Life satisfaction among individuals with opioid use disorder receiving extended-release naltrexone: A 12-week randomized controlled trial and a 36-week follow-up

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Abstract

Introduction Life satisfaction (LS) in opioid-dependent individuals is lower than in the general population. This study aimed to explore changes in LS during short- and long-term treatment with extended-release naltrexone (XR-NTX).

Methods This open-label 12-week clinical trial randomized 159 participants to either monthly XR-NTX or daily buprenorphine-naloxone (BP-NLX). In a subsequent 36-week follow-up study on XR-NTX, participants either continued or switched to XR-NTX. The study collected data on the Temporary Satisfaction with Life (TSWL) and illicit opioid use every fourth week. The research team assessed changes in TSWL by a linear mixed model and growth mixture model. The study assessed relationship between opioid use and TSWL by a linear mixed model.

Results Change in LS differed significantly between the groups in both study periods. TSWL scores were significantly higher in the XR-NTX group at week 4 ($p = 0.013$) and week 8 ($p = 0.002$). In the follow-up period, the groups were significantly different only at week 16 ($p = 0.031$) and week 48 ($p = 0.025$), with the higher TSWL scores in the XR-NTX continued group. Increase in opioid use by one day was associated with a 0.12 point lower mean TSWL score. Both study periods identified groups with low and high LS levels. In the trial period, the TSWL scores exhibited a significant increase from baseline to week 12 in both groups, $p < .001$ and $p = 0.011$ in the low and high LS group, respectively. In the follow-up period, the TSWL scores exhibited a significant increase from week 16 to week 48 ($p = 0.003$) in the high LS group, while the low LS group showed persistently lower values throughout that period.

Conclusions XR-NTX treatment given once monthly is associated with higher LS, as measured by TSWL, compared to daily use of BP-NLX. The majority of the participants had relatively low TSWL scores and did not report any change in TSWL during longer-term treatment. The study found a significant association between more frequent illicit opioid use and a low or decreased LS during follow-up.

Keywords life satisfaction; extended-release naltrexone; buprenorphine-naloxone; opioid use disorder

Highlights

Life satisfaction (LS) increased significantly in the XR-NTX group.

Declined LS was associated with more use of illicit opioids.

Most of the participants showed a rather low Temporary Satisfaction with Life (TSWL).

In the low and high LS groups, the TSWL scores increased from baseline to week 12.

The TSWL scores did not change in the low LS group during follow-up treatment.

1. Introduction

The American Society of Addiction Medicine recognizes opioid dependence as a chronic, recurrent disease (American Society of Addiction Medicine, 2011). Research has shown that opioid maintenance treatment (OMT) is considered the most effective intervention (Volkow & Blanco, 2020; WHO, 2009), because it reduces overdose mortality rates, illicit opioid use, and the risk of relapse (Andersson, Wenaas, & Nordfjærn, 2019; Sordo et al., 2017; Zhang, Friedmann, & Gerstein, 2003). Unlike OMT treatment, the opioid antagonist extended-release naltrexone (XR-NTX) blocks opioid receptors without the potential for abuse and diversion. Several studies have shown that XR-NTX is a promising treatment for opioid dependence, when compared to OMT (Alderks, 2017; Jarvis et al., 2018; Lee et al., 2018; Solli et al., 2018; Tanum et al., 2017).

OMT patients seek to abstain from illicit opioids, promote recovery, and improve quality of life (QoL). The field has increasingly used patient-reported outcome research to evaluate the QoL of OMT patients (Carlsen et al., 2019). While research has had an interest in how specific areas of life are important for enhancing well-being, research has also had an interest in how these specific elements may lead to a general sense of well-being. For well-being in general, research has used the term life satisfaction (LS). The most commonly used definition of LS is the degree to which people evaluate the overall quality of life based on the factors that matter most to them, that is, by comparing their life circumstances with the standard that is set by each person (Diener et al., 1985).

LS does not focus on any particular moment in time or specific areas of life, such as employment or health. Yet LS strongly influences health and well-being and a higher LS is associated with longer life expectancy, better disease tolerance, and fewer mental disorders (Diener & Chan, 2011; Koivumaa-Honkanen et al., 2001). Self-reported low LS is associated not only with poor health, but also with a higher risk of suicide, including drug-related deaths (Koivumaa-Honkanen et al., 2001; Oquendo & Volkow, 2018). Opioid-dependent individuals seeking treatment have a rather low LS compared to the general population (Luty & Arokiadass, 2008; Pavot & Diener, 2008, 2009).

Limited research exists on how OMT programs influence global LS (Krook et al., 2002; Laudet, 2011). For example, Laudet et al. (2009) found that higher overall LS was associated with an increased likelihood of prolonged abstinence among individuals with substance dependence. Another study by Krook et al. (2002) showed an increase in LS among participants inducted to buprenorphine compared to a control group during a three-month trial. However, participants emphasized that their lives were still not good, only somewhat better than before (Krook et al.,

2002). While these studies often show similar results, we know less about the LS trajectories among individuals with OUD during treatment (Laudet et al., 2009). Therefore, we aimed to identify potential homogeneous groups of participants following distinct LS trajectories.

Earlier assessments of the main outcomes of our trial have shown that XT-NTX was non-inferior to buprenorphine-naloxone (BP-NLX) in terms of retention and abstinence from illicit opioids, and in secondary analyses, it performed better than BP-NLX (Tanum et al., 2017). To our knowledge, no previous study has explored how treatment with XR-NTX influences LS compared to BP-NLX. Hence, this is the first study to assess LS among opioid-dependent individuals receiving XR-NTX treatment in a randomized open-label trial phase.

The main objective of this study was to assess changes in LS in the course of treatment. We hypothesized that treatment with short-term XR-NTX would be associated with increased LS among opioid dependent individuals compared to treatment with BP-NLX, and with further increased LS during longer-term treatment with XR-NTX. In addition, we aimed to assess the association between LS and illicit opioid use; years of opioid use; and subjective measures of social relationships such as satisfaction with civil status, with living arrangements, and with leisure time.

2. Methods

2.1 Design

An open-label controlled 12-week clinical trial, with either monthly intramuscular injection of XR-NTX or daily sublingual BP-NLX, performed randomization using a permuted block algorithm. A subsequent 36-week open-label follow-up study included participants who continued on XR-NTX and participants who switched from BP-NLX to XR-NTX (Fig. 1). A more detailed description of the study design is available in Kunoe et al. (2016) and Tanum et al. (2017). The study took place at 5 research hospitals in south east and western Norway between November 2012 and July 2016.

Study staff obtained informed consent from eligible participants. The Regional Committee for Medical and Health Research Ethics, South-Eastern Norway, the Norwegian Medicines Agency, and the boards of research ethics at the participating hospitals in 2011 approved the study (#2011/1320).

2.2 Measures

2.2.1 Life satisfaction 'present' item

At baseline and every 4 weeks during randomization and follow-up, the study assessed participants for global LS using the Temporal Satisfaction with Life Scale (TSWLS) "present" items (Pavot et al., 1998), based on the Satisfaction with Life Scale (SWLS) (Diener et al., 1985). Research has demonstrated the original SWLS to have a strong internal consistency and a moderate temporal stability with Cronbach's alpha of 0.87, a 2-month test-retest reliability of 0.82 (Diener et al., 1985), and an acceptable convergent validity (Pavot & Diener, 2008). The short 5-item instrument has a 7-point Likert-type scale ranging from 1 (strongly disagree) to 7 (strongly agree).

2.2.2 Covariates

The study used the European version of the Addiction Severity Index (EuropASI) every 4 weeks to register the number of days of heroin and other illicit opioid use (Kokkevi & Hargers, 1995), using the time-line follow-back method. In addition, study staff performed weekly urine drug tests in the randomized controlled trial. The study collected the number of years of opioid use at inclusion.

The study measured social relationships with three questions from the EuropASI. The questions were: "Are you satisfied with your civil status?"; "Are you satisfied with your living arrangements?"; and "Are you satisfied with spending your leisure time like this?" The questions had three possible responses: no (0), indifferent (1), and yes (2).

2.3 Procedures

Men or women aged 18 to 60 years with physical dependence on opioids according to the DSM-IV criteria were eligible to participate in the study. Alcohol dependence, pregnancy or breastfeeding, and serious mental (based on MINI 6.0) or somatic illness that could interfere with study participation were exclusion criteria. Women of childbearing potential had to use contraceptive methods.

After screening for psychiatric disorders and serious somatic diseases, eligible participants were referred to the in-patient detoxification before they were randomly allocated to either 380 mg XR-NTX every 4th week (Vivitrol®) or daily sublingual BP-NLX, 4:1–24:6 mg/d, with a target dose of 16 mg/day (Suboxone®). BP-NLX was administered during daily or near daily visits at the local OMT clinic, resulting in often more than 20 visits every month. XR-NTX was administered every 28 days at the study sites. Both groups had scheduled follow-up visits with

data collection every 4 weeks. All participants were requested to attend regular OMT program counseling.

After the completion of the 12-week trial, all participants, including those who had dropped out, could choose one of the two study medications. Only five participants chose BP-NLX, and no participant switched from XR-NTX to BP-NLX. Due to this distribution of participants in the follow-up period, the research team changed the original trial design to a cohort design, splitting the participants into one group that continued on XR-NTX from the randomized phase and another group that switched from BP-NLX to XR-NTX on entering follow-up. Participants on BP-NLX underwent detoxification and were in a controlled environment for a minimum of 72 h before entering the follow-up study. Participants did not receive any monetary payments for taking part in the study.

2.4 Statistical analyses

The study team estimated a mixed model with random effects for participants and fixed effects for non-linear time (in weeks), group, and the interaction between time and group to assess the differences between the groups in the TSWL trend. The study performed the analyses separately for the randomized period between the XR-NTX and BP-NLX groups and the follow-up period between continuers and switchers. Research staff performed post hoc analyses to assess the between-group differences at different time points.

The study team estimated three linear mixed models with random effects for participants to assess the association between simultaneously measured TSWL and the use of opioids, adjusted for age and gender; between simultaneously measured TSWL and satisfaction with civil status, satisfaction with living arrangements, and satisfaction with leisure time; and between TSWL and years of opioid use measured at baseline. The models included fixed effects for non-linear time (in weeks) and covariates, but the study did not include stratification by treatment group. We included interactions between time and the covariates. The study used Bayes Information Criterion (BIC), where the smaller value means a better model, to reduce the models for excessive interactions.

As an exploratory approach, the research team estimated a growth mixture model (Nagin & Nagin, 2005) with the attempt to identify potential homogeneous groups of participants following distinct LS trajectories separately in the randomization and follow-up phases of the study. In this analysis, the study assessed all participants simultaneously, i.e. not stratified by treatment group. The approach is designed to identify groups of participants based on individual profiles by using a combination of several statistical criteria. The study used the following criteria: BIC, which assesses model fit by balancing between model complexity and goodness of fit; average within-group probabilities representing classification accuracy of at

least 0.80; reasonable group sizes; and non-overlapping 95% confidence intervals (CIs) for trajectories in identified groups. The logistic regression model assessed the associations between group belonging and several covariates assessed at baseline (treatment group; sex; age; use of opioids; years of opioid use; and satisfaction with civil status, living arrangements, and leisure time).

The study presents results as regression coefficients, standard errors (SE), p-values, and illustrated graphically. We considered results with p-values below 0.05 statistically significant. The research team performed analyses using STATA SE16, SPSS v25, and SAS v9.4.

3. Results

3.1 Participants characteristics

The study randomized a total of 159 participants to either XR-NTX (n = 80) or BP-NLX (n = 79). In the follow-up study, 56 participants continued with XR-NTX and 61 switched to XR-NTX (shown in Fig. 1). Detailed demographic and clinical characteristics for each group are previously published in Tanum et al. (2017) and Latif et al. (2019). Men accounted for 73% of all participants. The average age of individuals was 36.1 years [SD = 8.5]. Prior to the study, 79% were never married; 40% lived alone, 20% had no stable living accommodation, lived with friends, in institutions or in prisons; 40% spent their leisure time with friends and family without drug problems (i.e., stable in OMT), and 36% spent their leisure time alone (see Table 1). At baseline, the XR-NTX and BP-NLX groups displayed similar TSWL distributions (mean [SD], 11.0 [6.9] and 11.3 [7.5], respectively).

3.2 Life satisfaction in study groups

In the trial period, the interactions between time and study group in the mixed model were significant, implying that the groups differed concerning trends in TSWL, presented in Table 2A. The trend in the BP-NLX group was flatter than in the XR-NTX group (see Fig. 2A). According to post hoc analyses, the groups were significantly different at week 4 (p = 0.013) and week 8 (p = 0.002), but not at week 0 or week 12.

At the beginning of the follow-up period, the group continuing on XR-NTX showed a higher TSWL score than the group switching from BP-NLX to XR-NTX (15.4 [7.7] and 13.1 [6.7], respectively). The interactions in the mixed model were significant, implying that the groups differed with respect to the trend in TSWL (see Table 2A). The trend in the group continuing on XR-NTX was flatter than in the group that switched (Fig. 2B). Even though the tendencies in both groups were statistically different, according to post hoc analyses, the groups were

significantly different only at week 16 (p = 0.031) and week 48 (p = 0.025), with the higher TSWL scores in the continuing group.

3.3 Life satisfaction and covariates

In the trial period, a significant trend occurred in TSWL when assessed for all participants, but this trend differed with varying levels of reported use of opioids (see Table 2B and Fig. 3). For those not using opioids at all or using only a few days a month, the TSWL scores were stable through the RCT, with a small increase from baseline to week 12. For those using opioids frequently (20 or more days a month), more use of opioids was associated with lower TSWL scores, particularly at weeks 4 and 8. The differences in TSWL scores were significant for varying use of opioids at week 0 (p = 0.019), week 4 (p = 0.001), and week 8 (p = 0.026). However, at week 12 the LS level was more or less the same independently of the use of opioids (p = 0.562). In the follow-up period, no significant trend occurred in TSWL when including all participants. More use of opioids was associated with, on average, lower TSWL both before (p = 0.027) and after adjustment (p = 0.028) for age and sex. An increase in the use of opioids by one day was associated with a TSWL reduction of, on average, 0.12 points.

Associations between LS and satisfaction with civil status, satisfaction with leisure time, satisfaction with living arrangements, and years of opioid use are presented in Table 2C. In the RCT period, those rating their satisfaction with leisure time as “indifferent” had significantly higher LS than those who were not satisfied (p < 0.001). Satisfaction with civil status, satisfaction with living arrangements, and years of opioid use were not associated with TSWL. In the follow-up period, those rating their satisfaction with living arrangements and with leisure time as “indifferent” had significantly higher TSWL than those who were not satisfied (p = 0.003 and p < 0.001, respectively). The study found no association between TSWL and satisfaction with civil status and years of opioid use in the follow-up period.

3.4 Life satisfaction trajectories

A growth mixture model identified two distinct groups of participants with similar TSWL profiles in the randomization phase of the study and two groups in the follow-up phase, called the low LS and high LS groups (see Table 2D and 2E). In both cases, the average group probabilities were high and well above the pre-specified level, and 95% CIs were not overlapping.

In the randomized phase of the study, the low LS group, constituting the majority of participants (n = 116), had a significantly lower TSWL score at baseline than the high LS group (n = 35) (non-overlapping 95% CIs), as Table 2D shows. The low LS group showed a significant nonlinear development with a slight increase toward week 8, which flattened out toward week

12 (see Fig. 2C). In the low LS group, a significant increase occurred in TSWL scores from week 0 to 12 ($p < 0.001$). In the high LS group, the increase in scores was nearly linear and weaker but still significant from week 0 to 12 ($p = 0.011$).

According to the multiple logistic regression model, odds for belonging to the high LS group were significantly lower among those using more opioids at baseline (OR 0.95 (0.90; 1.00), $p = 0.047$). Moreover, the odds of belonging to the high LS group were significantly higher among those who rated their satisfaction with leisure time as "indifferent" compared to those who answered "not satisfied" (OR 12.88 (3.18; 52.23), $p < 0.001$). The study identified no other significant associations (numbers not shown).

In the follow-up period, the low LS group also constituted the majority of the participants (n = 77); see Table 2E. The low LS group showed stable and significantly lower TSWL scores at week 16 and throughout the follow-up compared to the high LS group (n = 41). The high LS group showed a non-linear increase in scores toward week 28 but flattened out toward week 48, as Fig. 2D shows. An increase in TSWL scores was significant from week 16 to week 48 ($p = 0.003$). In the multiple logistic regression model, the only covariate associated with the group belonging in the follow-up period was satisfaction with leisure time. Odds of belonging to the high LS group were significantly higher among those who answered "indifferent" compared to those who answered "not satisfied" (OR 3.47 (1.18; 10.18), $p = 0.023$).

4. Discussion

To our knowledge, this is the first study assessing changes in LS in the course of short-term XR-NTX treatment compared to BP-NLX among opioid-dependent individuals, and further LS changes during longer-term treatment with XR-NTX using the TSWL scale.

We found a moderate increase in TSWL scores in both randomized treatment groups, with a significant difference between the groups at weeks 4 and 8 in favor of the XR-NTX group. As shown for the main outcomes of our trial, XR-NTX was non-inferior and actually performed better than BP-NLX (Tanum et al., 2017), thus the difference in LS trends favoring XR-NTX may not be surprising.

Possible explanations for the difference in LS between the treatment groups may be the treatment structure and motivation for treatment with XR-NTX. The observed daily or near daily dosing of BP-NLX may have had a negative impact on participants' LS, especially among participants who joined the study to obtain XR-NTX treatment but were randomized to BP-NLX. Patients may perceive the daily supervised dosing at OMT outpatient clinics or pharmacies as an act of mistrust and suspicion. In a previous qualitative study of OMT, patients

reported a better life with OMT despite having to comply with rules and regulations such as observing dose intake (Granerud & Toft, 2015).

Although OMT is widely available and fully funded by the government in Norway (Riksheim et al., 2014), most participants were highly interested in receiving the prolonged-release opioid antagonist naltrexone. In fact, the study attracted more than 40% of participants who were not in the OMT program (Solli et al., 2019). Our previous study found that participants who received XR-NTX were satisfied with it and were willing to recommend XR-NTX to others (Tanum et al., 2017). This finding may indicate that not all opioid dependent people are satisfied with the present structure of OMT, probably because it can be time-consuming, stigmatizing, and tempting to use illicit drugs (Steiro et al., 2020; Velasquez et al., 2019; Yarborough et al., 2016).

In the follow-up period, no significant trend occurred in LS scores when the study assessed all participants together, but in a stratified analysis, we found a significant difference between the groups. The group that continued XR-NTX treatment showed higher LS at the beginning and the end of the follow-up period and had a flatter trend throughout the entire follow-up compared to the group that switched to XR-NTX. The changes in LS among our study participants appeared to be closely associated with a high use of illicit opioids, and continued abstinence from opioids seemed important to maintain higher LS. A recent study of first-time OMT patients reported the same trend, where higher LS was related to lower opioid use over the course of one year of treatment (Carlsen et al., 2020). Likewise, the study by Hagen et al. (2017) found a link between LS and opioid use, with absentees reporting higher LS compared to the relapse group. The relationship between LS and opioid use may be explained, in part, by the motivation to focus on the recovery process and thereby abstain from substance use (Laudet et al., 2009). Previous XR-NTX studies have suggested that participants' higher motivation for abstinence might be related to reduction in opioid use (Kunoe et al., 2009; Lee et al., 2018; Tanum et al., 2017).

LS among adults with opioid dependence is heterogeneous. In this study, LS followed two different trajectories identified by the growth mixture model: a high and a low level. Most of the participants belonged to the group with the low LS level. The low LS group showed a slight improvement in the randomized part of the study and, surprisingly, remained relatively stable and low during the follow-up part of the study. That those participants did not show any change in LS during long-term treatment is worrisome. Even though the majority were initially highly interested in XR-NTX treatment, for a number of reasons they seemed to be disappointed with their life situation, expressing it in unchanged LS. These participants may have had higher expectations for the treatment than were met during the study (Muthulingam et al., 2019).

For some individuals, long-acting naltrexone treatment may have acted as a physiological and social stressor due to forced abstinence from opioids and, thus, eliminating the option to address stress by using opioids (Inagaki et al., 2019). Therefore, the LS changes may be further explained by individual differences in coping strategies (Hyman et al., 2007; Kornør & Nordvik, 2007) or even having a low desire to cope with increased stress at all (Hyman et al., 2009), depending on the personality traits. Variation in personality traits and individual genetics may be related to how participants expressed their well-being and LS (Røysamb et al., 2018).

Limitations

Our findings should be interpreted with caution. The study findings can only be generalized to opioid-dependent individuals with high motivation for opioid abstinence. Our participants were probably more motivated for treatment with XR-NTX compared to most individuals being offered such treatment in a clinical setting. Further, they did not suffer from any serious mental or physical illness or alcoholism. The number of participants was also too limited to provide any therapeutic conclusions. In our study, participants reported indifference toward satisfaction with living arrangements and leisure time, which was associated with their LS. This finding should be interpreted with caution, since participants did not elaborate on their answers but only indicated being indifferent toward their social circumstances.

Conclusions

XR-NTX treatment given once a month is associated with higher LS, as measured by TSWL, compared to daily use of BP-NLX. The majority of participants had relatively low TSWL scores throughout the study and did not report any change in TSWL during longer-term treatment. The study found a significant relationship between more frequent use of illicit opioids and a low or decreased LS during the follow-up phase of the study.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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Table 1. Baseline demographic and clinical characteristics of participants (n = 159).

Characteristics	Frequencies or mean (SD)
Sex, *n. (%)**	
Men	115 (73)
Women	44 (27)
Age, *mean (SD), y**	36.1 (8.5)
Civil status, *n. (%)*	
never married	123 (79)
married	8 (5)
other (divorced, separated, widowed)	25 (16)
Satisfaction with civil status, *n. (%)*	
no	42 (27)
indifferent	100 (65)
yes	11 (7)
Common living situation past 3 years, *n. (%)*	
alone	61 (40)
with partner only	27 (18)
with family	33 (22)
no stable living situation	31 (20)
Satisfaction with living arrangements, *n. (%)*	
no	58 (40)
indifferent	73 (51)
yes	13 (9)
Leisure time mostly spent, *n. (%)*	
alone	42 (36)
with family/friends *without* drugs problem	47 (40)
with family/friends *with* drugs problem	28 (24)
Satisfaction with leisure time, *n. (%)*	
no	60 (51)
indifferent	47 (40)
yes	10 (9)
Years of illicit opioid use, *mean (SD)**	7.6 (6.4)
Years of injecting substance use, *mean (SD)**	10.1 (9.0)
Life satisfaction 'present' item, *mean (SD)*	11.1 (7.2)

***Demographic and clinical characteristics for each group are published in Tanum et al., 2017 and Latif et al., 2019.**

Table 2. Linear mixed model assessing the differences between **(A)** the extended-release naltrexone (XR-NTX) and buprenorphine-naloxone (BP-NLX) groups in Temporary Satisfaction with Life (TSWL) trend during the randomized trial and between continuers and switchers in the follow-up period (BP-NLX group was a reference in the trial. Switch group was a reference in the follow-up); (**B**) TSWL and the use of opioids, adjusted for age and gender; (**C**) TSWL and satisfaction with civil status, satisfaction with living arrangements, and satisfaction with leisure time; and between TSWL and years of opioid. Growth mixture model assessing groups among study participants in TSWL in **(D)** the trial and **(E)** the follow-up period. Two groups of participants were identified in each study period, the low LS and high LS.

	Trial period		**Follow-up**	
Parameter	Regression coefficient (SE)	p-value	Regression coefficient (SE)	p-value
(A) Study groups				
Intercept	11.26 (0.84)	**<0.001**	6.76 (2.47)	**0.006**
Week	0.38 (0.25)	0.125	0.55 (0.16)	**0.001**
Week x Week	-0.02 (0.02)	0.373	-0.008 (0.003)	**0.001**
Group (BP-NLX – ref.)*	0.07 (1.19)	0.951	10.75 (3.58)	**0.003**
Week x Group	0.93 (0.35)	**0.008**	-0.74 (0.23)	**0.002**
Week x Week x Group	-0.06 (0.03)	**0.028**	0.01 (0.004)	**0.001**
(B) Use of illicit opioids				
Intercept	11.96 (2.63)	**<0.001**	12.01 (3.60)	**0.001**
Week	0.79 (0.22)	**<0.001**	0.18 (0.12)	0.122
Week x Week	-0.05 (0.02)	**0.004**	-0.002 (0.002)	0.181
Use of opioids	-0.09 (0.04)	**0.020**	-0.12 (0.06)	0.028
Week x Use of opioids	-0.07 (0.03)	**0.009**		
Week x Week x Use of opioids	0.006 (0.002)	**0.011**		
Age	-0.003 (0.06)	0.961	-0.002 (0.07)	0.981
Sex	0.35 (1.09)	0.749	0.20 (1.45)	0.889
(C) Covariates				
Satisfaction with civil status				
No – ref.	0		0	
Indifferent	0.23 (0.90)	0.795	0.90 (0.71)	0.207
Yes	-0.82 (1.36)	0.543	0.12 (0.99)	0.902
Satisfaction with living arrangements				
No – ref.	0		0	
Indifferent	1.40 (0.80)	0.083	1.75 (0.60)	**0.003**
Yes	0.65 (1.22)	0.596	1.09 (0.98)	0.268
Satisfaction with leisure time				
No – ref.	0		0	
Indifferent	4.11 (0.79)	**<0.001**	2.47 (0.60)	**<0.001**
Yes	1.88 (1.25)	0.132	1.20 (0.91)	0.189
Years of opioid use	-0.08 (0.08)	0.318	-0.17 (0.11)	0.125
(D) Trajectories, Trial period	**Low LS (N=116, 76.8%)**		**High LS (N=35, 23.2%)**	
Intercept	7.16 (0.76)	**<0.001**	19.53 (1.62)	**<0.001**
Linear	1.19 (0.28)	**<0.001**	0.86 (0.53)	**0.104**
Quadratic	-0.07 (0.02)	**0.002**	-0.04 (0.04)	0.345
Average group probability		0.96		0.86
(E) Trajectories, Follow-up	**Low LS (N=77, 65.3%)**		**High LS (N=41, 34.7%)**	
Intercept	10.53 (0.94)	**<0.001**	9.14 (4.32)	**0.035**
Linear	0.02 (0.03)	0.571	0.89 (0.30)	**0.003**
Quadratic			-0.01 (0.005)	**0.009**
Average group probability		0.97		0.92

Figure 1. CONSORT Flowchart

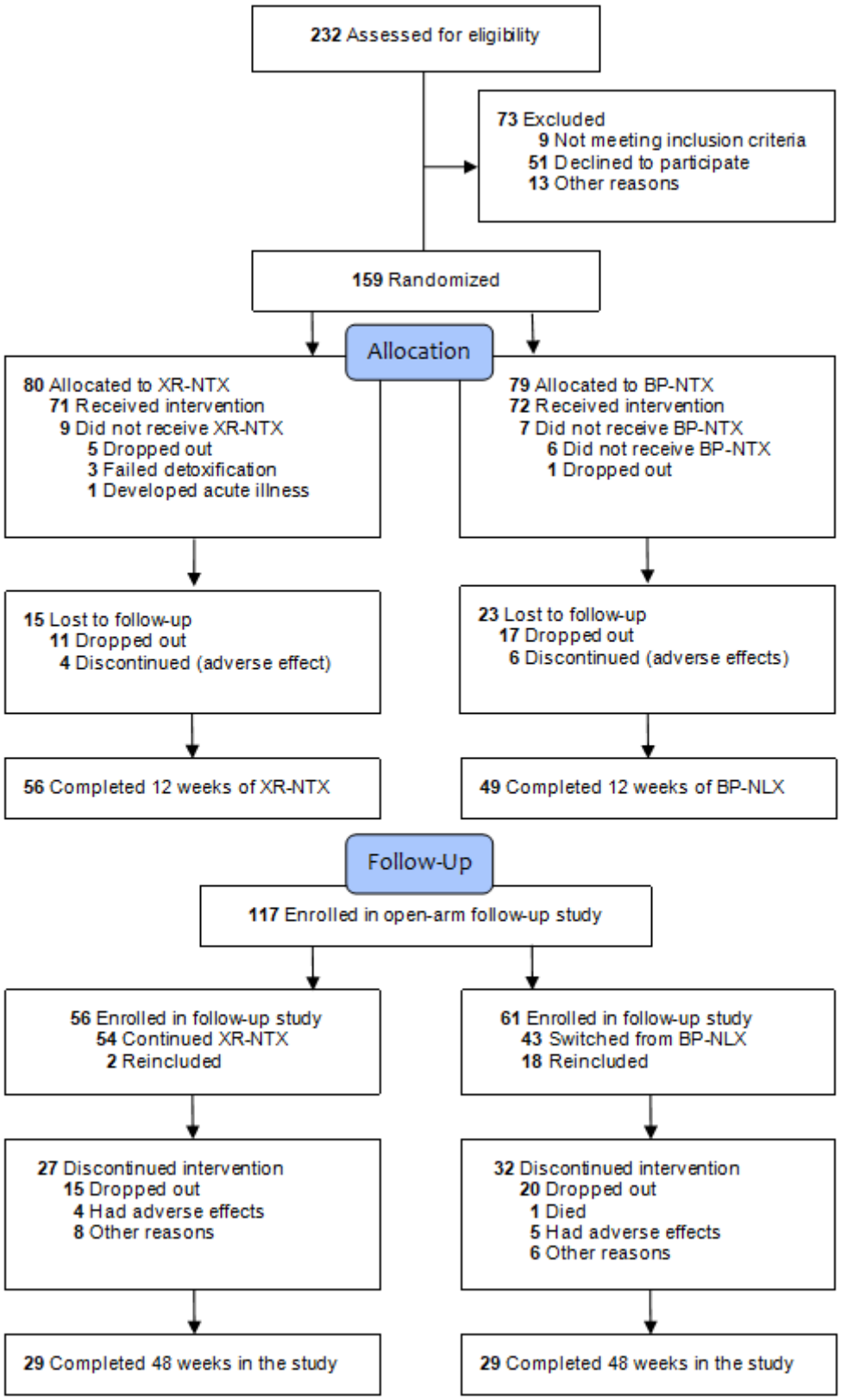

Figure 2. Changes in life satisfaction among study participants in the randomized trial (from weeks 0 to 12) and follow-up period (from weeks 16 to 48) measured by the TSWL, 'present' item questionnaire. **(A)** TSWL scores among participants randomized to XR-NTX and BP-NLX treatment and **(B)** In the follow-up period, the TSWL scores among the group continuing with XR-NTX and the group switched from BP-NLX to XR-NTX treatment; results of mixed model. Trajectories of life satisfaction in two groups of participants identified by growth mixture model not stratified by treatment group **(C)** in the trial and **(D)** in the follow-up period.

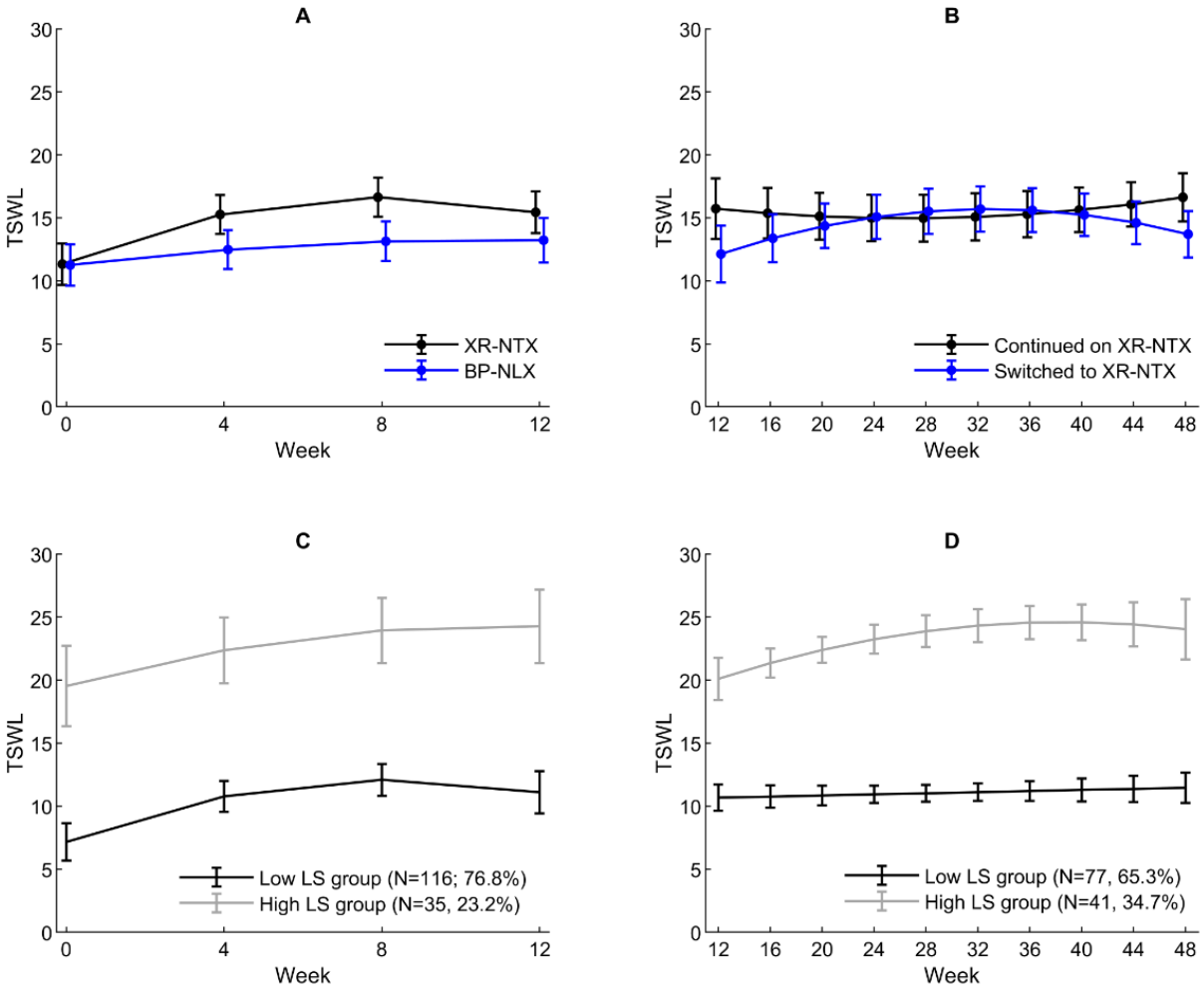

Figure 3. A trend in Temporary Satisfaction with Life (TSWL) by use of illicit opioids when assessing for all participants together every four weeks using EropASI questionnaire in the randomized study. The different colors indicate the number of days of opioid use.