**Appendix**

**Appendix 1:**

**Algorithm to define lifetime prescription opioid misuse:** Lifetime prescription opioid misuse was coded as “yes” if a) an age of first nonmedical use of prescription opioids (>0) was reported, OR b) “not sure” was indicated for age of first nonmedical use of prescription opioids, OR c) prescription opioid nonmedical use was reported in the past 30 days via product-specific responses.

**Algorithm to define lifetime prescription stimulant misuse:** Lifetime prescription stimulant misuse was coded as “yes” if a) an age of first nonmedical use of prescription stimulants (>0) was reported, OR b) “not sure” was indicated for age of first nonmedical use of prescription stimulants, OR c) prescription stimulant nonmedical use was reported in the past 30 days via product-specific responses.

**Appendix 2:**

**Algorithm to define *misuse* of prescription opioids as the primary lifetime substance use problem:** *Misuse* of prescription opioids as the primary lifetime substance use problem was coded as “yes” if 1) prescription opioid *use* was selected as the primary lifetime substance use problem AND 2) Either a) an age of first nonmedical use of prescription opioids (>0) was reported, OR b) “not sure” was indicated for age of first nonmedical use of prescription opioids, OR c) prescription opioid nonmedical use was reported in the past 30 days via product-specific responses.

**Appendix 3:**

**STROBE Statement**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Item No** | **Recommendation** | **Page** |
| **Title and abstract** | 1 | (*a*) Indicate the study’s design with a commonly used term in the title or the abstract | 3 |
| (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 3 |
| **Introduction** | | |  |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 4 |
| Objectives | 3 | State specific objectives, including any pre-specified hypotheses | 4 |
| **Methods** | | |  |
| Study design | 4 | Present key elements of study design early in the paper | 4-7 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 4-7 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants | 4-7 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 7-8 |
| Data sources/ measurement | 8\* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 7-8 |
| Bias | 9 | Describe any efforts to address potential sources of bias | 8 |
| Study size | 10 | Explain how the study size was arrived at | 9 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 8-9 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | 8-9 |
| (*b*) Describe any methods used to examine subgroups and interactions | NA |
| (*c*) Explain how missing data were addressed | 9 |
| (*d*) If applicable, describe analytical methods taking account of sampling strategy | NA |
| (*e*) Describe any sensitivity analyses | 9 |
| **Results** | | |  |
| Participants | 13\* | (a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 9-10 |
| (b) Give reasons for non-participation at each stage | NA |
| (c) Consider use of a flow diagram | - |
| Descriptive data | 14\* | (a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders | 10-11 |
| (b) Indicate number of participants with missing data for each variable of interest | NA |
| Outcome data | 15\* | Report numbers of outcome events or summary measures | NA |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 12,31 |
| (*b*) Report category boundaries when continuous variables were categorized | 12 |
| (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | NA |
| Other analyses | 17 | Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses | 13,34 |
| **Discussion** | | |  |
| Key results | 18 | Summarise key results with reference to study objectives | 13 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 17 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 13-17 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 17 |
| **Other information** | | |  |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 19 |

**Supplemental Files**

**Supplemental Table 1. Sensitivity Analysis: Multivariable logistic regression model examining predictors of reporting illicitly manufactured fentanyl use (versus any other substance use) as the primary lifetime substance use problem, restricted to assessments reporting IMF use in the past 30 days (N=29,758) a**

|  |  |
| --- | --- |
|  | **Adjusted Odds Ratio**  **(95% Confidence Interval)** |
| **Sex** | |
| Female | 0.90 (0.73, 1.12) |
| Male | Reference |
| **Age (years)** | |
| 18-24 | 2.28 (1.49, 3.48) |
| 25-34 | 1.66 (1.16, 2.38) |
| 35-44 | 1.37 (0.94, 2.00) |
| ≥55 | 0.71 (0.38, 1.32) |
| 45-54 | Reference |
| **Race/Ethnicity** | |
| Non-Hispanic Black | 1.31 (0.96, 1.78) |
| Non-Hispanic American Indian or Alaska Native | 0.41 (0.13, 1.28) |
| Non-Hispanic other | 0.82 (0.48, 1.41) |
| Hispanic | 1.09 (0.75, 1.58) |
| Non-Hispanic White | Reference |
| **Education Level** | |
| Less than high school | 0.98 (0.60, 1.61) |
| Some college | 1.09 (0.86, 1.37) |
| 4 years of college or more | 1.17 (0.76, 1.79) |
| High school | Reference |
| **United States Census Region (ASI-MV site)** | |
| Northeast | 17.93 (8.48, 37.90) |
| Midwest | 6.50 (3.04, 13.92) |
| South | 4.80 (2.33, 9.91) |
| West | Reference |
| **Moderate to Extreme Domain Severity Rating** | |
| Medical | 1.34 (1.05, 1.70) |
| Employment | 1.09 (0.87, 1.37) |
| Alcohol | 0.55 (0.43, 0.72) |
| Drug | 6.05 (3.97, 9.23) |
| Legal | 0.80 (0.62, 1.04) |
| Family | 0.95 (0.72, 1.26) |
| Psychiatric | 0.72 (0.57, 0.92) |
| **Route of Use for Any Substance in the lifetime** | |
| Injection drug use with or without also reporting swallowed, snorted, or smoked | 1.07 (0.85, 1.34) |
| Swallowed, snorted, or smoked without reporting any injection drug use | Reference |
| **Insurance type** | |
| Medicare only | 3.87 (2.35, 6.36) |
| Self-pay | 0.51 (0.32, 0.80) |
| Uninsured/Exhausted benefits | 1.32 (0.94, 1.85) |
| Commercial payer | 0.70 (0.25, 1.93) |
| Other | 0.61 (0.47, 0.79) |
| Medicare/Medicaid | Reference |
| **Urban-Rural Status (ASI-MV site)** | |
| Metropolitan | 1.62 (1.13, 2.32) |
| Micropolitan | 0.67 (0.41, 1.09) |
| Rural | Reference |
| **In inpatient controlled environment during the past 30 days** | |
| Yes | 1.36 (1.07, 1.72) |
| No | Reference |
| **Any income in the past 30 days** | |
| Yes | 1.12 (0.90, 1.39) |
| No | Reference |
| **Received treatment as part of an official medications for substance use disorders program in the past 30 days (%)** | |
| Yes | 1.42 (1.14, 1.78) |
| No | Reference |
| **Attended any outpatient treatment or counseling for alcohol or drug problems in the past 30 days** | |
| Yes | 1.22 (0.96, 1.57) |
| No | Reference |
| **Attended self-help meeting in the past 30 days** | |
| Yes | 0.54 (0.42, 0.68) |
| No | Reference |
| **Lifetime overdoses on any drug** | |
| 1 lifetime overdose | 2.03 (1.52, 2.72) |
| 2 lifetime overdoses | 2.00 (1.44, 2.79) |
| 3 or more lifetime overdoses | 2.42 (1.87, 3.14) |
| None | Reference |

a The sensitivity result is consistent with the main analysis except for the variables “non-Hispanic black”, “moderate to extreme severity problems for the medical domain”, “uninsured/exhausted benefits”, and “attended self-help meeting in the past 30 days”.

**Supplemental Table 2. Sensitivity Analysis: Multivariable logistic regression model examining predictors of illicitly manufactured fentanyl use** **as the primary lifetime substance use problem versus any other primary lifetime substance use problem (unit of analysis: individual level) (N=27,280) a**

|  |  |
| --- | --- |
|  | **Adjusted Odds Ratio**  **(95% Confidence Interval)** |
| **Sex** | |
| Female | 0.89 (0.74, 1.08) |
| Male | Reference |
| **Age (years)** | |
| 18-24 | 1.65 (1.15, 2.38) |
| 25-34 | 1.31 (0.97, 1.77) |
| 35-44 | 1.18 (0.86, 1.61) |
| ≥55 | 0.71 (0.43, 1.18) |
| 45-54 | Reference |
| **Race/Ethnicity** | |
| Non-Hispanic Black | 1.41 (1.07, 1.85) |
| Non-Hispanic American Indian or Alaska Native | 0.66 (0.31, 1.42) |
| Non-Hispanic other | 0.78 (0.49, 1.27) |
| Hispanic | 0.95 (0.67, 1.34) |
| Non-Hispanic White | Reference |
| **Education Level** | |
| Less than high school | 1.21 (0.81, 1.82) |
| Some college | 1.14 (0.93, 1.40) |
| 4 years of college or more | 1.13 (0.77, 1.65) |
| High school | Reference |
| **United States Census Region (ASI-MV site)** | |
| Northeast | 15.79 (8.49, 29.39) |
| Midwest | 5.80 (3.11, 10.84) |
| South | 4.26 (2.36, 7.72) |
| West | Reference |
| **Moderate to Extreme Domain Severity Rating** | |
| Medical | 1.16 (0.93, 1.44) |
| Employment | 1.09 (0.89, 1.33) |
| Alcohol | 0.50 (0.40, 0.63) |
| Drug | 3.67 (2.69, 5.01) |
| Legal | 0.88 (0.70, 1.10) |
| Family | 1.00 (0.78, 1.27) |
| Psychiatric | 0.72 (0.58, 0.89) |
| **Route of Use for Any Substance in the lifetime** | |
| Injection drug use with or without also reporting swallowed, snorted, or smoked | 1.17 (0.96, 1.44) |
| Swallowed, snorted, or smoked without reporting any injection drug use | Reference |
| **Insurance type** | |
| Medicare only | 2.74 (1.68, 4.47) |
| Self-pay | 0.70 (0.49, 1.00) |
| Uninsured/Exhausted benefits | 1.50 (1.11, 2.04) |
| Commercial payer | 1.00 (0.45, 2.20) |
| Other | 0.73 (0.58, 0.91) |
| Medicare/Medicaid | Reference |
| **Urban-Rural Status (ASI-MV site)** | |
| Metropolitan | 1.61 (1.17, 2.22) |
| Micropolitan | 0.75 (0.50, 1.13) |
| Rural | Reference |
| **In inpatient controlled environment during the past 30 days** | |
| Yes | 1.61 (1.31, 1.97) |
| No | Reference |
| **Any income in the past 30 days** | |
| Yes | 0.89 (0.73, 1.08) |
| No | Reference |
| **Received treatment as part of an official medications for substance use disorders program in the past 30 days (%)** | |
| Yes | 1.49 (1.23, 1.82) |
| No | Reference |
| **Attended any outpatient treatment or counseling for alcohol or drug problems in the past 30 days** | |
| Yes | 1.26 (1.02, 1.56) |
| No | Reference |
| **Attended self-help meeting in the past 30 days** | |
| Yes | 0.80 (0.66, 0.98) |
| No | Reference |
| **Lifetime overdoses on any drug** | |
| 1 lifetime overdose | 1.91 (1.47, 2.48) |
| 2 lifetime overdoses | 2.13 (1.60, 2.84) |
| 3 or more lifetime overdoses | 2.24 (1.78, 2.81) |
| None | Reference |

a The sensitivity result is consistent with the main analysis except for the variables “attended self-help meeting in the past 30 days”, “aged 25-34 years”, “self-pay”, and “attended any outpatient treatment or counseling for alcohol or drug problems in the past 30 days”.