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Fentanyl-related harm reduction and structural determinants of overdose in the United States: An umbrella review with AMSTAR-2 Appraisal

Mary Najjemba *

Brown School at Washington University in St. Louis, USA.

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Abstract

Background: Illicitly manufactured fentanyl has reshaped the U.S. overdose crisis, driving unprecedented mortality and intensifying demand for harm reduction and policy responses. Although numerous systematic and scoping reviews have examined naloxone distribution, fentanyl test strips (FTS), supervised consumption services, and structural determinants of overdose, the review-level evidence remains fragmented and methodologically heterogeneous. This umbrella review synthesizes existing reviews and appraises their methodological quality using AMSTAR-2.

Methods: A systematic PubMed search identified systematic and scoping reviews published between 2020 and 2025 examining U.S.-focused fentanyl-related harm reduction strategies, behavioral health policy, and structural determinants of overdose. Study selection followed PRISMA 2020 guidance. Methodological quality was assessed using AMSTAR-2. Findings were synthesized narratively and interpreted according to methodological confidence.

Results: Seven reviews met inclusion criteria (three systematic, four scoping). Interventions included naloxone distribution, fentanyl test strips, supervised consumption services, law enforcement drug seizure practices, and equity-focused harm reduction strategies. Naloxone expansion was consistently associated with reduced overdose mortality and improved bystander response. FTS demonstrated high acceptability and self-reported behavioral modification. Structural marginalization including poverty, housing instability, and criminal legal involvement was strongly associated with overdose vulnerability. However, five of seven reviews (71.4%) were rated critically low confidence under AMSTAR-2, primarily due to absence of protocol registration and lack of formal risk-of-bias assessment.

Conclusions: Fentanyl-related harm reduction strategies show consistent directional promise, but the review-level evidence base remains methodologically fragile. Strengthening systematic synthesis and equity-focused evaluation is essential to inform durable overdose prevention policy.

Keywords: Fentanyl; Harm Reduction; Umbrella Review; Amstar-2; Structural Determinants; Naloxone; Fentanyl Test Strips; Opioid Overdose; Health Equity; United States

1. Introduction

Illicitly manufactured fentanyl has fundamentally transformed the epidemiology of opioid-related overdose in the United States. Its high potency, rapid onset, and increasing contamination of the unregulated drug supply have driven escalating mortality and heightened unpredictability of overdose risk (van Draanen et al., 2020; Simha et al., 2023). Unlike earlier phases of the opioid crisis characterized primarily by prescription opioid misuse, the current fentanyl-dominated landscape reflects complex interactions among structural vulnerability, drug market instability, and policy environments (van Draanen et al., 2020; Cano et al., 2024). Related behavioral health syntheses have similarly

* Corresponding author: Mary Najjemba

demonstrated that fragmented service delivery systems, workforce shortages, and rural treatment inequities substantially undermine engagement across substance-use care continuums, particularly among structurally marginalized populations (Najjemba and Ohene-Djan, 2026).

In response, public health systems and policymakers have expanded harm reduction strategies to mitigate fentanyl-related mortality. These strategies include broad naloxone distribution, supervised consumption services, legalization and dissemination of fentanyl test strips (FTS), and community-based overdose prevention initiatives (Levengood et al., 2021; Kutscher et al., 2024; Luna et al., 2024). Evidence from recent systematic reviews further suggests that integrated and multidisciplinary behavioral-health models improve continuity of care and treatment engagement among individuals with co-occurring substance-use and mental health conditions, reinforcing the importance of coordinated harm reduction infrastructures (Najjemba and Solomon, 2026). Review-level evidence indicates that naloxone expansion is associated with reductions in fatal overdose events and increased bystander response capacity (Levengood et al., 2021). Fentanyl test strips demonstrate high acceptability among people who use drugs and are frequently associated with self-reported behavioral modification following positive detection (Kutscher et al., 2024; Luna et al., 2024).

Concurrently, structural determinants including poverty, housing instability, racial inequities, and criminal legal system involvement are consistently linked to elevated overdose vulnerability (van Draanen et al., 2020; Ezell et al., 2025). Emerging syntheses further suggest that enforcement-driven drug seizure practices may destabilize local drug markets and potentially exacerbate overdose risk by increasing supply unpredictability (Cano et al., 2024). Multiple reviews also document persistent disparities in harm reduction access among racial and ethnic minority populations, particularly Latinx communities (Luna et al., 2024; Ezell et al., 2025).

Despite the growing volume of systematic and scoping reviews addressing discrete aspects of fentanyl-related harm reduction and overdose determinants, the review-level evidence remains fragmented across intervention types, population subgroups, and structural domains. Heterogeneity in methodological rigor particularly the predominance of scoping reviews lacking formal risk-of-bias assessment limits the ability to draw confidence-weighted policy conclusions (Cano et al., 2024; Kutscher et al., 2024; Luna et al., 2024).

Umbrella reviews, defined as systematic syntheses of systematic and scoping reviews, facilitate higher-order integration of review-level evidence while enabling formal appraisal of methodological quality (Aromataris et al., 2015; Shea et al., 2017). Application of AMSTAR-2 allows structured evaluation of confidence in included reviews and strengthens interpretation of heterogeneous evidence bases (Shea et al., 2017). To date, no umbrella review has synthesized fentanyl-related harm reduction and structural policy evidence in the United States while concurrently appraising methodological rigor.

Accordingly, this umbrella review aims to; synthesize review-level evidence examining fentanyl-related harm reduction interventions and structural determinants of overdose in the United States; and evaluate the methodological quality of included reviews using AMSTAR-2 to inform confidence in policy-relevant conclusions.

2. Methods

2.1. Study Design

This study was conducted as umbrella review synthesizing evidence from systematic and scoping reviews examining fentanyl-related harm reduction interventions and structural determinants of overdose in the United States. Umbrella reviews enable higher-order integration of review-level evidence while permitting formal appraisal of methodological quality (Aromataris et al., 2015). Reporting adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines (Page et al., 2021).

2.2. Eligibility Criteria

Reviews were eligible if they were systematic or scoping reviews with clearly described search strategies and inclusion criteria; examined fentanyl-related harm reduction interventions, behavioral health policy, or structural determinants of opioid overdose; and focused on U.S. based populations or included substantive U.S. analyses. Eligible reviews were published between January 2020 and December 2025 and written in English.

Reviews were excluded if they were primary empirical studies, narrative reviews lacking systematic methodology, commentaries, editorials, dissertations, conference abstracts, or non-U.S. focused syntheses without contextual relevance to U.S. policy environments.

2.3. Information Sources and Search Strategy

A systematic search of PubMed was conducted to identify eligible reviews. Search terms combined concepts related to fentanyl and synthetic opioids, opioid overdose, harm reduction, behavioral health policy, structural determinants, and review-level study design. Filters were applied for publication date (2020–2025) and review article type. Search refinement emphasized U.S.-focused policy and harm reduction contexts to maximize retrieval of relevant review-level evidence.

2.4. Study Selection

The search identified 187 records. After application of publication type and date filters, 133 records remained. Search refinement yielded 52 records for title and abstract screening. Forty-five records were excluded for primary empirical design, non-U.S. focus, clinical pharmacology emphasis, or absence of systematic methodology. Seven reviews met eligibility criteria and were included in the final synthesis. One narrative review was excluded at full-text review due to lack of systematic or scoping methodology. The selection process is summarized in the PRISMA flow diagram.

2.5. Data Extraction

Data were extracted at the review level using a structured template. Extracted variables included publication year, review type (systematic or scoping), intervention focus, population characteristics, structural or equity emphasis, number of included primary studies, and principal findings. Extraction was limited to synthesized findings reported within each review; primary studies were not reanalyzed.

3. Methodological Quality Assessment

Methodological quality was assessed using AMSTAR-2, a validated instrument for evaluating confidence in systematic reviews of healthcare interventions (Shea et al., 2017). Critical domains included protocol registration, adequacy of literature search, risk-of-bias assessment, consideration of bias in interpretation, and publication bias evaluation. Reviews were categorized as high, moderate, low, or critically low confidence according to AMSTAR-2 guidance. Quality ratings were incorporated into the narrative synthesis to contextualize confidence in conclusions across intervention domains.

3.1. Data Synthesis

Given heterogeneity in intervention types, outcome measures, and review methodologies, quantitative meta-synthesis was not conducted. Findings were synthesized narratively at the review level. Intervention domains were grouped into thematic categories: naloxone distribution, fentanyl test strips, supervised consumption services, structural determinants of overdose, and law enforcement-related drug market dynamics. AMSTAR-2 confidence ratings informed interpretation of the strength and reliability of findings.

4. Results

4.1. Study Selection

The database search identified 187 records. After applying publication date and article type filters, 133 records remained. Search refinement emphasizing U.S.-focused harm reduction and policy domains yielded 52 records for title and abstract screening. Of these, 45 were excluded due to primary empirical design, non-U.S. focus, clinical pharmacology emphasis, or absence of systematic methodology. Seven reviews met eligibility criteria and were included in the final umbrella synthesis. One narrative review was excluded at full-text review due to lack of systematic or scoping methodology. The study selection process is illustrated in the PRISMA flow diagram.

4.2. Characteristics of Included Reviews

Seven reviews published between 2020 and 2025 were included, comprising three systematic reviews and four scoping reviews. Thematic domains included naloxone distribution, supervised consumption services, fentanyl test strips, racial and ethnic disparities in harm reduction utilization, socioeconomic marginalization and overdose vulnerability, and law enforcement–related drug seizure practices.

Two reviews explicitly focused on racial and ethnic minority populations, with particular emphasis on Latinx communities. One review included both U.S. and Canadian contexts, while the remaining reviews were exclusively U.S.-based. The number of primary studies per review ranged from 20 to more than 90. None conducted quantitative meta-analysis specific to fentanyl-related interventions.

4.3. Methodological Quality Assessment

Methodological quality varied substantially across included reviews. According to AMSTAR-2 appraisal, one review was rated moderate confidence, one low confidence, and five critically low confidence. The most frequent critical weaknesses were absence of protocol registration, lack of formal risk-of-bias assessment, and failure to incorporate study-level bias into interpretation.

All four scoping reviews were rated critically low under AMSTAR-2 criteria due to the absence of structured quality appraisal. The sole moderate-confidence review demonstrated prospective protocol registration, comprehensive database searching, and formal risk-of-bias assessment.

Overall, five of seven reviews (71.4%) were categorized as critically low methodological confidence. Appraisal findings are summarized in Table 1.

4.4. Evidence Synthesis

Across reviews, naloxone distribution was consistently associated with reductions in overdose mortality and improved bystander response. Supervised consumption services were similarly associated with reduced fatal overdose events and enhanced linkage to care. Fentanyl test strips demonstrated high acceptability and were frequently associated with self-reported behavioral modification, including dose reduction and increased naloxone carriage.

Structural determinants including poverty, housing instability, racial inequities, and criminal legal system involvement were consistently linked to elevated overdose vulnerability. Evidence examining law enforcement drug seizure practices suggested that intensified seizure activity may destabilize drug markets and contribute to overdose spikes; however, findings were primarily observational and heterogeneous.

Given methodological heterogeneity and limited quantitative synthesis within included reviews, findings were interpreted considering AMSTAR-2 confidence ratings. Characteristics and principal findings are presented in Table 2.

Table 1 Methodological Quality Assessment of Included Reviews Using AMSTAR-2

Review (Author, Year)	Review Type	Protocol Registered	Adequate Search	Risk of Bias Assessed	RoB Considered in Interpretation	Publication Bias Assessed	Overall Confidence
van Draanen et al., 2020	Systematic	Yes	Yes	Yes	Yes	Partial	Moderate
Levengood et al., 2021	Systematic	No	Yes	Partial	Yes	Partial	Low
Simha et al., 2023	Systematic	No	No	No	No	No	Critically Low
Ezell et al., 2025	Scoping	No	Yes	No	No	No	Critically Low
Cano et al., 2024	Scoping	No	Yes	No	No	No	Critically Low
Kutscher et al., 2024	Scoping	Yes	Yes	No	No	No	Critically Low
Luna et al., 2024	Scoping	No	Yes	No	No	No	Critically Low

Table 2 Characteristics and Key Findings of Included Reviews (Umbrella Synthesis Table)

Review (Author, Year)	Review Type	Primary Focus	Population Emphasis	Number of Included Studies	Key Findings	AMSTAR Confidence
van Draanen et al., 2020	Systematic	Socioeconomic determinants of overdose	Structurally marginalized populations	40+	Strong association between poverty, housing instability, and overdose risk	Moderate
Levengood et al., 2021	Systematic	Supervised consumption services	People who use drugs (PWUD)	30+	Reduced overdose mortality and improved service engagement	Low
Simha et al., 2023	Systematic	COVID-19 impact on overdose	U.S. and Canada	20	Overdose mortality increased during pandemic period	Critically Low
Ezell et al., 2025	Scoping	Harm reduction and treatment utilization	Racial/ethnic minorities	50+	Underutilization of harm reduction among minority populations	Critically Low
Cano et al., 2024	Scoping	Drug seizures and overdose mortality	U.S. populations	25+	Seizure intensity associated with supply instability and overdose spikes	Critically Low
Kutscher et al., 2024	Scoping	Fentanyl test strips (FTS)	PWUD	90+	High acceptability; behavioral modification after positive tests	Critically Low
Luna et al., 2024	Scoping	FTS and naloxone in Latinx communities	Latinx populations	20+	Limited culturally tailored interventions; equity gaps in access	Critically Low

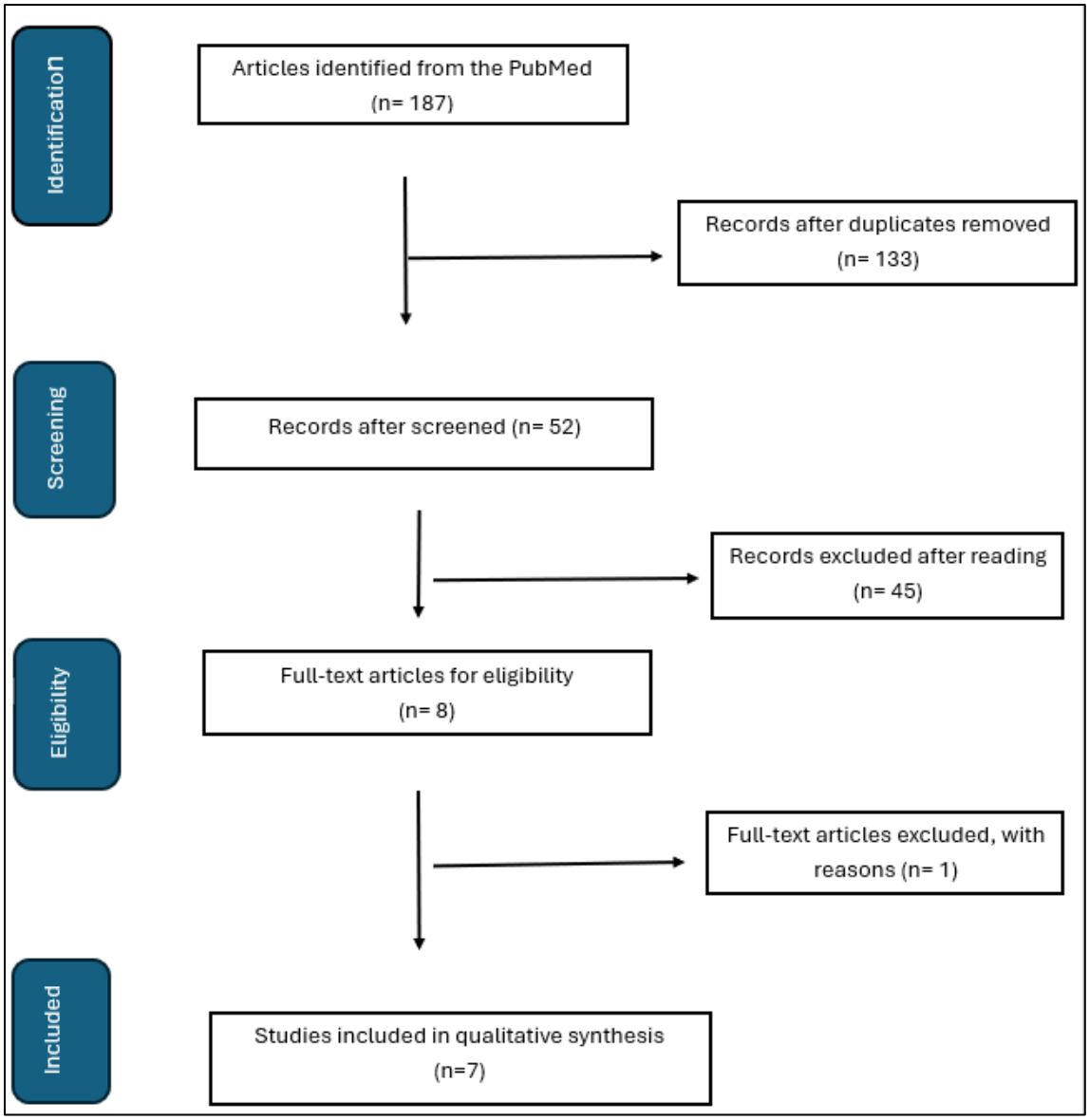

Figure 1 PRISMA 2020 flow diagram of study selection process

5. Discussion

5.1. Principal Findings

This umbrella review synthesizes review-level evidence examining fentanyl-related harm reduction strategies and structural determinants of overdose in the United States. Several patterns were consistently observed across intervention domains.

Naloxone distribution emerged as the most consistently supported harm reduction strategy. Across reviews, expansion of naloxone access was associated with reductions in fatal overdose events and increased bystander response capacity (van Draanen et al., 2020; Levengood et al., 2021). Although quantitative effect estimates were not consistently reported, the directional agreement across reviews strengthens confidence in naloxone as a core overdose prevention intervention.

Fentanyl test strips (FTS) were associated with high acceptability and self-reported behavioral modification following positive detection, including dose reduction and increased naloxone carriage (Kutscher et al., 2024; Luna et al., 2024). However, the supporting evidence remains primarily descriptive and derived from scoping-level syntheses without

pooled outcome estimation. Consequently, while FTS appears promising, the strength of causal inference remains limited.

Structural determinants including poverty, housing instability, racial inequities, and criminal legal system involvement were consistently associated with elevated overdose vulnerability (van Draanen et al., 2020; Ezell et al., 2025). These findings reinforce the understanding that overdose risk is embedded within broader social and policy environments rather than solely individual-level behavior. Comparable findings from behavioral-health implementation literature indicate that organizational readiness, workforce limitations, and fragmented coordination structures substantially influence treatment engagement and continuity across substance-use care systems (Najjemba and Solomon, 2026; Najjemba, 2026). Emerging review-level analyses also suggest that enforcement-driven drug seizure practices may destabilize local drug markets and contribute to overdose spikes, although these findings are primarily ecological and should be interpreted cautiously (Cano et al., 2024).

5.2. Methodological Interpretation

A central finding of this umbrella review is the limited methodological confidence of the current review-level evidence base. Under AMSTAR-2 appraisal, five of seven reviews (71.4%) were rated as critically low confidence, largely due to absence of protocol registration and lack of formal risk-of-bias assessment. Only one review achieved moderate confidence (van Draanen et al., 2020).

Importantly, all scoping reviews were rated as critically low under AMSTAR-2 criteria. This reflects structural differences between scoping review methodology and systematic review standards rather than necessarily poor conduct. Scoping reviews are designed to map emerging evidence and identify gaps rather than generate pooled effect estimates. Nevertheless, the predominance of scoping reviews limits the ability to draw confidence-weighted policy conclusions and underscores the need for higher-quality systematic syntheses.

5.3. Policy and Equity Implications

Despite methodological limitations, several policy-relevant implications emerge. First, naloxone expansion remains a foundational intervention and should be maintained and equitably distributed. Second, fentanyl test strips demonstrate behavioral impact and acceptability, supporting continued policy efforts to remove paraphernalia-related barriers to access. Recent implementation-science syntheses further suggest that long-term effectiveness of substance-use interventions depends heavily on leadership engagement, workforce training, organizational readiness, and sustained policy alignment within behavioral-health systems (Najjemba, 2026).

However, multiple reviews highlight persistent inequities in harm reduction utilization among racial and ethnic minority populations, particularly Latinx communities (Luna et al., 2024; Ezell et al., 2025). Addressing overdose risk therefore requires not only intervention expansion but also structural reform, including improved healthcare access, culturally tailored implementation strategies, and reconsideration of enforcement-centered approaches that may exacerbate supply instability.

5.4. Research Priorities

Future research should prioritize prospectively registered systematic reviews incorporating structured risk-of-bias assessment and, where feasible, quantitative meta-analysis. Comparative evaluation of intervention effectiveness across population subgroups is particularly needed. Additionally, policy-level natural experiments and longitudinal evaluations would strengthen causal inference in domains currently supported primarily by descriptive or ecological evidence.

Limitations

Several limitations should be considered when interpreting these findings.

First, the search strategy relied on a single database (PubMed), which may have limited identification of eligible reviews indexed exclusively in databases such as Scopus, Web of Science, or PsycINFO. Although search refinement procedures were applied to enhance relevance, the possibility of missed reviews cannot be excluded.

Second, eligibility was restricted to English-language publications and to reviews published between 2020 and 2025. This timeframe was selected to capture the fentanyl-dominant phase of the overdose crisis; however, earlier relevant syntheses may have been omitted.

Third, application of AMSTAR-2 resulted in all scoping reviews being rated critically low confidence due to the absence of formal risk-of-bias assessment. This reflects structural differences between scoping and systematic review methodologies rather than necessarily inadequate conduct. Nevertheless, the predominance of scoping reviews constrains the strength of causal inference and reduces confidence in aggregate policy conclusions.

Fourth, quantitative meta-synthesis was not conducted at the umbrella level due to heterogeneity in intervention types, outcome measures, and review methodologies. Similar methodological heterogeneity has been observed across recent behavioral-health and implementation-science syntheses examining substance-use interventions and integrated care systems in the United States (Najjemba and Solomon, 2026; Najjemba, 2026). Findings were therefore synthesized narratively, limiting the ability to estimate pooled intervention effects.

Finally, the fentanyl crisis remains dynamic, with rapidly evolving drug supply patterns and policy responses. Newly emerging evidence may not be captured within included reviews due to publication lag.

Despite these limitations, this umbrella review provides a structured, quality-weighted synthesis of review-level evidence addressing fentanyl-related harm reduction and structural determinants of overdose in the United States.

6. Conclusion

This umbrella review synthesizes review-level evidence examining fentanyl-related harm reduction strategies and structural determinants of overdose in the United States. Naloxone distribution and fentanyl test strips demonstrate consistent directional promise, while socioeconomic marginalization and structural inequities remain central drivers of overdose vulnerability. However, the predominance of scoping reviews lacking formal risk-of-bias assessment highlights the methodological fragility of the current evidence base.

Strengthening prospective registration, structured quality appraisal, and quantitative synthesis will be essential to improve confidence in policy-relevant conclusions. Advancing equitable implementation of harm reduction strategies alongside more rigorous evidence synthesis is critical to informing durable responses to the evolving fentanyl crisis

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare no conflicts of interest.

Statement of ethical approval

Ethical approval was not required as this study synthesized data from published literature.

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Author Contributions

All authors contributed to study conception and design. Data screening, extraction, and methodological appraisal were performed by the authors. The manuscript was drafted and critically revised by the authors. All authors approved the final version of the manuscript.

Data Availability

No new data was generated or analyzed in this study. All data included in this umbrella review are derived from previously published reviews.

References

[1] Aromataris, E., Fernandez, R., Godfrey, C. M., Holly, C., Khalil, H., and Tungpunkom, P. (2015). Summarizing systematic reviews: methodological development, conduct and reporting of an umbrella review approach. JBI Evidence Implementation, 13(3), 132-140.

[2] Cano, M., Timmons, P., Hooten, M., Sweeney, K., and Oh, S. (2024). A scoping review of law enforcement drug seizures and overdose mortality in the United States. International Journal of Drug Policy, 124, 104321.

[3] Ezell, J. M., Simek, E., Shetty, N., Pho, M. T., Bluthenthal, R. N., Goddard-Eckrich, D. A., and Choi, S. (2025). A scoping review of the utilization of opioid use treatment, harm reduction, and culturally tailored interventions among racial/ethnic minorities in the United States. International Journal of Mental Health and Addiction, 23(6), 4612-4653.

[4] Kutscher, E., Grossi, M. B., LaPolla, F., and Lee, J. D. (2024). Fentanyl test strips for harm reduction: a scoping review. Journal of addiction medicine, 18(4), 373-380.

[5] Levengood, T. W., Yoon, G. H., Davoust, M. J., Ogden, S. N., Marshall, B. D., Cahill, S. R., and Bazzi, A. R. (2021). Supervised injection facilities as harm reduction: a systematic review. American journal of preventive medicine, 61(5), 738-749.

[6] Luna, G., Dermid, G., and Unger, J. B. (2024). Fentanyl harm reduction strategies among Latinx communities in the United States: a scoping review. Harm Reduction Journal, 21(1), 150.

[7] Najjemba, M. (2026). Implementation-science strategies for scaling trauma-informed substance-use interventions in U.S. behavioral-health organizations. World Journal of Advanced Research and Reviews, 30(1), 1537–1548. https://doi.org/10.30574/wjarr.2026.30.1.0945

[8] Najjemba, M., and Ohene-Djan, D. (2026). Barriers to treatment engagement for alcohol use disorders in rural and community behavioral health settings: A systematic review. International Journal for Multidisciplinary Research, 8(1)

[9] Najjemba, M., and Solomon, D. (2026). Systematic review of the effectiveness of multidisciplinary care-coordination models for U.S. citizens with co-occurring disorders. Sarcouncil Journal of Internal Medicine and Public Health, 5(1), 21–29.

[10] Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., ... and Moher, D. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. bmj, 372.

[11] Shea, B. J., Reeves, B. C., Wells, G., Thuku, M., Hamel, C., Moran, J., ... and Henry, D. A. (2017). AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. bmj, 358.

[12] Simha, S., Ahmed, Y., Brummett, C. M., Waljee, J. F., Englesbe, M. J., and Bicket, M. C. (2023). Impact of the COVID-19 pandemic on opioid overdose and other adverse events in the USA and Canada: a systematic review. Regional Anesthesia and Pain Medicine, 48(1), 37-43.

[13] Van Draanen, J., Tsang, C., Mitra, S., Karamouzian, M., and Richardson, L. (2020). Socioeconomic marginalization and opioid-related overdose: a systematic review. Drug and alcohol dependence, 214, 108127.