were prison medical centers. The survey took place between 12/02/2018 and 05/31/2019. Inclusion criteria were as follows: 1) being aged 18 years or more; 2) initiating or being currently treated with an OAT for OUD; 3) providing written consent for participating in the survey; and 4) being capable of completing a self-administered questionnaire.

2.2. Study questionnaire

The questionnaire was developed by the authors and pre-tested on small group of treatment-seeking individuals with OUD, in order to ensure the acceptability and reproducibility of the collected data. The questionnaire aimed to explore: 1) the main sociodemographic features, clinical history, and characteristics of participants regarding their use of OAT; 2) the participants' objectives with respect to their OUD treatment; and 3) the perceptions of participants regarding the convenient or problematic aspects of OAT in their daily life. Subsequently, after a brief description outlining the features of weekly and monthly XR-BUP, participants were asked to score their potential interest in such a new formulation of OAT, using a 1−10 Likert scale. A final series of questions explored the expectations of participants regarding weekly and monthly XR-BUP. A copy of the questionnaire can be found in the **Supplemental Materials**.

2.3. Statistical analyses

Only some of the questions asked in the survey were analyzed in the present study. There was no a priori statistical analysis plan. Moreover, to avoid analyzing variables with small subgroup sizes, the answers to many multicategorical questions were binarized as defined in the 'parameter' column of Table 1 and Table 2. The 1−10 Likert scale assessing the level of interest in XR-BUP was binarized as follows: a score of 1–6 was defined as 'less interested', while a score or 7 or more out of 10 was defined as 'more interested'. The choice for this cut-off was based on the median score of the quantitative variable (see below).

Quantitative parameters are presented as the mean ± standard deviation (m ± SD), median and interquartile range [IQR], and minimum and maximum values. Categorical parameters are presented as the number and percentage (n; %). The association between the response to

Table 1
Influence of sociodemographic features, clinical parameters, and history of treatment, on the interest in XR-BUP.

Parameter	'More' vs. 'less' interested in XR-BUP n (%)	OR [95 %CI]	aOR [95 %CI] [a]
Gender			
Males (n = 265; 74.2 %)	145 (54.7 %) vs. 120 (45.3 %)	1	1
Females (n = 92; 35.8 %)	51 (55.4 %) vs. 41 (44.6 %)	1.03 [0.64–1.66]	1.02 [0.63–1.65]
Age category			
18 – 24 years (n = 14; 3.9 %)	10 (71.4 %) vs. 4 (28.6 %)	1.88 [0.56–6.32]	1.87 [0.56–6.33]
25–34 years (n = 94; 26.3 %)	45 (47.9 %) vs. 49 (52.1 %)	0.82 [0.48–1.40]	0.82 [0.48–1.40]
35–44 years (n = 128; 35.9 %)	73 (57.0 %) vs. 55 (43.0 %)	1	1
45 – 54 years (n = 95; 26.6 %)	48 (50.5 %) vs. 47 (49.5 %)	0.77 [0.45–1.31]	0.77 [0.45–1.31]
55 years and more (n = 26; 7.3 %)	16 (61.5 %) vs. 10 (38.5 %)	1.21 [0.51–2.86]	1.20 [0.51–2.86]
Professional status			
Employed (n = 99; 27.7 %)	55 (55.6 %) vs. (44.4 %)	1	1
Unemployed (n = 243; 68.1 %)	131 (53.9 %) vs. 112 (46.1 %)	0.94 [0.58–1.50]	0.93 [0.58–1.49]
Students (n = 8; 2.2 %)	5 (62.5 %) vs. 3 (37.5 %)	1.33 [0.30–5.89]	0.99 [0.19–4.99]
Retired (n = 7; 2.0 %)	5 (71.4 %) vs. 2 (28.6 %)	2.00 [0.37–10.81]	1.79 [0.29–11.14]
Marital status			
Single (n = 202; 56.6 %)	111 (55.0 %) vs 91 (45.0 %)	1	1
Having a stable partner (n = 102; 28.6 %)	55 (53.9 %) vs. (47 (46.1 %)	0.96 [0.59–1.55]	1.00 [0.61–1.61]
Separated / Divorced / Widowed (n = 53; 14.8 %)	30 (56.6 %) vs. 23 (43.4 %)	1.07 [0.58–1.97]	1.11 [0.60–2.07]
Has children (nmv = 1)			
No (n = 175; 49.0 %)	92 (52.6 %) vs. 83 (47.4 %)	1	1
Yes (n = 181; 51.0 %)	103 (56.9 %) vs. 78 (43.1 %)	1.19 [0.78–1.81]	1.25 [0.81–1.93]
Housing status			
Unstable (n = 127; 35.6 %)	70 (55.1 %) vs. 57 (44.9 %)	1	1
Stable (n = 230; 64.4 %)	126 (54.8 %) vs. 104 (45.2 %)	0.99 [0.64–1.52]	0.99 [0.63–1.57]
Level of Education			
Primary (n = 27; 7.6 %)	70 (55.1 %) vs. 57 (44.9 %)	1.06 [0.47–2.38]	1.05 [0.46–2.37]
Secondary (n = 251; 70.3 %)	126 (54.8 %) vs. 104 (45.2 %)	1	1
High school (n = 79; 22.1 %)	35 (44.3 %) vs. 44 (57.7 %)	**0.58 [0.35 – 0.97]** *	**0.56 [0.33 – 0.95]** *
Duration of opioid use (nmv = 6)			
Years (per one-year increase)	14.7 ± 8.8 vs. 15.3 ± 9.50	0.99 [0.97–1.02]	1.00 [0.97–1.02]
Comorbid HIV, HCV, or HBV (nmv = 17)			
No (n = 284; 83.5 %)	151 (53.2 %) vs. 133 (46.8 %)	1	1
Yes (n = 56; 16.5 %)	35 (62.5 %) vs. 21 (37.5 %)	1.19 [0.78–1.81]	1.25 [0.81–1.93]
Psychiatric comorbidity (nmv = 16)			
No (n = 148; 43.4 %)	83 (56.1 %) vs. 65 (43.9 %)	1	1
Yes (n = 193; 56.6 %)	107 (55.4 %) vs. 86 (44.6 %)	0.97 [0.63–1.50]	0.97 [0.63–1.51]
Other somatic comorbidity (nmv = 1)			
No (n = 262; 73.6 %)	149 (56.7 %) vs. 113 (43.3 %)	1	1
Yes (n = 94; 26.4 %)	47 (50 %) vs. 47 (50 %)	0.77 [0.48–1.23]	0.76 [0.47–1.23]
Concurrent use of benzodiazepines (nmv = 2)			
No (n = 163; 36.7 %)	85 (52.2 %) vs. 78 (47.8 %)	1	1
Yes (n = 192; 63.3 %)	110 (57.3 %) vs. 82 (42.7 %)	1.23 [0.81–1.87]	1.25 [0.82–1.92]
Concurrent use of prescription opioids (nmv = 0)			
No (n = 319; 89.4 %)	18 (47.4 %) vs. 20 (52.6 %)	1	1
Yes (n = 38; 10.6 %)	178 (55.8 %) vs. 141 (44.2 %)	0.71 [0.36–1.40]	0.66 [0.33–1.32]
Type of OAT (nmv = 0)			
BUP or BUP/NAL (n = 222; 62.5 %)	126 (57.3 %) vs. 94 (42.7 %)	1	1
Methadone (n = 135; 37.5 %)	70 (51.9 %) vs. 65 (48.1 %)	0.80 [0.52–1.24]	0.79 [0.51–1.23]
Average daily dose of OAT			
mg buprenorphine equivalent (per 1-mg increase)	9.2 ± 5.7 vs. 10 ± 7.4	0.98 [0.95–1.01]	0.98 [0.95–1.01]
First OAT			
No (n = 325; 91.0 %)	178 (54.8 %) vs. 147 (45.2 %)	1	1
Yes (n = 32; 9.0 %)	18 (56.3 %) vs. 14 (43.8 %)	1.06 [0.51−2.21]	1.03 [0.49–2.18]
Duration of OAT (nmv = 11)			
Years (per one-year increase)	9.3 ± 7.3 vs. 9.0 ± 9.3	1.01 [0.98–1.04]	1.00 [0.98–1.02]
Number or previous OAT attempts (nmv = 39)			
Number or attempts (per one-attempt increase)	1.9 ± 2.5 vs. 2.1 ± 2.8	0.97 [0.89–1.06]	0.98 [0.90–1.07]
Type of prescribing setting			
CSAPA = Outpatient Addiction Center (n = 169; 47.3 %)	95 (56.2 %) vs. 74 (43.8 %)	1	1
GP (n = 87; 24.4 %)	48 (55.2 %) vs. 39 (44.8 %)	0.96 [0.57–1.61]	0.93 [0.55–1.57]
UCSA = Prison Medical Center (n = 101; 28.3 %)	53 (52.5 %) vs. 48 (47.5 %)	0.86 [0.52–1.41]	0.86 [0.52–1.44]
Subjective satisfaction about OAT (nmv = 36)			
1−10 Likert scale (per one-point increase)	9.3 ± 7.3 vs. 9.0 ± 9.3	1.05 [0.93–1.19]	1.06 [0.93–1.20]
Frequency of dispensing (nmv = 34)			
Daily or several times per week (n = 49; 15.2 %)	26 (53.1 %) vs. 23 (46.9 %)	1	1
Weekly (n = 78; 24.1 %)	42 (53.9 %) vs. 36 (46.1 %)	1.02 [0.48–2.12]	1.01 [0.48–2.10]
Every two weeks (n = 54; 16.7 %)	53 (52.5 %) vs. 48 (47.5 %)	1.11 [0.50–2.43]	1.10 [0.49–2.43]
Monthly (n = 142; 44.0 %)	53 (52.5 %) vs. 48 (47.5 %)	1.06 [0.55–2.07]	1.06 [0.54–2.08]
Full treatment is taken (nmv = 35)			
Never, rarely, or sometimes (n = 30; 9.3 %)	14 (46.7 %) vs. 16 (53.3 %)	1	1
Always or often (n = 292; 90.7 %)	161 (55.1 %) vs. 131 (44.9 %)	1.40 [0.66–2.98]	1.53 [0.71–3.29]
Dose of OAT is split in several daily intakes (nmv = 35)			

(*continued on next page*)

Table 1 (*continued*)

Parameter	'More' vs. 'less' interested in XR-BUP n (%)	OR [95 %CI]	aOR [95 %CI] [a]
Never, rarely, or sometimes (n = 178; 55.3 %)	95 (53.4 %) vs. 83 (46.6 %)	1	1
Always or often (n = 144; 44.7 %)	81 (56.3 %) vs. 63 (43.7 %)	1.12 [0.72–1.75]	1.12 [0.72–1.76]
Daily dose OAT may be insufficient (nmv = 36)			
No (n = 182; 56.7 %	100 (55.0 %) vs 82 (45.0 %)	1	1
Yes (n = 139; 43.3 %)	75 (54 %.0%) vs. 64 (46.0 %)	0.96 [0.62–1.50]	0.91 [0.58–1.45]
May feel craving (nmv = 37)			
No (n = 197; 61.6 %)	110 (55.8 %) vs. 87 (44.2 %)	1	1
Yes (n = 123; 39.4 %)	65 (52.9 %) vs. 58 (47.1 %)	0.89 [0.56–1.39]	0.84 [0.53–1.34]
Has reduced the use of illicit opioids with OAT (nmv = 44)			
No (n = 85; 27.2 %)	123 (54.0 %) vs. 105 (56.0 %)	1	1
Yes (n = 228; 72.8 %)	47 (55.3 %) vs. 38 (44.7 %)	0.95 [0.57–1.56]	0.92 [0.58–1.46]
Has stopped the use of illicit opioids with OAT (nmv = 37)			
No (n = 120; 37.5 %)	65 (54.2 %) vs. 55 (45.8 %)	1	1
Yes (n = 200; 62.5 %)	110 (55.0 %) vs. 90 (45.0 %)	1.03 [0.66–1.63]	1.07 [0.68–1.69]
Has increase the use of alcohol with OAT (nmv = 38)			
No (n = 262; 82.1 %)	146 (55.7 %) vs. 116 (44.3 %)	1	1
Yes (n = 57; 17.9 %)	30 (52.6 %) vs. (27 (47.4 %)	0.88 [0.50–1.57]	0.86 [0.48–1.53]
Has increase the use of other drugs with OAT (nmv = 36)			
No (n = 241; 75.1 %)	128 (53.1 %) vs. 113 (46.9 %)	1	1
Yes (n = 80; 24.9 %)	48 (60 %) vs. 32 (40 %)	1.32 [0.79–2.71]	1.42 [0.84–2.41]
Forgets to take the OAT (nmv = 36)			
Never, rarely, or sometimes (n = 240; 74.8 %)	122 (50.8 %) vs. 118 (49.2 %)	1	1
Always or often (n = 81; 25.2 %)	53 (65.4 %) vs. 28 (34.6 %)	**1.83 [1.08–3.09]** *	**1.81 [1.06–3.10]** *
Situations in which taking OAT is impractical (nmv = 38)			
Never, rarely, or sometimes (n = 198; 62.1 %)	100 (50.5 %) vs. 98 (59.5 %)	1	1
Always or often (n = 121; 37.9 %)	74 (61.2 %) vs. 47 (38.8 %)	1.54 [0.97–2.44] †	**1.69 [1.05–2.73]** *
Injects the OAT (nmv = 36)			
Never (n = 289; 90.0 %)	154 (53.3 %) vs. 135 (46.7 %)	1	1
Always, often, sometimes, or rarely (n = 32; 10 %)	20 (62.5 %) vs. 12 (37.5 %)	1.46 [0.69–3.10]	1.45 [0.68–3.12]
Snorts / smoke the OAT (nmv = 39)			
Never (n = 248; 78.0 %)	137 (55.2 %) vs. 111 (44.8 %)	1	1
Always, often, sometimes, or rarely (n = 70; 22.0 %)	34 (48.6 %) vs. (51.4 %)	0.77 [0.45–1.30]	0.77 [0.45–1.32]

Abbreviations: OR: odds ratio; aOR: adjusted OR ; ([a] adjusted on gender and age category, expect for age category which was adjusted only for gender, and reciprocally); 95 %CI: 95 % confidence interval; nmv: number of missing values; OAT: opioid agonist treatment; BUP: buprenorphine; NAL: naltrexone; HIV: human immunodeficiency virus; HCV: hepatitis C virus; HBV: hepatitis B virus; XR-BUP: Extended-release buprenorphine.

** $p<0.001$.

*** $p<0.0001$.

† $p<0.1$.

* $p<0.05$.

each variable and the binarized category of interest in XR-BUP was explored using logistic regression modeling through unadjusted bivariable comparisons, providing an odds ratio and the 95 % confidence interval (OR [95CI%], and comparisons adjusted for age category and gender, providing an adjusted OR (aOR) and the 95 %CI. Individuals with missing values were not integrated in the models. There was no a priori sample size calculation, but we estimated, based on the results of a previous similar quantitative survey (Larance et al., 2020), that not less than 30 % of participants would declare being 'less interested' in XR-BUP. Given the "one in ten" rule for estimating the sample size of a logistical regression analysis (Peduzzi et al., 1996), we calculated that a 300-participant survey would allow a nine-predictor logistic regression model, which was deemed sufficient. As a result, the survey aimed to recruit between 300 and 400 participants during the inclusion period.

Statistical analyses were performed using the XLSTAT2019 software (https://www.xlstat.com/en/).

2.4. Ethical aspects

In accordance with the French law on clinical research (Loi Jardé), the study protocol was submitted to and approved by the CNIL (#2,211,988).

3. Results

Descriptive results of the entire sample can be found in **Supplemental Materials**. Data from 357 participants were included in the analyses, as the responses provided by nine of the 366 recruited participants were aberrant or provided no answer to all of the main explanatory variables. Among participants, the average level of interest in XR-BUP, according to the 1−10 Likert scale, was 6.2 ± 3.2, with a median value and IQR of 7 [3–9]. The cut-off for binarizing the variable into 'more interested' and 'less interested' participants was thus based on this median score of interest. In total, 196 (54.9 %) participants were categorized as 'more interested' in XR-BUP, whereas 161 others (45.1 %) were categorized as 'less interested'.

The associations between the binarized category of interest in XR-BUP ('more interested' vs. 'less interested') and participants' sociodemographic and clinical features are displayed in Table 1. Overall, very few parameters were associated with being more or less interested in XR-BUP. In the sociodemographic variables, only a high-school level of education was negatively associated with being interested in XR-BUP, compared to lower levels of education. Among the main clinical features, only the respondents that reported frequently forgetting to take their OAT, and those frequently experiencing situations in which taking their OAT was impractical, were significantly more interested in XR-BUP, relative to other participants. More significant associations with the interest in XR-BUP were found with respect to the objectives of treatment (Table 2). Being 'more interested' in XR-BUP was significantly more frequent among participants expecting that the treatment would help them discontinue illicit drug use (aOR = 1.67; 95 %CI [1.02–2.70], $p < 0.05$), reduce health risks (aOR = 3.57; 95 %CI [1.67–7.69], $p < 0.001$), save daily costs (aOR = 1.61; 95 %CI [1.01–2.56], $p < 0.05$); reduce injecting or snorting drugs (aOR = 1.88; 95 %CI [1.20–2.94], $p < 0.05$); reduce craving (aOR = 2.38; 95 %CI [1.39–4.02], $p < 0.001$), improve social / family (aOR = 1.81; 95 %CI [1.03–3.13], $p < 0.05$) and professional recovery (aOR = 2.33; 95 %CI [1.43–3.85], $p < 0.001$). The

Table 2
Influence of personal objectives of treatment and representations about OAT on the interest in XR-BUP.

Parameter	'More' vs. 'less' interested in XR-BUP n (%)	OR [95 %CI]	aOR [95 %CI] [a]
Personal objective of treatment Stopping any illicit use of drugs			
No (n = 92; 25.8 %)	42 (45.5 %) vs. 50 (54.3 %)	1	1
Yes (n = 265; 74.2 %)	154 (58.1 %) vs. 111 (41.9 %)	**1.67 [1.02–2.70]** *	**1.67 [1.02–2.70]** *
Reducing illicit use of drugs			
No (n = 333; 93.3 %)	12 (50.0 %) vs. 12 (50.0 %)	1	1
Yes (n = 24; 6.7 %)	184 (55.0 %) vs. 149 (45.0 %)	1.41 [0.60–3.23]	1.39 [0.59–3.21]
Managing the illicit use of drugs			
No (n = 333; 93.0 %)	187 (56.3 %) vs. 145 (43.7 %)	1	1
Yes (n = 25; 7.0 %)	9 (36.0 %) vs. 16 (64.0 %)	0.44 [0.19–1.02] †	**0.41 [0.18 – 0.97]** *
Reducing healthcare risks (nmv = 6)			
No (n = 38; 10.8 %)	11 (28.9 %) vs. 27 (71.1 %)	1	1
Yes (n = 313; 89.2 %)	183 (58.5 %) vs. 130 (41.5 %)	**3.45 [1.64–7.14]** ***	**3.57 [1.67–7.69]** ***
Stopping withdrawal (nmv = 3)			
No (n = 15; 4.2 %)	1 (6.7 %) vs. 14 (93.3 %)		
Yes (n = 339; 95.8 %)	193 (56.9 %) vs. 146 (43.1 %)	**Not calculated**	**Not calculated**
Saving money (nmv = 7)			
No (n = 106; 30.3 %)	50 (47.2 %) vs. 56 (52.8 %)	1	1
Yes (n = 244; 69.7 %)	145 (59.4 %) vs. 99 (40.6 %)	**1.64 [1.04–2.63]** *	**1.61 [1.01–2.56]** *
Reducing injecting / snorting / smoking OAT (nmv = 14)			
No (n = 187; 45.5 %)	90 (48.1 %) vs. 97 (51.9 %)	1	1
Yes (n = 156; 54.5 %)	98 (62.8 %) vs. 58 (37.2 %)	**1.82 [1.18–2.78]** *	**1.88 [1.20–2.94]** **
Reducing craving (nmv = 10)			
No (n = 76; 45.5 %)	30 (39.5 %) vs. 46 (60.5 %)	1	1
Yes (n = 271; 54.5 %)	164 (60.5 %) vs. 107 (39.5 %)	**2.33 [1.36–4.00]** ***	**2.38 [1.39–4.02]** ***
Improving social / family recovery (nmv = 6)			
No (n = 64; 45.5 %)	28 (43.7 %) vs. 36 (56.3 %)	1	1
Yes (n = 287; 54.5 %)	167 (58.2 %) vs. 120 (41.8 %)	**1.81 [1.03–3.13]** *	**1.81 [1.03–3.13]** *
Improving professional recovery (nmv = 8)			
No (n = 96; 25.5 %)	39 (40.6 %) vs. 57 (59.4 %)	1	1
Yes (n = 253; 74.5 %)	153 (60.5 %) vs. 100 (39.5 %)	**2.22 [1.39–3.57]** ***	**2.33 [1.43–3.85]** ***
Representations about OAT Daily OAT intake is a problem (nmv = 4)			
No or no opinion (n = 209; 59.2 %)	100 (47.9 %) vs. 109 (52.1 %)	1	1
Yes (n = 144; 40.8 %)	94 (65.3 %) vs. 50 (34.7 %)	**2.05 [1.32–3.17]** ***	**2.18 [1.39–3.41]** ***
The fact that OAT may be diverted is a problem (nmv = 7)			
No or no opinion (n = 266; 59.2 %)	148 (55.6 %) vs. 118 (44.4 %)	1	1
Yes (n = 84; 40.8 %)	43 (51.2 %) vs. 41 (48.9 %)	0.84 [0.51–1.37]	0.83 [0.51–1.37]
Splitting the daily dose of OAT is convenient (nmv = 7)			
No or no opinion (n = 248; 59.2 %)	143 (57.7 %) vs. 105 (42.3 %)	1	1
Yes (n = 102; 40.8 %)	49 (48.0 %) vs. 53 (52.0 %)	0.68 [0.43–1.08] †	0.68 [0.43–1.09]
Giving or reselling the OAT is convenient (nmv = 3)			
No or no opinion (n = 335; 94.6 %)	182 (54.3 %) vs. 153 [45.7 %)	1	1
Yes (n = 19; 5.4 %)	12 (63.2 %) vs. 7 (36.2 %)	1.32 [0.55–3.75]	1.38 [0.53–3.63]
Stopping the OAT to use drugs is convenient (nmv = 4)			
No or no opinion (n = 297; 84.1 %)	163 (54.9 %) vs. 134 (45.1 %)	1	1
Yes (n = 56; 15.9 %)	31 (55.4 %) vs. 25 (44.7 %)	1.02 [0.57–1.81]	1.02 [0.57–1.83]

Abbreviations: OR: odds ratio; aOR: adjusted OR ; ([a] adjusted on gender and age category, expect for age category which was adjusted only for gender, and reciprocally); 95 %CI: 95 % confidence interval; nmv: number of missing values; OAT: opioid agonist treatment; BUP: buprenorphine; NAL: naltrexone; HIV: human immunodeficiency virus; HCV: hepatitis C virus; HBV: hepatitis B virus; XR-BUP: Extended-release buprenorphine.

† $p < 0.1$.
* $p < 0.05$.
** $p < 0.001$.
*** $p < 0.0001$.

aOR and 95 %CI are not provided for the personal objective of preventing withdrawal, because sample size limitations. By contrast, participants 'more interested' in XR-BUP were less likely to aim to manage their drug use, relative to the 'less interested' group (aOR = 0.41; 95 %CI [0.18−0.97], $p < 0.05$).

Regarding the personal opinions about oral or sublingual OATs, participants 'more interested' in XR-BUP were more likely to consider taking an OAT on a daily basis to be a constraint compared to those 'less interested' in XR-BUP (aOR = 2.18; 95 %CI [1.39–3.41], $p < 0.001$). Opinions regarding the possibility of diverting, splitting, or reselling the current formulations, or being able to stop the OAT if the patient wishes to use illicit opioids, were not significantly associated with belonging to a specific group.

4. Discussion

The aim of this study was to identify which treatment seekers among French people treated for OUD were 'more' or 'less' interested in XR-BUP formulations. This question was warranted as the first XR-BUP has recently been approved in France. In France, the treatment

coverage with OATs is very important, since, in 2017, 80 % of people with OUD were estimated to receive at least one prescription of OAT within the previous year (European Monitoring Centre for Drugs and Drug Addiction, 2017).

Overall, we found that, with the exception of level of education, no sociodemographic parameter was associated with being 'more interested' in XR-BUP. In terms of clinical features, only specific subgroups, i.e., individuals that frequently forget to take their OAT, and those frequently experiencing personal or professional situations in which taking an oral OAT is impractical, were significantly 'more interested' in XR-BUP.

Interestingly, the characteristics related to the individual objectives of treatment were more predictive of greater interest in XR-BUP. In particular, those who were more concerned with reducing their health risks, reducing craving, and improving their psychosocial recovery, were more likely to be interested in XR-BUP. To a lesser extent, this was also the case for participants who were expecting that the treatment would help them discontinue illicit drug use, reduce injecting / snorting / smoking their OAT, or reduce withdrawal symptoms. Caution is required, however, regarding the latter, because the small sample size did not allow calculation of a reasonable 95 %CI. By contrast, participants who sought treatment to help them manage the use of illicit drug were significantly 'less interested' in XR-BUP. Overall, this suggests that, among treatment seeking people with OUD, those who might be more interested in XR-BUP are those willing to discontinue illicit drug use, and/or those concerned by functional outcomes, i.e., reducing craving or improving psychosocial recovery. Practical issues, such as forgetting to take daily OAT, or finding daily medication a burden for social or professional reasons, were also predictive of being more interested in XR-BUP.

Overall, our results suggest that no predefined category of people with OUD constitute a specific target population for XR-BUP. By contrast, individual opinions and objectives seem to be the strongest predictors for being more interested in these new formulations, irrespective of age, gender, history of OUD, or comorbid conditions. This appears relatively consistent with the conclusions of previous qualitative surveys that found that individual objectives and practical issues were the most frequent factors associated with interest in XR-BUP (Neale et al., 2018b; Tompkins et al., 2019). Similarly, the fact that neither the type of OAT, nor the type of prescribing setting, seemed to have an influence on the interest in XR-BUP is notable. First, it suggests that patients treated with methadone, similarly to those treated with BUP, may also be potentially interested in XR-BUP, and should be able to benefit from this new treatment option if they wish. Furthermore, the findings suggest that the incarcerated patients treated with OAT are not specifically reluctant to receive XR-BUP. As sublingual formulations are commonly smuggled and misused in prison (Bi-Mohammed et al., 2017), if acceptance of XR-BUP by people with OUD in prison is satisfactory, these new treatment options could thus particularly interest patients who want to avoid pressure for diversion, and risks of extortion of their OAT in prison (Vorspan et al., 2019).

Only two previous studies have quantitively assessed the preferences of people with OUD regarding XR-BUP, in Australia, and in the US, respectively (Larance et al., 2019; Saunders et al., 2020). A greater proportion of interviewees in Australia were interested in XR-BUP, compared to their French counterparts, with more than two thirds of them reporting that they deemed that XR-BUP could be a good treatment option for them. Moreover, a study among 40 American participants with previous or current OAT, found that only 40 % of the responders were interested in XR-BUP formulations. In Australia, stricter supervision of treatment compared with other medicines may increase their preference for XR-BUP compared to countries where treatment is less monitored, such as in France or the USA where unsupervised office-based opioid treatment (OBOT) with buprenorphine is standard practice (Jin et al., 2020). Another difference in the interest for XR-BUP might be the affordability and cost of daily OUD treatment in Australia with dispensing fees payed by the patients for pharmacy dispensing compared to the free provision of daily sublingual BUP in France (Winstock et al., 2007; Fatseas and Auriacombe, 2007). However, when comparing the figures between countries and studies, it should also be taken into account that the way of determining the preference for XR-BUP was different across the three surveys. In particular, in our study, the cut-off used to determine the level of interest was high (i.e., 7 or more out of 10, using the Likert scale). This made us categorize respondents with a mild level of interest as 'less interested'.

To our knowledge, only one quantitative survey was conducted with a similar objective of exploring the determinants of interest in XR-BUP. This study was undertaken in 2017–2018 among 396 Australian individuals with OUD (Larance et al., 2019). Questions were partially similar, but the sample was different, insofar as one third of participants were not treated with OAT. Overall, our results partially overlap with the results from this Australian survey. In particular, they found a statistically significant gender gap in the interest in XR-BUP, with females being more interested in XR-BUP, when compared to males. Moreover, they found a significantly reduced interest for XR-BUP in more educated individuals, which is in line with what we found in the present survey. Reasons for this consistent finding in both France and Australia are difficult to explain at this stage. There were also some differences between the results from the Australian survey and those from our French one. In Larance et al., being a recent heroin user was associated with an increased interest in XR-BUP formulations. Australian patients who were on OAT for more than two years were less interested in XR-BUP than those who had started their treatment for less than two years. Last, patients who received more than seven unsupervised ('take-home') doses of buprenorphine per months were significantly less interested in XR-BUP than those receiving no take-home doses. By contrast, we found no significant influence of recent opioid use, treatment duration, or dispensing frequency, on the interest in XR-BUP formulations among French patients treated with OAT. Many other findings from our survey, in particular regarding treatment preferences, were not investigated in the Australian study and thus provides new information regarding the overall determinants of interest in XR-BUP formations among treatment-seeking people with OUD.

Despite the relatively large sample size, our survey has some limitations. In particular, the fact that participants were not randomized or selected using quotas may result in the population being not entirely representative of French people with OUD. Nevertheless, in practice, this population is very difficult to characterize epidemiologically, because of the illicit nature of their opioid use, which makes the issues about representativeness relatively challenging. Similarly, the fact that only patients treated with an OAT were included might be a limitation. However, this is the likely population of people with OUD that will firstly have the option of receiving treatment with XR-BUP in France. Another limitation of the survey is that it is unclear whether the willingness of being treated with XR-BUP expressed in the survey would translate to actual treatment choice. Last, the fact that we chose not to use all the initial questions of the survey for investigating the main objective of this specific study main appear somewhat arbitrary, but as specified in the Methods, some questions were relatively redundant, and their respective answers were too much correlated to be integrated into the same multivariable model.

In conclusion, we found that, in France, in which the access to and the monitoring of buprenorphine treatment is less restrictive than in many other countries, the population of treatment-seeking patients with OUD was to a large extent interested in receiving XR-BUP formulations. Moreover, we found that the interest in such formulations was not predicted by sociodemographic features or by parameters related to the individual history of drug use, but more on by treatment objectives, and by very practical considerations related to the constraints of taking sublingual formulations on a daily basis. This suggests that weekly and monthly XR-BUP formulations will be likely to find a place among the very heterogeneous population of populations with OUD.

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Contributors

GB, BT, JB, PN, PH, and MK designed the study.
BR, BT, MC, PB, FM, JB, PN, and GB recruited participants.
BR and MN analyzed the data.
BR wrote the first draft of the manuscript.
All authors read and approved the final draft.

Declaration of Competing Interest

BR received fees for lectures and consultancy from Camurus, Individor, Recordati, and Ethypharm. BT received fees for consultancy from Camurus. JB received fees for lectures or consultancy from Camurus and Indivior. MK and PH are employed by Camurus, France, and Camurus, Sweden, respectively. FM received fees for lectures or consultancy from Camurus and Indivior. PN received fees for lectures or consultancy from Camurus. GB received fees for lectures or consultancy from Camurus and Indivior. Other authors declare having no conflict of interest.

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Appendix A. Supplementary data

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