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| Supplemental Table A. Prevalence and adjusted odds of heroin use over 17 years as a function of medical use and nonmedical misuse history of prescription opioids during adolescence | | | | | |
| Baseline opioid exposure (modal age 18) | Heroin use  ages 19 to 35  % | Heroin use  ages 19 to 35  AOR (95% CI)a | Heroin use  ages 19 to 35  AOR (95% CI)a | Heroin use  ages 19 to 35  AOR (95% CI)a | Heroin use  ages 19 to 35  AOR (95% CI)a |
| Lifetime medical use/nonmedical misuse  No medical or nonmedical use (n = 6,444)b  Medical use only (n = 992)b  Medical use followed by nonmedical use (n = 408)b  Nonmedical misuse followed by medical use (n = 197)b  Nonmedical use only (n = 408)b | 2.1%  3.7%  5.5%  15.1%  16.4%  b(n = 8449) | Reference  1.65 (1.06, 2.57)\*  1.93 (1.05, 3.55)\*  4.30 (2.41, 7.67)\*\*\*  5.52 (3.67, 8.29)\*\*\*  c(n = 8143) | 0.60 (0.38, 0.93)\*  Reference  1.17 (0.59, 2.31)  2.59 (1.33, 5.04)\*\*  3.33 (1.96, 5.66)\*\*\*  c(n = 8143) | 0.52 (0.28, 0.95)\*  0.85 (0.43, 1.69)  Reference  2.21 (1.00, 4.91)\*  2.84 (1.47, 5.52)\*\*  c(n = 8143) | 0.23 (0.13, 0.41)\*\*\*  0.38 (0.19, 0.74)\*\*  0.45 (0.20, 0.99)\*  Reference  1.28 (0.50, 2.45)  c(n = 8143) |
| p<.05\*, p<.01\*\*, p<.001\*\*\*  aAll analyses control for race/ethnicity (i.e., White, Black, Hispanic, Other race), sex (i.e., Male and Female), highest level of parental education, geographic region (i.e., Northeast, Northcentral, South and West), metropolitan statistical area (i.e., large MSA, other MSA, and non-MSA), and baseline cohort year, and baseline measures of past two week binge drinking, past 30 day marijuana use, and past 30 day cigarette use.  bSample size drops based on attrition in the panel sample (sample sizes are unweighted). cSample size drops due to attrition and missing data on control variables (sample sizes are unweighted).. Individuals who reported any lifetime heroin use at baseline (modal age 18) were excluded (n = 179). A random one-sixth of the overall panel sample received the questions regarding medical and nonmedical prescription opioid use. All percentages and adjusted odds ratios (AOR) use attrition weights at age 35. | | | | | |

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| Supplemental Table B. Prevalence and adjusted odds of heroin use over 17 years as a function of medical use and nonmedical misuse history of prescription opioids during adolescence | | | | |
| Baseline opioid exposure (modal age 18) |  | **ORIGINAL OUTCOME**  Heroin use  ages 19 to 35  AOR (95% CI)a | **SUPPLEMENTAL OUTTCOME**  Heroin use  between age 19 to 22d  AOR (95% CI)a | **SUPPLEMENTAL OTUCOME**  Mean Frequency of Heroin use between age 19 to 35e  IRRf (95% CI)a |
| Lifetime medical use/nonmedical misuse  No medical or nonmedical use (n = 6,444)b  Medical use only (n = 992)b  Medical use followed by nonmedical use (n = 408)b  Nonmedical misuse followed by medical use (n = 197)b  Nonmedical use only (n = 408)b |  | Reference  1.65 (1.06, 2.57)\*  1.93 (1.05, 3.55)\*  4.30 (2.41, 7.67)\*\*\*  5.52 (3.67, 8.29)\*\*\*  c(n = 8143) | Reference  1.40 (0.44, 4.41)  3.56 (1.14, 11.0)\*  2.60 (0.76, 8.93)  6.57 (2.88, 15.0)\*\*\*  c(n = 8143) | Reference  0.74 (0.31, 1.72)  3.59 (1.36, 9.46)\*\*  4.23 (1.00, 17.9)\*  4.11 (1.88, 8.98)\*\*\*  c(n = 8143) |
| p<.05\*, p<.01\*\*, p<.001\*\*\*  aAll analyses control for race (i.e., White, Black, Hispanic, Other race), sex (i.e., Male and Female), highest level of parental education, geographic region (i.e., Northeast, Northcentral, South and West), metropolitan statistical area (i.e., large MSA, other MSA, and non-MSA), and baseline cohort year, and baseline measures of past-year alcohol use, past-year marijuana use, and past-year other drug use.  bSample size drops based on attrition in the panel sample. cSample size drops due to attrition and missing data on control variables. dThis outcome used past-year heroin use to capture when respondents first started using heroin after the age of 18. eThis outcome used the average frequency of past-year heroin use between age 19 and 35 (the seven possible response options ranged from ‘0 occasions’ to ’40 or more occasions’. fThese models used negative binomral regression due to the continuous nature of the outcome variable.  Individuals who reported any lifetime heroin use at baseline (modal age 18) were excluded (n = 179). A random one-sixth of the overall panel sample received the questions regarding medical and nonmedical prescription opioid use. All percentages and adjusted odds ratios (AOR) use attrition weights at age 35. | | | | |

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| Supplemental Table C. Prevalence and adjusted odds of heroin use over 17 years as a function of medical use and nonmedical misuse history of prescription opioids during adolescence | | | | |
|  |  | **ORIGINAL OUTCOME**  Heroin use  between ages 19 to 35  AOR (95% CI)a | **SUPPLEMENTAL OUTCOME**  Heroin use  between age 19 to 22d  AOR (95% CI)a | **SUPPLEMENTAL OUTCOME**  Heroin use frequency (mean) ages 19 to 35e  IRRe (95% CI)a |
| Lifetime medical use/nonmedical misuse (at age 18 and earlier & between ages 19 to 35)  No medical or nonmedical use (n = 3,385; never exposed to opioids during the entire study period)b  Medical use only by age 18 (n = 992)b  Medical use followed by nonmedical use by age 18 (n = 407)b  Nonmedical use followed by medical use by age 18 (n = 196)b  Nonmedical use only by age 18 (n = 405)  Prescription opioid use between ages of 19 and 35 (not exposed at baseline [age 18 or younger]) (n = 3051) |  | Reference  5.30 (2.84, 9.90)\*\*\*  6.25 (2.93, 13.3)\*\*\*  14.1 (6.76, 29.5)\*\*\*  18.1 (9.87, 33.4)\*\*\*  5.60 (3.32, 9.44)\*\*\*  c(n = 8130) | Reference  3.06 (0.63, 14.8)  7.77 (1.62, 37.4)\*\*  5.80 (1.12, 29.9)\*  14.6 (3.83, 56.1)\*\*\*  3.39 (0.86, 13.3)  c(n = 8130) | Reference  3.21 (1.04, 9.91)\*  15.8 (4.87, 51.3)\*\*\*  19.3 (3.99, 93.4)\*\*\*  18.4 (6.58, 51.7)\*\*\*  7.70 (2.94, 20.1)\*\*\*  c(n = 8130) |
| p<.05\*, p<.01\*\*, p<.001\*\*\*  aAll analyses control for race (i.e., White, Black, Hispanic, Other race), sex (i.e., Male and Female), highest level of parental education, geographic region (i.e., Northeast, Northcentral, South and West), metropolitan statistical area (i.e., large MSA, other MSA, and non-MSA), and baseline cohort year, and baseline measures of past two week binge drinking, past 30 day marijuana use, and past 30 day cigarette use.  bSample size drops based on attrition in the panel sample (sample sizes are unweighted). cSample size drops due to attrition and missing data on control variables (sample sizes are unweighted).  dThis outcome used past-year heroin use to capture when respondents first started using heroin after the age of 18. eThis outcome used the average frequency of past-year heroin use between age 19 and 35 (the seven possible response options ranged from ‘0 occasions’ to ’40 or more occasions’. fThese models used negative binomral regression due to the continuous nature of the outcome variable.  Individuals who reported any lifetime heroin use at baseline (modal age 18) were excluded (n = 179). A random one-sixth of the overall panel sample received the questions regarding medical and nonmedical prescription opioid use. All percentages and adjusted odds ratios (AOR) use attrition weights at age 35. | | | | |

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| Supplemental Table D. Descriptive statistics for lifetime heroin users at baseline (n = 179) | |
| Baseline prescription opioid/heroin use behaviors (modal age 18) | % (n = 179) |
| **Medical use and nonmedical misuse of prescription opioids at baseline** |  |
| Non-use of prescription opioids | 26.0% |
| Medical use of prescription opioids only | 1.8% |
| Nonmedical misuse followed by medical use of prescription opioids | 6.5% |
| Medical use followed by nonmedical misuse of prescription opioids | 20.7% |
| Nonmedical misuse of prescription opioids only | 45.0% |
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| **Initiation sequences of heroin and nonmedical use of prescription opioids at baseline** |  |
| Heroin use only | 25.4% |
| Heroin use followed by nonmedical misuse of prescription opioids | 13.5% |
| Heroin use and nonmedical misuse of prescription opioids in the same year | 38.9% |
| Nonmedical use of prescription opioids followed by heroin use | 22.2% |
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