Caponnetto P, Triscari S, Prezzavento GC, et al. Exploring the Psychological Side of Fentanyl: A Scoping Review to Disclose the Psychosocial Dimensions of Illicitly Manufactured Fentanyl Users. *Health Psychology Research*. 2024;12. doi:10.52965/001c.120958

General

Exploring the Psychological Side of Fentanyl: A Scoping Review to Disclose the Psychosocial Dimensions of Illicitly Manufactured Fentanyl Users

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Keywords: Fentanyl, Illicitly Manufactured Fentanyl, Fentanyl and Psychology, Fentanyl and Psychological Dependence, Clinical psychology

https://doi.org/10.52965/001c.120958

Health Psychology Research

Vol. 12, 2024

Background

Fentanyl is a powerful opioid. The abuse and overdoses related to Illicitly Manufactured Fentanyl (IMF) have become more prevalent. The majority of clinical studies on fentanyl have focused on its medical and biological aspects, particularly its addictive properties. Few studies have delved into the psychological aspects of illicit fentanyl use, and there is currently no comprehensive review providing a structured psycho-social profile of the population groups most vulnerable to its effects. The goal of this Scoping Review was to construct a psychological and social profile of individuals at risk of using illicit fentanyl. This profile will serve as a guiding force for shaping behavioral policies and public health prevention efforts necessary to face the recent pandemic.

Methods

Following the PRISMA guidelines we conducted a Scoping Review focused on the following research question: What are the practical psycho-social implications of illicit fentanyl use in the global population?

Results

The bibliographic research was carried out in the databases of Medline, Scopus, and PsycNet. The articles resulting from the research phase in the databases listed above produced a total of 17737 reports. After the screening process, 10 studies were included in the scoping review.

Discussion and Conclusion

This scoping review was the first to consistently and systematically outline the psychosocial implications of fentanyl dependence. Users of IMF are consistently younger than other drug users. People using fentanyl have a relatively low perception of risk. On the psycho-social levels, there is a significant correlation between fentanyl use and mental disorders such as suicidal thoughts, anxiety disorders, and depression. The development of psychotherapy, along with digital tools such as apps and online platforms, can be an initial step in addressing this challenge.

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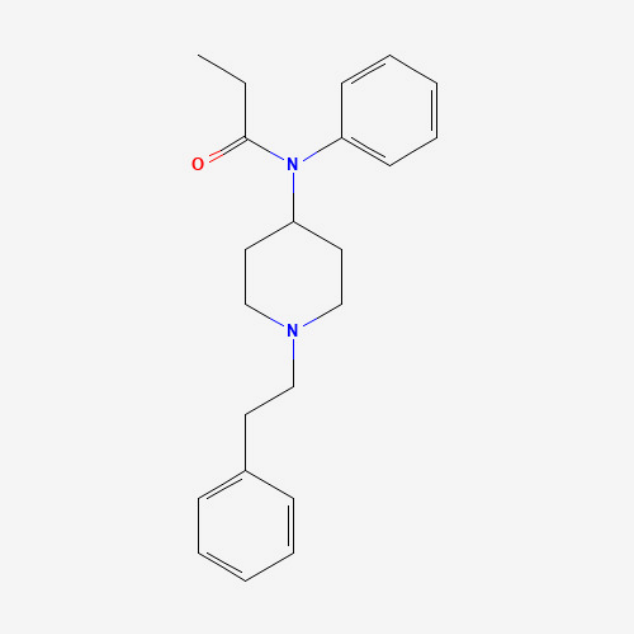

Figure 1. Fentanyl Structure 2D

1. INTRODUCTION

Fentanyl (N-1-(2-phenylethyl)-4-piperidinyl-N-phenyl-propionamide) (Figure 1) was synthesized for the first time by the Belgian company Janssen Pharmaceutica in the late 1950s during the search for effective, fast-acting, and highly potent analgesics.[1,2] Initially designed and synthesized as a valuable therapeutic agent for anesthesia and the management of severe pain, fentanyl exerts analgesic and rewarding effects by binding to and activating μ-opioid receptors (MORs).[3,4] Fentanyl possesses unique pharmacological properties, including rapid onset of action, high potency in activating MOR-associated signaling in vivo (100 times more potent than morphine), high lipophilicity, and induction of muscle rigidity.[5] While fentanyl has a legitimate and important role in the management of pain in the medical field, there has been a worrying increase in the use of this substance as an illicit drug in recent years.[6,7] The abuse and overdoses related to fentanyl use have become more prevalent. Improper and non-compliant use of fentanyl can result in addiction, overdose, and other severe side effects. Additionally, there has been a troubling expansion of fentanyl in the illegal drug market.[8] We will classify this unauthorized use of fentanyl as Illicitly Manufactured Fentanyl (IMF).[9]

According to the latest World Health Organization report, around 296 million people worldwide used drugs at least once in 2021, with about 60 million using opioids. In the United States, drug overdose deaths have increased significantly, with about 70,630 deaths in 2019, half of which involved synthetic opioids like fentanyl.[10]

IMF is frequently mixed with cocaine, methamphetamine, heroin, and other illicit drugs among addicts.[11] Recently, fentanyl has been mixed with xylazine, a sedative for cattle and horses. xylazine, commonly known as "Tranq" or "Zombie Drug," is used to prolong fentanyl's effects.[12] The main acute effects of xylazine include central nervous system depression, bradycardia, and hypotension. Prolonged use may lead to the development of skin lesions and ulcerations, which could necessitate amputation.[13] Combined use of fentanyl and xylazine raises the likelihood of severe poisoning. Since xylazine is not an opioid, its effects cannot be reversed with naloxone, which complicates emergency management.[14]

According to the literature, certain part of the population seem to have a higher susceptibility to the illicit use of fentanyl.[15,16] Socio-cultural characteristics and mental health status emerge as significant factors in identifying these at-risk groups.[17]

The majority of clinical studies on fentanyl have focused on its medical and biological aspects, particularly its addictive properties.[1,18-22] However, there is a lack of cohesive research on the socio-psychological factors and mental health implications of fentanyl use. Few studies have delved into the psychological aspects of illicit fentanyl use, and there is currently no comprehensive review providing a structured psycho-social profile of the population groups most vulnerable to its effects.

The purpose of this Scoping Review is to examine the current state of the art regarding the growing phenomenon of fentanyl abuse and its psychosocial implications. The study aims to specifically contextualize the abuse of IMF, with particular attention to the psycho-social characteristics of typical fentanyl abusers. It also analyzes a fundamental aspect related to the abuse of fentanyl: the perception of the risk of overdose and the associated suicidal behavior. Additionally, in line with the objective of the review, the correlation with psychological and psychiatric disorders is explored. Finally, an overview of the new perspectives of prevention and treatment is provided. In sum, this review seeks to provide a comprehensive understanding of the current state of the art about this global phenomenon, offering insights to guide future research in the field, which is still relatively unexplored, particularly regarding the psychosocial implications of fentanyl abuse.

2. MATERIAL AND METHODS

This scoping review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Extension for Scoping Reviews[23] and focused on the following research question: "*What are the practical psycho-social implications of IMF use in the global population?*"

The review's primary goal was to construct a psychological and social profile of individuals at risk of using illicit fentanyl. This profile will serve as a guiding force for shaping behavioral policies and public health prevention efforts necessary to combat the recent pandemic.

2.1. INFORMATION SOURCES

The bibliographic research was carried out from January 2024 to May 2024 in the databases of MEDLINE, Scopus, and PsycNet using the following string of searches: "Fen-

tanyl and Psychology" or "Fentanyl and Psychological Abuse" or "Fentanyl and Psychological Dependence" or "Fentanyl and Abuse" or "Fentanyl and Dependence" or "Fentanyl and Psychological traits" or "Fentanyl and Motivational traits" or "Fentanyl and Motivation" or "Illicitly manufactured fentanyl and Psychology" or "Illicitly manufactured fentanyl and Psychological Abuse" or "Illicitly manufactured fentanyl and Psychological Dependence" or "Illicitly manufactured fentanyl and Abuse" or "Illicitly manufactured fentanyl and Dependence" or " "Illicitly manufactured fentanyl and Psychological traits" or "Illicitly manufactured fentanyl and Motivation" or " "Illicitly manufactured fentanyl and Motivational Traits" or "Fentanyl and Mental illness" or "Fentanyl and Street Drugs" or "Fentanyl and Psychological Disorders" or "Illicitly manufactured fentanyl and Psychological Disorders" or "Illicitly manufactured fentanyl and Mental Illness".

2.2. ELIGIBILITY CRITERIA

We considered randomized controlled trial (RCT); pilot trial; cross sectional study; qualitative studies; and observational studies that evaluated the psycho-social implications associated with the use of illicit fentanyl. We only included studies that were written in English, with no time limit.

2.3. EXCLUSION CRITERIA

We excluded any studies that evaluated the medical use of fentanyl. We also left out studies that evaluated illicit fentanyl but did not use any measure to assess psycho-social variables.

2.4. DATA COLLECTION PROCESS

We conducted a bibliographic search and we independently screened each resulting article to ensure its adherence to the eligibility criteria. We did not use any automatic screening tools for this purpose.

To extract data from each article, we used a specific format that included the author's name, year of publication, title, nation where the research was conducted, type of study, sample, psychological measures used, and results (Table 1).

The articles that we agreed upon were included in the next screening process. However, in cases where there was no agreement between the evaluators, a brief discussion was held, and a final decision was made jointly by the team on whether to include the articles in the next step.

During the data extraction process, each author selected both qualitative and quantitative psychological results from each study that was included.

2.5. RISK OF BIAS

In the Scoping Review, four rigorous tools were employed to meticulously assess the Risk of Bias. Specifically, the Cochrane risk-of-bias tool for randomized trials (RoB 2)[24] was utilized for the Randomized Controlled Trial; Risk of Bias in Non-randomized Studies - of Exposure (ROBINS-E)[25] for the Cross-Sectional Study; Mixed Methods Appraisal Tool (MMAT)[26,27] for the Mixed Studies, and JBI's critical appraisal tools for the Qualitative Study.[28] The results of the risk assessment are showed in Figures 3, 4, 5, 6.

3. RESULTS

3.1. STUDY SELECTION

The articles resulting from the research phase in the databases listed above produced a total of 17737 reports. The duplicate manuscripts were deleted until a number of 10171 unique reports were produced. These unique reports were examined by the title and abstract and 288 were selected. 279 reports were opened and analyzed in full-text version; of 9 report it was not possible to find the full-text. In conclusion following full-text screening 10 studies were included in the systematic review (Figure 2).

3.2. PSYCHOLOGICAL CHARACTERISTICS OF ILLICITLY MANUFACTURED FENTANYL USERS

Hochstatter et al.[17] and Morales et al.[29] sought to characterize the preference for IMF in 250 and 308 participants, respectively, appropriately stratified. In both cases, the preference for fentanyl was evaluated through surveys. The analysis of the results showed a preference for fentanyl ranging from 21%[17] to 27%[29] among people who use drugs (PWUD), with a peak preference of 31%[17] for those who preferred the mixture of heroin and fentanyl. Consumers who preferred fentanyl were significantly younger than those who preferred other substances.[17,29] The preference for fentanyl of younger subjects was also confirmed by Gun et al.[30] They were also more likely to be white.[17,29] Receiving a prescription for legal fentanyl did not show significant differences between the preference groups for illicit fentanyl[29]; In Morales et al.,[29] the preference for fentanyl was related to the participation of individuals in the underground and illegal economy, which can promote exposure to illicit drugs not prescribed. Kasson et al.,[31] in line with previous research, has observed how the use of fentanyl is declared by anonymous consumers populating online subreddits as a strategy to overcome the problems related to social and employment difficulties. This may be in line with Morales et al.,[29] which points out that fentanyl abuse comes from low socio-economic groups.

3.3. TOLERANCE, ABSTINENCE, AND CRAVING

A study conducted by Hochstatter et al.[17] demonstrated that, compared to those who preferred the heroin-fentanyl mixture, those with an exclusive preference for fentanyl were more prone to experiencing acute drug-related problems such as addiction, inability to stop, and withdrawal symptoms. A further investigation by Kasson et al.[31] highlighted that approximately one-fifth of online posts/comments mentioned high tolerance to fentanyl or withdrawal experiences, with users describing severe symptoms and difficulties in reducing usage. Users frequently discussed

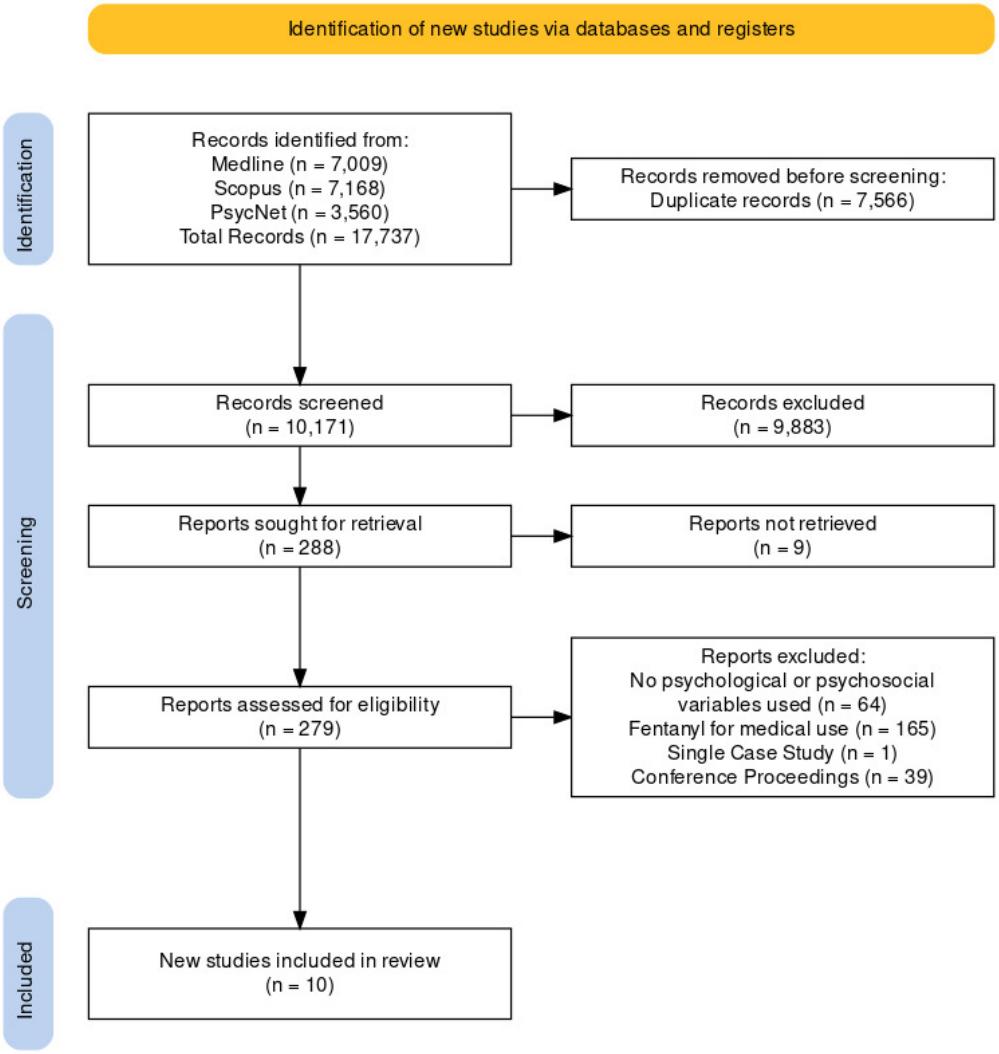

Figure 2. Prisma Flow Chart.

their craving experiences and the challenges of maintaining abstinence due to intense withdrawal symptoms.

These studies underscore the significant challenges faced by individuals using fentanyl, including a greater propensity to develop addiction, high tolerance requiring increasingly higher doses to achieve the same effects, and particularly intense withdrawal symptoms. The persistent craving and difficulties in maintaining abstinence represent further obstacles in the recovery journey of these individuals, highlighting the need for targeted therapeutic interventions and adequate support.[32]

3.4. RISK PERCEPTION AND OVERDOSE

In the study by Morales et al.[29] the participants had witnessed or had direct experience of overdose; nevertheless, this experience did not deter them from continuing to take the substance. This behavior is taken up again in the Brar et al.[33] and Kasson et al. ,[31] where the majority of IMF users did not report a change in their use patterns of the substance, despite awareness of the high risk of experiencing an overdose. Awareness of the risk of fentanyl overdose prompts individuals to change their preferred route of administration to oral or inhalation, rather than intravenous. However, this change alone is insufficient to prevent overdose.[33] In McKnight et al.[34] although some consumers implement strategies that they believe are preventative, such as taking fentanyl in the presence of other people, fentanyl test strips, or having a dose of naloxone available, these strategies are often not enough and make the perception of risk generally low, associated with a high impulsiveness.[31] Harris et al.[35] in line with other research emphasizes a general desensitization against the risk of overdose, also caused by a predetermined vision of life, an external locus of control for which their actions will not remove them from death. Similarly, Gunn et al.,[30] found it challenging to convey risk information to young adults. Most young people described their fentanyl use with confidence and a sense of immunity, dismissing the risk of overdose.

In general, the perception of overdose risk varies considerably between individuals, and is influenced by factors such as education, personal experience and information received.

Table 1. STUDIES CHARACTERISTICS

Authors	*Year*	*Title*	*Nation*	*Study Design*	*Sample*	*Psychological Measures*	*Outcome*
Kasson E, Filiatreau LM, Kaiser N, Davet K, Taylor J, Garg S, El Sherief M, Aledavood T, De Choudhury M, & Cavazos-RehgP.	2023	Using Social Media to Examine Themes Surrounding Fentanyl Misuse and Risk Indicators	USA	Qualitative study	365	Observation and analysis of subreddit data on fentanyl	The analysis revealed that nearly a third of the discourse focused on how substance misuse impairs functionality and quality of life. Polysubstance use was discussed in 27% of the content, while issues of tolerance, dependence, and withdrawal symptoms were featured in 20%. Other notable themes included the identification of drugs through photos, the cutting of substances with other drugs, injectable drugs, and experiences with past overdoses. It was also observed that r/fentanyl users frequently engaged with media-centric subreddits and other drug-related online communities.
He Y, Tang Z, Sun G, Cai C, Wang Y, Yang G, Bao Z	2023	Effectiveness of a Mindfulness Meditation App Based on an Electroencephalography-Based Brain-Computer Interface in Radiofrequency Catheter Ablation for Patients With Atrial Fibrillation: Pilot Randomized Controlled Trial	China	Randomized Controlled Trial	84	Survey	Experimental group with App significantly reduced the use of fentanyl (used as a pain sedative drug) compared to the control group. These results lead us to hypothesize the possibility of replicating this study in contexts where subjects make illicit use of fentanyl.
Karli R. Hochstatter, Mishka Terplan, Shannon Gwin Mitchell, Robert P. Schwartz, Kristi Dusek, Kim Wiremann, Jan Gryczynski	2022	Characteristics and correlates of fentanyl preferences among people with opioid use disorder	U.S.A.	Mixed Methods	250	Survey	The study shows that of the 250 patients, 21% preferred fentanyl The study shows that of the 250 patients, 21% preferred fentanyl alone and 31% preferred the heroin-fentanyl mixture. People who preferred fentanyl were younger, more likely to be white, have a mental illness, be impulsive, and be involved in illegal, for-profit activities. The fentanyl group also had higher scores on risk-taking and hostility. Furthermore, groups with a preference for fentanyl were more likely to report that the effect of fentanyl was stronger than that of heroin.
Alexandria Macmadu, Lisa Frueh,	2022	Drug use behaviors, trauma, and emotional affect following the	U.S.A.	Qualitative study	25	Semi-Structured Interview	This study examines how the ongoing overdose crisis affects people who use drugs, focusing on the emotional trauma and changes in drug use behaviors after knowing someone who has overdosed. The study reveals

Authors	*Year*	*Title*	*Nation*	*Study Design*	*Sample*	*Psychological Measures*	*Outcome*
Alexandra B. Collins, Roxxanne Newman, Nancy P. Barnett, Josiah D. Rich, Melissa A. Clark, and Brandon D.L. Marshall.		overdose of a social network member: A qualitative investigation					that such experiences lead to significant grief, bereavement, and trauma, which can result in increased drug use to cope with negative emotions. The research highlights the need for enhanced overdose prevention interventions that include network-based strategies, bereavement support, and mental health services.
Harris MTH, Bagley SM, Maschke A, Schoenberger SF, Sampath S, Walley AY, Gunn CM.	2021	Competing risk of women and men who use fentanyl: "The number one thing I worry about would be my safety and number two would be overdose"	U.S.A.	Qualitative study	21	interview	The results showed that men and women described overdose as a chronic condition and expressed desensitization at overdose risk. Women feared infection, physical and sexual violence and gave priority to childcare and maintaining relationships with child protection services. While men feared injection infections, violence resulting from obtaining and using street drugs and incarceration
M Gunn C, Maschke A, Harris M, Schonberger SF, Sampath S, Walley AY, Bagley SM	2020	Age-based preferences for risk communication in the fentanyl era: 'A lot of people keep seeing other people die and that's not enough for them	U.S.A.	Qualitative study	21	Interview	The results showed potential age-based differences in perceptions of fentanyl overdose, including that younger participants appeared to display more perceptions of an immunity to fentanyl's lethality, while older people seemed to express a stronger aversion to fentanyl due to its heightened risk of fatal overdose, shorter effects and potential for long-term health consequences. Compassionate harm reduction communication was preferred by all participants and perceived to be delivered most effectively by community health workers and peers
R Brar , Concessione C , KDeBeck , MJ Milloy , N Fairbairn, E Legno , T Kerr , Kanna Hayashi	2020	Changes in drug use behaviors coinciding with the emergence of illicit fentanyl among people who use drugs in Vancouver, Canada	U.S.A.	Cross-Sectional Study	999	Survey	This study aims to examine changes in drug use among people who use drugs, following the emergence of illicit fentanyl. The study found that despite a high prevalence of fentanyl exposure, the majority of PWUD did not change their drug use behavior. There is a need for targeted behavior change messaging and overdose prevention efforts to address the risk of overdose among PWUD
Morales KB, Park JN, Glick JL, Rouhani S, Green TC, Sherman SG	2019	Preference for drugs containing fentanyl from a cross-sectional survey of people who use illicit opioids in three United States cities	U.S.A.	Cross-Sectional Study	308	Survey	This study found that a quarter of people who use street drugs have tried Fentanyl, often combined with other drugs like heroin. The study also revealed that individuals who prefer Fentanyl tend to be younger than those who use other drugs. This highlights the pressing need for public health policies to address this issue. In this study, the use of legal Fentanyl is not associated with an increased preference for this illicit drug.

Authors	*Year*	*Title*	*Nation*	*Study Design*	*Sample*	*Psychological Measures*	*Outcome*
Connery HS, Taghian N, Kim J, Griffin M, Rockett IRH, Weiss RD, Kathryn McHugh R.	2019	Suicidal motivations reported by opioid overdose survivors: A cross-sectional study of adults with opioid use disorder	U.S.A.	Cross-Sectional Study	356	Opioid Overdose Questionnaire, opioid History Questionnaire, ASI-3, Brief Pain Inventory	This study aims to quantify the frequency and intensity of ratings of desire to die and perceived overdose risk proximal to the most recent opioid overdose event among individuals admitted for opioid use disorder detoxification/stabilization. A significant portion of participants reported a desire to die before their most recent overdose. with varying perceptions of overdose risk. Suicidal motivation prior to opioid overdose is common and varies in severity, suggesting the need for suicide preventions to potentially reduce opioid overdose risks
C McKnight, D C Des Jarlais	2018	Being "hooked up" during a sharp increase in the availability of illicitly manufactured fentanyl: Adaptations of drug using practices among people who use drugs (PWUD) in New York City	U.S.A.	Qualitative Study	55	Semi-Structured Interview	The study explores how drug users are adapting their practices to reduce the risk of overdose from fentanyl and opioids, and the variations in the effectiveness of these adaptations. Common methods include test injections, naloxone use, and purchasing from reliable suppliers, although many users do not consistently apply these practices. Fentanyl test strips (FTS) are relatively new but show potential in reducing risks.

3.5. SUICIDE RISK

The study by Kasson et al.[31] delved into the potential link between severe functional impairments and suicidal ideation among fentanyl users. Descriptions of expressed despair in some comments, coupled with references to severe withdrawal symptoms, may indicate a potential increase in suicide risk among these individuals. Concurrently, Connery et al.[36] sought to measure the frequency and intensity of suicidal ideation assessments among opioid-using patients. Notably, the authors found that participants who had experienced an overdose were more likely to use heroin and/or fentanyl compared to other types of opioids. Many opioid users reported life weariness, an inability to cope with events, or apathy towards death. The study aimed to address the literature gap regarding the number of people who reported intentional suicide ideations and attempts before an opioid overdose, and demonstrated a very high prevalence. The results of this study suggest that a significant number of patients seeking treatment for OUD experience suicidal motivation before a non-fatal opioid overdose. In the sample, nearly 60% of participants reported some suicidal motivation, and 36% reported a high level. These findings indicate that some degree of desire to die may be common before an overdose. Moreover, the combination of perceived low overdose risk but some presence of suicidal desire can be particularly dangerous in facilitating potentially lethal opioid use behaviors (e.g., using alone, using more than usual, impulsive use from an unknown or unsafe provider, and polydrug use) even in the absence of a clear intention to die by suicide. Macmadu et al.[37] further revealed that a subset of participants increased drug use with suicidal intentions and suicidal ideation after witnessing an overdose event of someone within their social network

3.6. FENTANYL AND MENTAL DISORDERS

Hochstatter et al.[17] demonstrated that individuals who prefer fentanyl are more likely to have comorbidity with severe mental illness. Connery[36] stressed the link between opioid use, including fentanyl, and depression, anxiety, substance use disorders, severe or chronic trauma, and suicidal ideation. This indicates the importance of identifying comprehensive treatment services for substance use and mental health in fentanyl users. Specifically, mental illness seems to be more common in those who prefer IMF alone rather than a fentanyl-heroin mix. Morales et al.,[29] in line with the theme of mental health, highlight a strong association between improper and sometimes illicit use of benzodiazepines or tranquilizers and a preference for fentanyl, suggesting a comorbidity between fentanyl dependence and anxiety disorders not adequately treated by specialists. The research of Kasson et al.[31] also shows that many IMF users on SubReddit are interested in mental health issues, indicating that these patients may seek treatment without consulting specialist psychotherapists. These findings unequivocally highlight the critical need for an integrated approach to treat patients with fentanyl dependence. This approach must comprehensively address psychological comorbidities and associated socio-emotional factors. It is imperative to prioritize the development of a psychological profile of individuals abusing fentanyl as a public health necessity. This will effectively address both the problem of intervening on untreated symptoms that can lead to addiction and the problem of preventing IMF dependence from exacerbating mental illness.

3.7. NEW PREVENTION PERSPECTIVES

Technological advances offer new possibilities for rehab. For instance, He et al.[38] tested a brain-computer interface mindfulness app to reduce fentanyl use. AI monitored relaxation via EEG, with the app guiding patients. The intervention group significantly cut fentanyl use vs. controls, suggesting similar apps could aid illicit fentanyl users, aiding rehab affordably and effectively. Kasson et al.[31] indicated that social media could be used to disseminate information about harm reduction and treatment strategies for substance use disorder. Also, Macmadu et al.[37] highlight the need to invest more in the prevention of overdose based on social networks, the power of influence of social, especially among teenagers, should not be underestimated by the scientific community. Developing digital tools, such as apps or online platforms, to identify people with recovery intentions and provide support through mentors could represent a significant opportunity for prevention and treatment. These comprehensive measures are crucial to addressing the multifactorial challenges associated with fentanyl dependence and related health consequences. The risk perceptions identified among younger participants in Gunn et al.[30] confirm that young adults often feel invulnerable to harm, complicating the effectiveness of risk communication as a prevention tool. Some participants minimize the risk of death from fentanyl use but express a need for concrete information on overdose prevention and response. An effective approach could involve a continuum of services, from harm reduction to pharmacological treatment. Fentanyl users appreciate risk communication that is based on empathetic relationships and communication methods that include personal connections, active listening, and consistent and encouraging messages. The perceived power dynamics between physicians and users can undermine harm reduction efforts. Most participants seek the involvement of individuals with lived experiences, suggesting that peer support can be an effective channel for risk communication.

3.8. RISK OF BIAS ANALYSIS

The paragraph visually presents the results of the bias analysis using appropriate tools based on the research design of the included studies.

4. DISCUSSION

Fentanyl was originally developed as an effective medication for anesthesia and chronic pain management. However, its high potential for abuse has led to a concerning in-

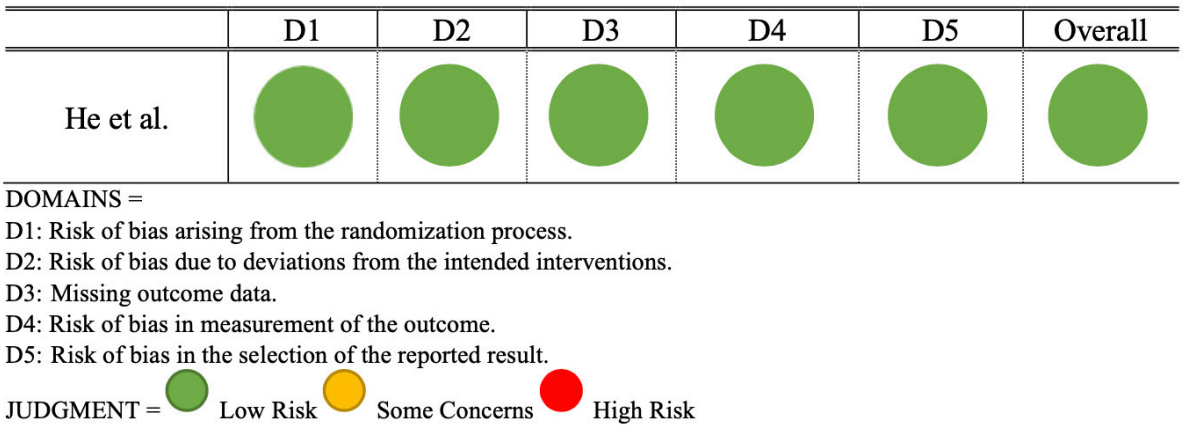

Figure 3. Cochrane risk-of-bias tool for randomized trials, version 2 (RoB 2)

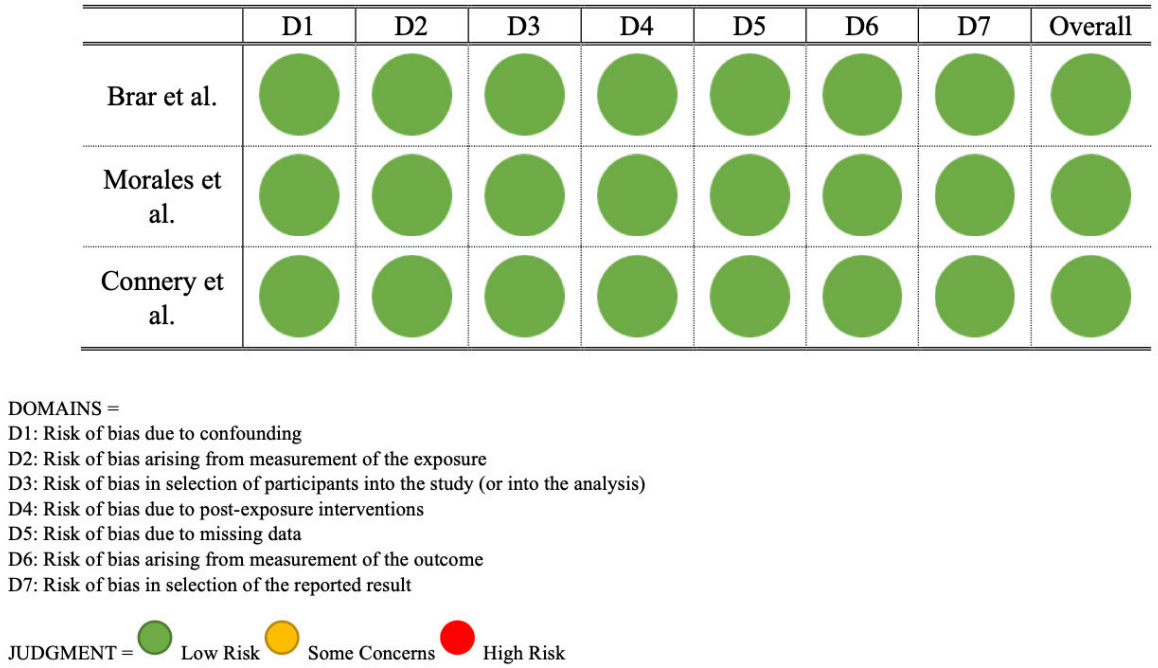

Figure 4. Risk of Bias in Non-randomized Studies - of Exposure (ROBINS-E)

crease in its use as an illicit drug, especially in recent years. This trend started in America and has now spread to Europe. Existing literature on the subject mainly focuses on the medical and biological aspects of fentanyl abuse, analyzing its physical health consequences. However, there is a noticeable gap in understanding the typical profile of a fentanyl abuser and the associated psychological and social implications. The main goal of this scoping review was to examine the current state of the growing Fentanyl abuse phenomenon and its psychosocial implications.

According to established literature, users of IMF (IMF) are consistently younger than other drug users.[17,29,30] These individuals frequently engage in illegal and underground activities, bringing them into frequent contact with street drugs.[29] Fentanyl's popularity on the street can be attributed to its potent effects, affordability, and ease of transport. Fentanyl is associated with acute dependency and seems to have a high tolerance, which contributes to the users' need to increase their doses continually. The difficulty in maintaining abstinence and the particularly intense withdrawal symptoms perpetuate the vicious cycle typical of craving and addiction.[17,31] Risk perception regarding abuse is another crucial dimension. The perception of risk among people who use fentanyl (PWUF) is relatively low.[37] Specifically, they are aware of the risk of overdose and may have experienced an overdose themselves or indirectly, but this does not lead to significant changes in their behavior. This desensitization and sense of immunity may be due to the mistaken belief that they can mitigate the risk by using maladaptive strategies, such as using fentanyl in the presence of others or having naloxone available.[29,30,33,

	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	Overall
Kasson et al.	Yes	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	Include
Macmadu et al.	Yes	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	Include
Harris et al.	Yes	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	Include
Gun et al.	Yes	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	Include
McKnight et al.	Yes	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	Yes	Include

DOMAINS:
D1= Is there congruity between the stated philosophical perspective and the research methodology?
D2= Is there congruity between the research methodology and the research question or objectives?
D3= Is there congruity between the research methodology and the methods used to collect data?
D4= Is there congruity between the research methodology and the representation and analysis of data?
D5= Is there congruity between the research methodology and the interpretation of results?
D6= Is there a statement locating the researcher culturally or theoretically?
D7= Is the influence of the researcher on the research, and vice- versa, addressed?
D8= Are participants, and their voices, adequately represented?
D9= Is the research ethical according to current criteria or, for recent studies, and is there evidence of ethical approval by an appropriate body?
D10=Do the conclusions drawn in the research report flow from the analysis, or interpretation, of the data?

Figure 5. JBI's critical appraisal tools for the Qualitative Study.

Category of study designs	Methodological quality criteria	Responses			
		Yes	No	Can't tell	Comments
Screening questions (for all types)	S1. Are there clear research questions?	x			
	S2. Do the collected data allow to address the research questions?	x			
	Further appraisal may not be feasible or appropriate when the answer is 'No' or 'Can't tell' to one or both screening questions.				
1. Qualitative	1.1. Is the qualitative approach appropriate to answer the research question?	x			
	1.2. Are the qualitative data collection methods adequate to address the research question?	x			
	1.3. Are the findings adequately derived from the data?	x			
	1.4. Is the interpretation of results sufficiently substantiated by data?	x			
	1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?	x			
2. Quantitative randomized controlled trials	2.1. Is randomization appropriately performed?				
	2.2. Are the groups comparable at baseline?				
	2.3. Are there complete outcome data?				
	2.4. Are outcome assessors blinded to the intervention provided?				
	2.5 Did the participants adhere to the assigned intervention?				
3. Quantitative non-randomized	3.1. Are the participants representative of the target population?				
	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?				
	3.3. Are there complete outcome data?				
	3.4. Are the confounders accounted for in the design and analysis?				
	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?				
4. Quantitative descriptive	4.1. Is the sampling strategy relevant to address the research question?	x			
	4.2. Is the sample representative of the target population?	x			
	4.3. Are the measurements appropriate?	x			
	4.4. Is the risk of nonresponse bias low?			x	not specified
	4.5. Is the statistical analysis appropriate to answer the research question?	x			
5. Mixed methods	5.1. Is there an adequate rationale for using a mixed methods design to address the research question?	x			
	5.2. Are the different components of the study effectively integrated to answer the research question?	x			
	5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted?	x			
	5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed?		x		
	5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?	x			

Figure 6. Mixed Methods Appraisal Tool (MMAT) for the mixed methods study by Hochstatter et al.[17]

[34] These strategies only reduce the perceived risk associated with use.

On the psychosocial level, there is a significant and interesting comorbidity between fentanyl use and mental health symptoms or disorders such as suicidal thoughts, anxiety disorders, and depression.[17,29,31,36,37] In more detail, IMF users report high levels of functional difficulties, despair, trauma, depressive, and anxious symptoms.[36] Indeed, the high potential of fentanyl to induce an overdose episode is associated with the risk of suicidal behaviors.

The despair linked to severe withdrawal symptoms can contribute to an increased risk of suicide among fentanyl abusers,[31] and some degree of suicidal ideation may be common prior to an overdose.[36] This aspect is fundamental in highlighting the substance's danger.

During our scoping review, we found that properly prescribed fentanyl does not lead to a subsequent preference for illicit fentanyl.[29,39] On the contrary, it appears that PWUF have reported previous misuse and non-prescription use of benzodiazepines or other tranquilizers.[29] They also show an interest in online mental health issues.[31] This suggests that PWUF may have untreated mental health issues, which could have led to fentanyl abuse. Conversely, fentanyl abuse may have exacetbated their mental health condition. It's also worth nothing that mental health problems seem to be associated with a preference for pure fentanyl over a fentanyl-heroin mix.[36]

It is crucial to take action by creating public health policies that consider the behavioral aspect of illicit fentanyl addiction and it is essential to develop psychoeducation tailored to this population at risk. This should be a top public health priority. The development of psychotherapy, along with digital tools such as apps and online platforms, can be an initial step in addressing this challenge.[38] Considering the prevalence of young people with fentanyl use, it is important for the scientific community not to underestimate the importance of using "social" services and peer support programs to provide accurate information.[30,31] .

Our review has some limitations. Due to the limited research on psychosocial variables and psychological dependence, it's challenging to generalize the results widely, as noted by the small number of studies included. Most of the research was conducted in the American context,[17,29-31,33,35-37] so further investigation is needed to understand the dynamics in other cultural contexts such as Europe and Asia. Additionally, some of the research had weak methodologies.

Beyond these limitations, this scoping review also presents several significant strengths. This review is the first to focus on the psychological aspects of fentanyl use, extending beyond the traditional medical and biological perspectives on addiction. It offers a comprehensive overview of the psychological profile of fentanyl addicts, which helps identify populations most at risk of developing this addiction. These insights make the review an important reference for understanding the complex impact of fentanyl and for guiding future research and targeted interventions.

5. CONCLUSIONS

This scoping review was the first to consistently and systematically outline the psychosocial implications of fentanyl dependence. Future research on fentanyl must consider not only the medical aspect but also the psychological implications. It is crucial to explore fentanyl abuse in different socio-cultural contexts, such as Europe. Finally, it is imperative to establish research avenues to develop innovative prevention and treatment interventions facilitated by technological advancements. Particularly, the development of mobile applications, online platforms, and digital tools could represent an effective way to reach and engage at-risk populations, especially young fentanyl users. These tools could provide psychoeducation, peer support, symptom monitoring, and facilitated access to treatment services. Additionally, they could be used to collect real-time data on fentanyl use and its psychosocial consequences, enabling timely and targeted interventions.

It is imperative to establish multidisciplinary collaborations involving healthcare professionals, researchers, policymakers, local communities, and non-governmental organizations. Only through a coordinated effort and a holistic understanding of the phenomenon can effective strategies be developed to address the fentanyl epidemic and its severe psychosocial consequences.

List of Abbreviations

IMF: illicitly manufactured fentanyl
PWUD: people who use drugs
MORs: μ-opioid receptors
OUD: opioid use disorder
PWUF: people who use fentanyl

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Each author has made an equal contribution.

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FUNDING

This research received no external funding.

INSTITUTIONAL REVIEW BOARD STATEMENT

Not applicable.

INFORMED CONSENT STATEMENT

Not applicable.

Submitted: July 06, 2024 EST, Accepted: July 25, 2024 EST

CONFLICTS OF INTEREST

The authors have not declared any conflicts of interest pertaining to the topic addressed in the article.

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