

Title

Observational Characterization of Self-Reported SR-17018 Exposure and Outcomes in Individuals With Prior Opioid Use Histories

Author

Mark Picard

Independent Researcher
Denver, Colorado, USA

ORCID: [<https://orcid.org/0009-0004-5138-0637>]

Email: [nngozo@protonmail.com]

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Conflict of Interest Statement

The author reports no commercial or financial relationships related to SR-17018 at the time of publication.

Ethical Statement

This study involved anonymous, voluntary self-reported survey responses. No personally identifying information was collected.

Abstract

Opioid withdrawal remains a significant challenge in both clinical and harm reduction settings, particularly among individuals with repeated unsuccessful attempts at cessation. SR-17018 is a μ -opioid receptor agonist with atypical signaling properties that has demonstrated altered receptor regulation and signaling dynamics in preclinical studies, although the translational relevance of these findings in humans remains unknown. Prior work involving biased or functionally selective μ -opioid receptor agonists has also demonstrated that preclinical signaling profiles do not necessarily predict improved clinical outcomes, underscoring the need for cautious interpretation of translational hypotheses.

This study presents a descriptive analysis of a self-reported observational registry (N = 36) examining real-world SR-17018 exposure among individuals with prior opioid use histories. Participants represented a heterogeneous population with varied substance use backgrounds, including kratom-derived 7-hydroxymitragynine products, fentanyl-associated street opioids, methadone, buprenorphine, oxycodone, heroin, and research chemical opioids (Table 1). A substantial proportion of participants reported repeated prior detoxification attempts using other methods, with 72.2% reporting three or more prior unsuccessful attempts (Figure 1A).

Within this observational cohort, 38.9% of participants reported full cessation of opioid use during SR-17018 exposure, while 52.8% reported meaningful reduction in opioid use (Figure 1B). Smaller proportions reported no change (5.6%) or relapse to prior opioid use patterns (2.8%). These outcomes were self-reported and were not independently verified.

Temporal characteristics of SR-17018 use varied across participants. Most respondents reported dosing SR-17018 three or more times daily (77.8%), with perceived effects commonly lasting approximately 4–8 hours per dose (58.3%) (Figure 2). Continued SR-17018 exposure following opioid discontinuation most commonly lasted between 4–7 days or 1–2 weeks.

Reported adverse effects included anxiety, sweating, sedation, drowsiness, insomnia, and gastrointestinal symptoms, although most participants described overall side effect severity as mild to moderate. A minority of respondents reported subjective breathing-related concerns or significant functional impairment associated with SR-17018 exposure.

These findings provide preliminary observational data describing self-reported SR-17018 exposure patterns and perceived outcomes in a treatment-experienced population with prior opioid use histories. However, the uncontrolled, self-reported, cross-sectional nature of the registry substantially limits interpretation. No conclusions regarding safety, efficacy, or clinical applicability can be drawn from these data. Controlled human studies are required to further characterize the pharmacology, tolerability, misuse potential, and clinical relevance of SR-17018 and related atypical μ -opioid receptor agonists.

1. Overview

Opioid dependence continues to present substantial challenges across both clinical and harm reduction settings, particularly in the context of high-potency synthetic opioids and repeated treatment failure. While established pharmacotherapies such as methadone and buprenorphine provide effective stabilization for many individuals, their mechanisms of action involve sustained μ -opioid receptor activation and often require long-term maintenance or gradual tapering [1,2]. As a result, alternative pharmacological approaches that may influence withdrawal trajectories or stabilization patterns remain an area of ongoing interest.

Recent developments in opioid receptor pharmacology have highlighted the concept of biased agonism, in which ligands may differentially engage intracellular signaling pathways [3,4]. SR-17018 is a μ -opioid receptor agonist that has been characterized in preclinical studies as exhibiting altered signaling and receptor regulatory properties, including reduced β -arrestin2 recruitment relative to some conventional opioids [5,6]. In animal models, these properties have been associated with context-dependent differences in tolerance development, antinociception, and withdrawal-related outcomes. However, the translational relevance of these findings in humans remains unclear, and prior investigations involving atypical or biased μ -opioid receptor agonists have demonstrated that preclinical signaling differences do not necessarily predict improved clinical outcomes.

Despite these pharmacological observations, there is limited information regarding real-world SR-17018 exposure in human populations, particularly within harm reduction environments. Informal reports and online discussions have described potential signals related to withdrawal management and opioid use reduction; however, these observations remain largely unstructured and insufficiently characterized.

To address this gap, the present study analyzes data from a self-reported observational registry of individuals reporting SR-17018 use in the context of prior opioid exposure. The aim is not to establish efficacy or clinical utility, but rather to describe participant characteristics, usage patterns, temporal characteristics of exposure, self-reported outcomes, and adverse effects within a real-world observational cohort. These findings are intended to generate descriptive observational data and inform future controlled research efforts.

2. Methods

2.1 Study Design and Data Source

This study presents a descriptive analysis of data obtained from a self-reported observational registry of individuals using SR-17018 in the context of opioid dependence and withdrawal. The registry was designed to capture real-world experiences, including substance use history, SR-17018 usage patterns, and self-reported outcomes.

Data were collected anonymously through a structured online survey. Participation was voluntary, and no incentives were provided. Responses were recorded without identifying information to preserve participant anonymity.

The survey instrument is available at: [<https://www.sr17018study.com/>]

2.2 Participants

A total of 36 participants were included in the analysis. Inclusion criteria consisted of:

- self-reported history of opioid use or dependence
- self-reported use of SR-17018
- completion of key survey fields related to substance use history and outcomes

No exclusion criteria were applied beyond incomplete or unusable responses.

2.3 Measures

The survey captured the following domains:

Substance Use History

- primary opioid or substance of use
 - duration of opioid use (categorized)
 - number of prior detoxification or withdrawal attempts
-

SR-17018 Use

- self-reported use in the context of withdrawal or opioid reduction
 - qualitative descriptions of dosing patterns (not standardized)
-

Outcomes

Participants were asked to describe outcomes associated with SR-17018 use. Responses were categorized into:

- **Full cessation** – complete discontinuation of opioid use
- **Reduction in use** – meaningful decrease without full cessation
- **Other improvement** – subjective improvements (e.g., reduced withdrawal severity, improved function, reduced cravings) without clear reduction or cessation
- **No change**
- **Worsening/relapse**

For analysis, “any improvement” was defined as the combination of full cessation, reduction in use, or other reported improvements.

Safety and Tolerability

Participants reported side effects, which were categorized as:

- none
- mild
- moderate
- severe

Participants were also asked whether SR-17018 use was discontinued due to adverse effects.

2.4 Data Processing and Analysis

Data were reviewed and manually categorized to standardize free-text responses into predefined outcome and safety categories. Descriptive statistics were calculated, including counts and percentages for all variables.

No inferential statistical analyses were performed due to the observational, self-reported nature of the dataset and the limited sample size. The analysis is intended to be descriptive and hypothesis-generating.

2.5 Ethical Considerations

This study did not involve intervention, identifiable data collection, or direct interaction with participants beyond voluntary survey completion. All responses were collected anonymously, and no personal identifiers were obtained.

Given the observational and anonymized nature of the dataset, and the absence of intervention, this study is consistent with commonly accepted criteria for research not requiring formal ethical review. However, interpretations should be made with caution due to the self-reported nature of the data.

2.6 Disclaimer

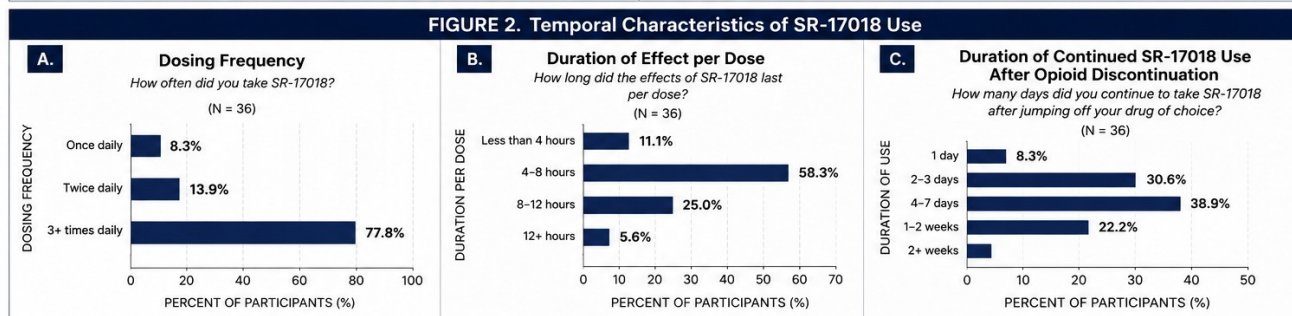
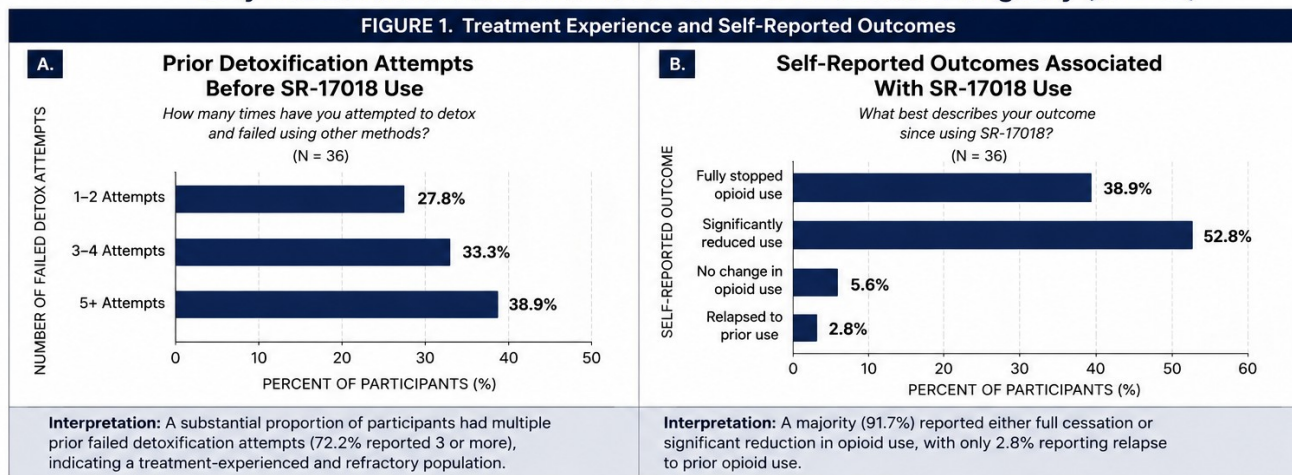
This report is based on observational, self-reported data and is intended for research and informational purposes only. It does not constitute medical advice or clinical guidance. SR-17018 has not been evaluated in controlled clinical trials for safety or efficacy in humans, and any interpretation of these findings should be made with caution.

3. Results

3.1 Participant Characteristics

Participant characteristics and self-reported outcomes associated with SR-17018 use are summarized in Figures 1 and 2.

Early Observational Data From the SR-17018 Outcome Registry (N = 36)



SR-17018 Outcome Registry is an anonymous, voluntary survey. Findings reflect self-reported data and are not intended to establish efficacy.

Figure 1. Participant outcomes and prior cessation attempts (N = 30).

(A) Distribution of self-reported number of prior detoxification or withdrawal attempts, highlighting a population with repeated prior treatment failure.

(B) Distribution of self-reported outcomes associated with SR-17018 use, including, full cessation, reduction in use, other improvement, no change, and worsening. “Any improvement” reflects the combined proportion of cessation, reduction, and other reported benefits.

Figure 2. Temporal Characteristics of SR-17018 Use and Self-Reported Effect Duration.

Most participants reported dosing SR-17018 three or more times daily (77.8%), with the majority describing effects lasting approximately 4–8 hours per dose (58.3%). Continued use following discontinuation of the participant’s prior opioid most commonly lasted between 4–7 days (38.9%) or 1–2 weeks (22.2%). These findings provide preliminary observational insight into self-reported temporal patterns of SR-17018 use, including dosing frequency, perceived duration of effects, and duration of continued administration following opioid discontinuation.

3.2 Self-Reported Outcomes

Self-reported outcomes associated with SR-17018 exposure are summarized in Figure 1B. Within the observational cohort, 38.9% of participants reported full cessation of opioid use during SR-17018 exposure, while 52.8% reported meaningful reduction in opioid use without complete discontinuation. Smaller proportions of participants reported no meaningful change (5.6%) or relapse to prior opioid use patterns (2.8%).

Reported reductions in opioid use were self-defined by participants and were not independently verified. In qualitative responses, some participants additionally described perceived reductions in withdrawal severity, decreased cravings, or improvements in overall stability or functional capacity during SR-17018 exposure. However, these observations were heterogeneous and remain inherently limited by the self-reported, uncontrolled nature of the registry.

These findings should be interpreted cautiously and are not intended to establish efficacy or clinical utility. Rather, they provide descriptive observational data regarding self-reported outcomes in a treatment-experienced population with prior opioid exposure histories.

3.3 Safety and Tolerability

Self-reported safety and tolerability findings are summarized in Figure 2 and Supplementary Table 1. Reported adverse effects associated with SR-17018 exposure varied across participants, although most respondents described overall side effect severity as mild to moderate. Specifically, 44.4% of participants characterized side effects as mild, 47.2% as moderate, and 8.3% reported no side effects. No participants reported severe side effect severity ratings within the structured severity assessment.

Commonly reported adverse effects included anxiety (19.4%), sweating (11.1%), constipation (11.1%), sedation or drowsiness-related effects, and other heterogeneous symptoms described in free-text responses, including vivid dreams, low motivation, and excessive daytime sleepiness.

A minority of participants (8.3%) reported subjective breathing-related concerns during SR-17018 exposure, although descriptions varied substantially and were not medically verified. Most participants reported that side effects interfered either slightly or moderately with daily functioning, while only a small minority described significant impairment.

Importantly, no participants reported discontinuation of SR-17018 exposure directly attributable to adverse effects within the observational period. However, interpretation of tolerability findings is substantially limited by the self-reported and uncontrolled nature of the registry, the absence of medical assessment, and the presence of concurrent substance use among some participants.

3.4 Summary of Observational Findings

Across this observational dataset, participants described a range of self-reported outcomes associated with SR-17018 exposure in the context of prior opioid use histories and attempted opioid reduction or

discontinuation. Reported outcomes included both full cessation and reduction in opioid use within a treatment-experienced population characterized by repeated prior detoxification attempts and heterogeneous substance exposure backgrounds.

Importantly, these findings reflect descriptive self-reported observations rather than controlled clinical outcomes. The registry design lacked standardized dosing protocols, medical verification, longitudinal follow-up, or objective outcome measurements, substantially limiting interpretation and preventing causal conclusions regarding efficacy or safety.

The observational context of the cohort is also important to consider. Participants were self-selected individuals reporting SR-17018 exposure specifically in relation to opioid withdrawal, reduction, or cessation attempts, frequently following multiple prior unsuccessful detoxification efforts. As shown in Figure 1A, 72.2% of participants reported three or more prior detoxification attempts using other methods.

These findings suggest that the cohort represents a population with substantial prior treatment exposure and repeated cessation difficulty. While some participants described perceived improvements during SR-17018 exposure, these observations should be interpreted cautiously and viewed primarily as hypothesis-generating descriptive data intended to inform future controlled research.

4. Discussion

This study presents a descriptive analysis of a self-reported observational registry examining SR-17018 exposure among individuals with prior opioid use histories. Within this cohort, many participants described self-reported improvement during SR-17018 exposure, including opioid cessation, reduction in use, or subjective changes such as reduced withdrawal severity, decreased cravings, or improved functional stability. These observations were reported within a heterogeneous population characterized by varied substance exposure histories and a high prevalence of repeated prior detoxification attempts.

The findings may be considered in the context of the known preclinical pharmacology of SR-17018. Prior studies have characterized SR-17018 as a μ -opioid receptor agonist exhibiting altered receptor signaling and regulatory properties relative to some conventional opioids, including reduced β -arrestin2 recruitment and differences in receptor phosphorylation dynamics [5–8]. In preclinical models, these properties have been associated with context-dependent differences in tolerance development, antinociceptive responses, and withdrawal-related outcomes. However, the translational significance of these signaling differences remains uncertain.

Importantly, prior investigations involving atypical or biased μ -opioid receptor agonists have demonstrated that altered intracellular signaling profiles do not necessarily translate into improved clinical safety or therapeutic outcomes in humans. Factors such as intrinsic efficacy, receptor regulation, pharmacokinetics, adaptive neurobiology, and polysubstance exposure may substantially influence clinical outcomes beyond simplified models of biased agonism alone. As a result, the

observational findings reported here should not be interpreted as validation of mechanistic hypotheses regarding biased signaling or reduced harm potential.

Nonetheless, some participants described subjective experiences suggesting altered withdrawal trajectories or perceived stabilization during SR-17018 exposure. Reported observations included reductions in withdrawal severity, reductions in opioid use, and improved ability to function during cessation attempts. While these findings remain entirely self-reported and uncontrolled, they may support further investigation into how atypical μ -opioid receptor agonists influence subjective withdrawal experiences and opioid use patterns in real-world settings.

The treatment history of the cohort is also relevant when interpreting the observational findings. A substantial proportion of participants reported repeated prior unsuccessful detoxification attempts using other approaches (Figure 1A), suggesting that the cohort represents a population with significant prior treatment exposure and cessation difficulty. This context may be important when considering the descriptive outcome patterns observed within the registry, although no conclusions regarding comparative efficacy can be drawn.

Temporal characteristics of SR-17018 exposure observed in this cohort may also warrant further study. Most participants reported dosing SR-17018 three or more times daily, with perceived effects commonly lasting between 4–8 hours per dose (Figure 2). These self-reported observations may suggest complex pharmacodynamic or behavioral use patterns that are not fully captured by existing preclinical literature and may be relevant to future observational or pharmacokinetic investigations.

Safety and tolerability findings should likewise be interpreted cautiously. Although many participants described side effects as mild or moderate, adverse effects including anxiety, sedation, excessive daytime sleepiness, sweating, and subjective breathing-related concerns were reported. Additionally, a proportion of participants reported concurrent benzodiazepine, alcohol, stimulant, or other opioid use during SR-17018 exposure, substantially complicating interpretation of tolerability findings and increasing the potential for confounding effects.

Several important limitations substantially restrict interpretation of the present findings. The dataset is entirely self-reported and subject to recall bias, reporting bias, selection bias, and variability in participant interpretation of survey items. Outcomes were not independently verified, dosing patterns were heterogeneous and uncontrolled, and no standardized instruments were used to assess withdrawal severity, craving, or functional outcomes. Additionally, the cross-sectional observational design precludes causal inference, and the modest sample size limits generalizability.

Despite these limitations, the present study contributes preliminary descriptive observational data regarding real-world SR-17018 exposure within a treatment-experienced population reporting prior opioid use. Rather than establishing efficacy or clinical utility, these findings may help inform future controlled observational, pharmacological, and clinical investigations examining atypical μ -opioid receptor agonists and their potential relevance to opioid withdrawal, dependence, and harm reduction contexts.

5. Limitations

This study has several important limitations. The dataset is based entirely on self-reported responses, introducing the potential for recall bias, reporting bias, and variability in interpretation of survey questions. Outcomes were not verified through objective measures, and no standardized clinical instruments were used to assess withdrawal severity, craving, sedation, respiratory effects, or functional outcomes.

The observational and cross-sectional design precludes any causal inference regarding the effects of SR-17018. Additionally, dosing patterns, exposure duration, co-administered substances, and prior opioid histories varied substantially across participants, limiting interpretation of dose-response relationships and preventing standardized comparison between respondents.

The sample size was modest (N = 36), and participants were self-selected individuals who voluntarily completed an online registry. This introduces the possibility of selection bias and limits generalizability to broader populations of individuals with opioid dependence or opioid use disorder.

Importantly, the registry reflects uncontrolled real-world SR-17018 exposure occurring within harm reduction environments rather than structured clinical conditions. Concurrent use of benzodiazepines, alcohol, stimulants, kratom-derived products, and other opioids was reported by some participants, further complicating interpretation of both outcome and tolerability findings.

Finally, while SR-17018 has demonstrated atypical signaling properties in preclinical studies, no controlled human studies currently exist evaluating its pharmacokinetics, safety profile, misuse liability, respiratory effects, or clinical applicability. As such, the present findings should be interpreted solely as preliminary observational data intended to inform future research questions rather than support clinical use.

6. Conclusion

This study presents a descriptive observational analysis of self-reported SR-17018 exposure among individuals with prior opioid use histories. Within this treatment-experienced cohort, many participants described perceived reductions in opioid use, withdrawal severity, or subjective functional impairment during SR-17018 exposure, often following multiple prior unsuccessful detoxification attempts.

These findings do not establish efficacy, safety, or clinical utility. Rather, they provide preliminary observational data describing real-world exposure patterns, temporal characteristics, self-reported outcomes, and adverse effects associated with SR-17018 use in uncontrolled harm reduction contexts.

Given the substantial translational uncertainty surrounding atypical or biased μ -opioid receptor agonists, the findings should be interpreted cautiously. However, the observational signals described in this registry may support further investigation through controlled pharmacological, observational, and clinical research examining SR-17018 and related compounds.

Future work should focus on standardized observational methodologies, pharmacokinetic characterization, longitudinal follow-up, safety assessment, and controlled human studies to better understand the pharmacology, tolerability, misuse potential, and clinical relevance of SR-17018 exposure.

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