



CAPT Decision-Support Tools

PREVENTING PRESCRIPTION DRUG MISUSE:
Understanding Who Is at Risk

Using Prevention Research to Guide Prevention Practice
SAMHSA's Center for the Application of Prevention Technologies
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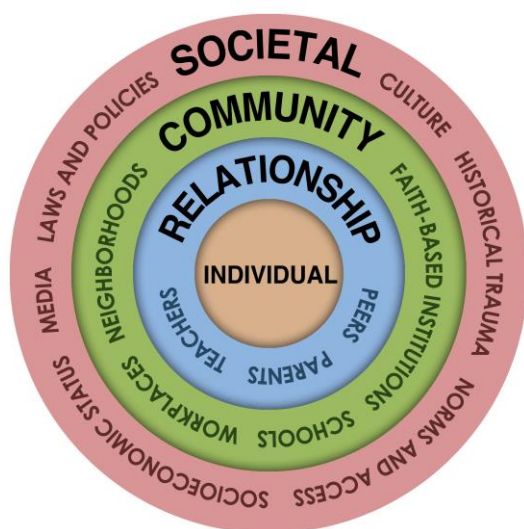
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INTRODUCTION

The nonmedical use of prescription drugs (NMUPD) has become an increasing public health concern in the United States, with abuse rates rising rapidly since the late 1990s. Yet preventing and reducing prescription drug misuse represents a major challenge for several reasons. First, we know less about the factors that contribute to NMUPD than about those that contribute to other drug use. Also, because of how prescription drugs are made available, these factors may differ from those that are associated with alcohol misuse and illicit drug use. This tool provides a starting point for understanding those factors that the research literature has identified as being associated with NMUPD and its consequences. Understanding these factors can help us assess, plan for, and select interventions designed to address them.

The factors included in this tool have been organized according to the **socio-ecological model**, a multi-level framework that allows us to consider the different contexts in which risk and protective factors exist. This model considers the different contexts and settings with which a person interacts and is based on the premise that we are influenced not only by traits specific to us or what we think and believe, but by our relationships with others, the institutions and communities to which we belong, and the broader society in which those institutions are embedded.



There are four levels to the socio-ecological model:^{1, 2, 3}

- **Individual level:** Includes factors specific to the individual, such as age, education, income, health, and psychosocial problems, which may correspond with substance use and misuse.
- **Relationship level:** Includes an individual’s closest social circle—family members, peers, teachers, and other close relationships—that contribute to his or her range of experiences and that may influence his or her behavior.
- **Community level:** Includes the settings in which social relationships occur, such as schools, workplaces, and neighborhoods. These factors can have both negative and positive associations with substance use and misuse.

¹ Centers for Disease Control and Prevention, 2015

² World Health Organization, 2016

³ Domains and sub-domains of the socio-ecological model often overlap or are nested within each other. For example, bullying is an individual-level risk factor that falls under the interpersonal behavior sub-domain; however, bullying in a school setting could also be considered a community-level risk factor that falls under the school sub-domain.

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- **Societal level:** Includes the broad societal factors, such as social and cultural norms. Other significant factors operating at this level include the health, economic, educational, and social policies that contribute to economic and/or social inequalities between populations.

Factors that influence future behavior are often categorized as either risk or protective factors. Here, a *protective factor* is a characteristic operating at the individual, relationship, community, or societal level that is associated with a lower likelihood of NMUPD or that reduces the negative impact of a risk factor on NMUPD. Conversely, a *risk factor* is a characteristic at each level of the socio-ecological model that precedes and is associated with a higher likelihood of NMUPD.⁴

Our search of the literature yielded many more risk than protective factors. In addition, the majority of factors are situated at the individual level of the socio-ecological model, which focuses on an individual's personal experience rather than contextual factors. We also found studies that included populations across the whole lifespan, ranging in age from 12 years old to over 70, and focused on special population groups or groups at increased risk for NMUPD and other types of substance abuse (such as homeless young adults, veterans, active duty service members, lesbian and gay youth, cancer patients, and Medicaid recipients). In addition, while our literature search included search terms that encompass various types of prescription drugs (see "[THE FINE PRINT: SEARCH METHODS AND INCLUSION CRITERIA](#)" section for search terms used), the class of drug that was represented most frequently in the identified studies was opioids.

RELATED TOOLS

Other CAPT tools that support the prevention of NMUPD include the following:

- ***Preventing Prescription Drug Misuse: Programs and Strategies***: Presents detailed descriptions of prevention strategies and associated interventions that have been evaluated to determine their effects on prescription drug misuse
- ***Sources of Consumption Data Related to Non-Medical Use of Prescription Drugs – 2012***: Includes national and local sources of consumption data on prescription drug misuse
- ***Sources of Consequence Data Related to Non-Medical Use of Prescription Drugs – 2012***: Includes national and local sources of consequence data on prescription drug misuse
- ***Other Sources of Data Related to Non-Medical Use of Prescription Drugs – 2012***: Includes four data sources related to non-medical use of prescription drugs

⁴ O'Connell, Boat, & Warner, 2009

THE FINE PRINT: SEARCH METHODS AND INCLUSION CRITERIA

To populate this tool, we conducted a thorough search of the academic literature to identify those factors that protect against or increase the risk for NMUPD. Searches were conducted using the PSYCHINFO, MEDLINE, PSYCHARTICLES, and SOCINDEX databases. Search terms included the following:

- **(Substance Key Words)** *Prescription drug** OR *Opioid** OR *Opiate** OR *Tranquilizer** OR *Sedative** OR *Stimulant*
- AND **(Abuse Key Words)** *Abuse* OR *Misuse* OR *Overdose* OR *Addiction* OR *Depend**
- AND **(Factors Key Words)** *Predictor** OR *Risk factor** OR *Protective factor** OR *Contributing factor**

The result was 42 studies that met our criteria for inclusion. Specifically, these studies were:

- Published in a peer-reviewed journal between 2005 and 2015.
- Available in full text.
- Implemented with a U.S.-based sample.
- Published in English.

These studies also:

- Included clearly articulated methods for establishing associations between specific risk or protective factors and NMUPD.
- Assessed at least one main outcome (dependent variable) specifically related to NMUPD use or consequences.
- Established a direct (and statistically significant) link between risk or protective factors and NMUPD outcomes⁵ of interest.
- Used quantitative data analyses.
- Included human participants.

In addition, articles were excluded that:

- Focused on the evaluation of prevention or treatment strategies.
- Did not identify any risk or protective factors statistically linked ($p < .05$) to NMUPD outcomes.
- Were literature reviews, non-primary sources, commentaries, news report, or historical perspectives. Note, however, that studies meeting inclusion criteria were distilled from literature reviews produced in our search.
- Included a combined or composite outcome measure of multiple types of drug use.

⁵ Although some studies demonstrated links between risk or protective factors and multiple substances, we report NMUPD outcomes only in this document.

USING THIS RESOURCE TO GUIDE PREVENTION PRACTICE

This tool comprises two sections, each organized according to the socio-ecological levels of influence—individual, relationship, community, and societal:

- Section 1 provides at-a-glance information on which risk or protective factors are linked to which outcomes for specific population groups. When reading through the tables in this section, you should be able to say that a given protective factor is associated with a specific outcome among a given population (according to this study). For example, referencing an entry from the table highlighting individual-level factors, we can say that: having a current depression diagnosis is associated with greater likelihood of prescription opioid misuse among youth from ages 12 to 17.⁶
- Section 2 provides detailed information on the research studies that identify these factors. Within each level of influence, we list relevant articles, the factors they identify, and details on participant characteristics, analyses, and any outcomes significantly associated with the identified factors.

Although there are several ways to approach and use these tools, here are some suggested steps or guidelines:

- **Conduct a needs assessment *before* looking at this tool.** Conducting a thorough needs and resource assessment is an important first step for every effort to prevent substance misuse. However, this tool should not be the starting point for this assessment. Instead, you should begin by examining local data to identify the relevant risk and protective factors that are driving NMUPD in your community. You may discover that certain factors are unique to your community that were not relevant in the communities studied. For instance, not all communities have a large number of high school students with a low perception of the risks associated with NMUPD.
- **Target factors addressed by available research literature.** Targeting established factors, even those with weak evidence, is more likely to influence NMUPD than targeting factors that lack any research supporting an association between them and NMUPD. Review the “Risk Factor” and “Protective Factor” columns of the tables in either Section 1 or Section 2 to quickly identify research-supported factors. Note that the same factors may appear in multiple studies, but be associated with different outcomes. Also note that certain factors may be strongly related to other factors that also affect NMUPD, and that it may be possible to implement a single intervention that improves both factors. For instance, if lack of parental disapproval of NMUPD *and* increased availability of prescription drugs at home are both significant risk factors for a

⁶ Ford & Rigg, 2015

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community, a single well-designed parental education strategy may be able to address both factors.

- **Reconcile factors identified via community assessment with those included here.** What if a risk or protective factor identified in your community's local needs assessment doesn't appear in this tool? First, determine whether this is simply because your assessment may have labeled the factor differently than the way the tool does. The factor labels in the tool reflect the language used in the articles, standardized as much as possible across the articles; as such, they can't capture all variations. To address this possibility, it's helpful to examine the original article (complete citations for all articles are provided below). If it is truly the case that the factor(s) identified in your assessment are not included in the tool, you may want to consider focusing on other factors that are supported by research literature, or attempt to identify and examine literature not included in this tool for research on your factor of interest.
- **Focus on factors that you have the greatest likelihood of changing.** There are some risk and protective factors that prevention strategies cannot modify (e.g., race, gender, or age) or are not easily modified (e.g., socio-economic status, geographic location, or level of educational attainment). However, these background or demographic factors may be useful in determining which high-risk populations a strategy should focus on or emphasize. Factors that are not easily addressed are included here; factors that cannot be addressed are not included.
- **Determine the relevance of identified risk and protective factors.** The "Population" column in Table 2 can help you determine the relevance of a factor to your community's local conditions. For instance, a study that focused on factors related to NMUPD among veterans may not be relevant to a community seeking to implement an intervention focusing on high school students. However, there are also common factors across populations, and a study focusing on a population not matching a community's needs may still provide valuable information. Similarly, the "Outcome(s)" column in either table can help you determine which studies provide the most direct support for the factors your community is interested in exploring. For instance, if "prescription opioid misuse" is your community's primary problem of interest, the tool can help you identify articles that list prescription opioid misuse as an outcome, as well as the factors significantly associated with that outcome.
- **Don't be fooled by frequency.** When trying to determine where to focus your prevention efforts, guard against selecting factors and assigning importance based on how often a specific factor appears in this tool. Although numerous studies may identify the same factor, the evidence in all the studies may be weak. Additionally, some study designs were created based on the availability of data, and some factors have more readily available data, and so appear more frequently. Comparing and weighing the evidence of the different studies is beyond the scope of this tool, although information is provided that allows you to determine whether study analyses established temporal relationships between risk/protective factors and

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outcomes (i.e., that the risk factors precede substance-using behaviors rather than the other way around), and/or whether they controlled for other factors. In general, it is best to leave rigorous study comparisons to researchers, evaluators, or others with appropriate training and experience.

- **Examine study details.** For each study identified in our search, Section 2 provides detailed information on the study's research design, geographic location, time frame, sample size, sample gender composition, and sample age range. These details can help you determine whether a factor is relevant, given your chosen focus, and also whether that factor is more likely to co-occur with (cross-sectional design) or precede (longitudinal design) NMUPD. Any study where this information is not provided is the result of study authors not reporting it. For more detailed information on study methods consult the full text articles.
- **Examine other literature about risk and protective factors.** If you believe that specific risk or protective factors may be missing from this tool, then consider searching databases, such as those discussed earlier, to retrieve any additional articles of interest. This search might include articles published before or after this tool's time range, literature reviews, studies using non-U.S.-based samples, qualitative studies, or studies not published in peer-reviewed journals. Communities may use the search terms listed at the start of this tool, variations on them, or other relevant terms.

The next step. Once you and your community have settled on the risk or protective factors you hope to change to impact NMUPD, the next step is to select one or more strategies that address them. The companion CAPT tool, [*Preventing Prescription Drug Misuse: Programs and Strategies*](#), may be useful in this process.

A FEW CAUTIONARY NOTES REGARDING USE

Please use prudence when interpreting information included in these tables. Here is why:

1. The findings are limited to the time frame, libraries, and search parameters described above. Expanding the time frame or examining risk and protective factors associated with other substances may uncover additional or conflicting factors. However, scientifically rigorous study of risk and protective factors associated with NMUPD is a relatively recent development, and there is not yet a robust number of completed studies. As such, in some cases there may be only one study supporting the claim of an association between a specific risk or protective factor and NUMPD.
2. The methodological rigor of the studies in this tool varies widely, from longitudinal studies that followed individuals over time to retrospective studies using readily available administrative or clinical data collected for other purposes. The majority of studies are cross-sectional designs

that cannot categorically determine whether a temporal relationship exists between a risk or protective factor and NMUPD (i.e., cannot determine whether the risk or protective factor occurred prior to the NMUPD outcome).

3. We do not include studies demonstrating insignificant or negative findings related to the risk or protective factors featured here. It is possible that for every study demonstrating a positive finding on any given factor, there is a study showing no findings—suggesting that the relationship between the contributing or associated factor and the outcome is inconclusive. For this reason, you may want to consider only those risk or protective factors supported by two or more studies.

GLOSSARY OF TERMS

To keep the tool as concise and consistent as possible, many technical terms are used without explanation. While many of these terms may be familiar to prevention experts, such as the difference between *misuse* and *dependence*, others are terms more commonly used in other fields. The following is a list of terms used in this tool with which prevention experts might be less familiar, accompanied by short definitions:

Bivariate analysis: A type of analysis in which only two variables from the selected outcomes, risk and protective factors, and other relevant variables are studied at a time to determine whether they are significantly associated. Not as robust as a multivariate analysis because it does not account for other factors that might be associated with NMUPD outcomes.

Cluster sampling: A sampling method that divides a population into groups or clusters based on a set of characteristics, then selects, at random, a given number of clusters to include in the sample. Each member of the population can be assigned to only one cluster.

Convenience sample: A sample composed of readily available individuals who meet the sample's inclusion criteria.

Control group: A group of individuals in a sample who did not receive the intervention. Their post-intervention data are compared to individuals in the sample who did receive the intervention to determine the effect of the intervention.

Cross-sectional study: Refers to a study for which data is collected from its sample members at only one point in time. The study may have taken place over a period of time to facilitate data collection, but each sample member's data is from a single point in time.

Descriptive analysis: A type of analysis that enables you to identify patterns in quantitative data. Types of statistics used to describe data include measures of central tendency (e.g., mode, median, mean), distribution (e.g., frequency distribution), and dispersion (e.g., standard deviation, range, variance).⁷

Drug dependence: A need for repeated doses of a drug to feel good or to avoid feeling bad.⁸

Drug misuse: The use of a substance for a purpose not consistent with legal or medical guidelines.⁹

ICD-10: Shorthand for the *International Statistical Classification of Diseases and Related Health Problems, 10th Edition* which is used to code and classify mortality data from death certificates.¹⁰

IMS® LRx: A longitudinal database that includes information on patient-level prescriptions based on pharmacy coding center data.

IMS® Dx: A database that includes information on patient diagnoses based on physician insurance claims. It can be linked to the *IMS® LRx*.

Longitudinal study: Refers to a study for which data is collected from its sample members at multiple points over a period of time. This type of study is considered more robust than a cross-sectional study due to its ability to compare data from before and after an intervention occurred.

Multivariate analysis: A type of analysis in which the selected outcomes, main risk and protective factors, and other relevant variables are all included in a single analysis to determine the statistically significant associations between main factors of interest, accounting for other factors.

Prospective study: A study that looks for the development of outcomes over the course of its time range. The study is seeking to determine what outcomes will derive from selected factors. Contrast with *retrospective study*.

Randomized sample: A sample composed of individuals selected at random. A study with a randomized sample is considered more robust due to its ability to eliminate threats to a study's validity, such as selection bias. Random sample studies are often not feasible to conduct.

Retrospective study: A study that looks at data where the outcome has already occurred. The study is seeking to determine what factors led to the outcome. Contrast with *prospective study*.

Sensitivity analyses: A technique used to determine how different risk or protective factor values will influence an outcome under different conditions.

⁷ Trochim, 2006

⁸ National Institute on Drug Abuse, 2007

⁹ World Health Organization, 2006

¹⁰ More information can be found here: <http://www.cdc.gov/nchs/icd/icd10cm.htm>

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Stratified sampling: A type of sampling method in which the researcher divides the population in groups (e.g., by sex, race, age), called strata. Then, he or she will draw a random sample from each group. Researchers often stratify samples in order to make sure that different groups are represented in the sample.

Tapentadol: A type of opioid pain medication.

Test group: A group of individuals in a sample that receive the intervention. Their post-intervention data are compared to individuals in the sample who did not receive the intervention to determine the effect of the intervention.

SECTION 1. RISK AND PROTECTIVE FACTORS, ORGANIZED BY FACTOR

INDIVIDUAL-LEVEL FACTORS

At the individual level, individuals most at risk of NMUPD include those with a history of **mental illness** (i.e., history of depression,¹¹ posttraumatic stress disorder,¹² anxiety¹³), **acute and chronic pain** (i.e., having a current painful physical disorder,¹⁴ chronic pain,¹⁵ past-year back pain¹⁶), **physical health problems** (i.e., fatigue,¹⁷ headaches¹⁸), and **heightened physiological reactions** to certain types of drugs (i.e., having a greater subjective euphoric reaction¹⁹). The link between pain, physical health problems, and opioid use seems likely because these drugs (e.g., opioids) are often prescribed to lessen pain.²⁰ It may be that people start by using opioids as prescribed, develop dependence, have a difficult time tapering off and, ultimately, find a way to access and use against original doctor's orders.²¹ Having prescription drugs on hand may perpetuate NMUPD because evidence suggests that individuals who have access to prescription drugs²² and who are prescribed opioids at a large dosage²³ or have multiple prescriptions²⁴ are at greater risk of NMUPD.

Having a past **history of other substance use or misuse** is also linked to NMUPD. People who have a history of substance use disorder, who use alcohol heavily, or who use illicit drugs are more likely to engage in NMUPD. These individuals have already engaged in risky behaviors; they have initiated substance use and some are abusing other substances. This finding also suggests that those who misuse prescription drugs are more likely to also be polydrug users.²⁵ It may also suggest that these individuals may benefit from prevention messages and interventions other than those that specifically target NMUPD. A broader, more comprehensive approach to preventing substance misuse in general may be appropriate to those in this category exhibiting risk for NMUPD.

¹¹ Boscarino et al., 2010; Ford & Rigg, 2015; Grattan, Sullivan, Saunders, Campbell, & Von Korff, 2012; Koyyalagunta et al., 2013; Park & Lavin, 2010

¹² Mackesy-Amiti, Donenberg, & Ouellet, 2015

¹³ Koyyalagunta et al., 2013; Mowbray & Quinn, 2015

¹⁴ Edlund, Steffick, Hudson, Harris, & Sullivan, 2007; Sullivan et al., 2010

¹⁵ Rosenblum et al., 2007

¹⁶ Cepeda, Fife, Kihm, Mastrogiovanni, & Yuan, 2014; Edlund et al., 2010; Sullivan et al., 2010

¹⁷ Koyyalagunta et al., 2013

¹⁸ Edlund et al., 2010

¹⁹ Bieber et al., 2008

²⁰ Haddox et al., 1997; Joranson, Ryan, Gilson, & Dahl, 2000

²¹ Lankenau et al., 2012

²² Edlund et al., 2014; Jeffery, Babeu, Nelson, Kloc, & Klette, 2013; Silva, Schragger, Kecojevic, & Lankenau, 2013

²³ Bohnert et al., 2011; Edlund, Steffick, Hudson, Harris, & Sullivan, 2007; Koyyalagunta et al., 2013; Sullivan et al., 2010

²⁴ Peirce, Smith, Abate, & Halverson, 2012

²⁵ McCabe & Teter, 2007; Sung, Richter, Vaughan, Johnson, & Thom, 2005

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Regarding protective factors, individuals who **commit to doing well**²⁶ and **finishing school**²⁷ are less likely to misuse prescription drugs. These include individuals who are current students,²⁸ have a high school diploma,²⁹ or have attended a prevention class.³⁰ Students who are committed to school and have a strong school bond are less likely to engage in risky behaviors. The Social Development Model³¹ suggests that this occurs because once a student has strong school bonds, they conform to the norms and values of the school; if the school norms discourage substance use or misuse, then a strongly bonded student will more likely remain faithful to the norms and not engage in substance use. It is worth noting, however, that one study found that having a college degree was associated with higher likelihood of unintentional fatal opioid overdose at home for New York City residents.³² This study differs from the other studies examining associations between academic achievement and NMUPD in that the sample studied included individuals who unintentionally overdosed on opioids at home or outside the home. It's possible that there is something about having a college education that propels opioid misuse at home rather than outside the home and requires further exploration.

Another common protective factor includes **perceptions about prescription drug misuse**. For example, if individuals don't think they are doing anything wrong when they take prescription drugs without a doctor's orders, then they are more likely to misuse them.³³ Conversely, those who are concerned about the dangers of prescription drugs are less likely to misuse them.³⁴ These findings mirror those from studies linking perception of harm and other kinds of substance abuse (e.g., alcohol).³⁵

²⁶ Collins, Abadi, Johnson, Shamblen, & Thompson, 2011

²⁷ Arkes & Iguchi, 2008

²⁸ Arkes & Iguchi, 2008

²⁹ Arkes & Iguchi, 2008

³⁰ Ford & Rigg, 2015

³¹ Catalano & Hawkins, 1996

³² Siegler, Tuazon, O'Brien, & Paone, 2014

³³ Collins, Abadi, Johnson, Shamblen, & Thompson, 2011

³⁴ Ford & Rigg, 2015

³⁵ Henry, Slater, & Oetting, 2005

INDIVIDUAL-LEVEL FACTORS

How to read this table: “Factor is associated with Outcome among Population(s) of Interest.”

INDIVIDUAL-LEVEL FACTORS

| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
|---|-------------------|--|---|--|
| Mental Health | | | | |
| Ever being admitted to a psychiatric hospital | | <ul style="list-style-type: none"> • Non-fatal prescription drug overdose | Individuals (mostly homeless) who misused prescription drugs at least three times in the past 90 days (age range = 16–25) | Silva, Schrage, Kecojevic, & Lankenau, 2013 |
| Having a history of depression | | <ul style="list-style-type: none"> • Opioid addiction | Individuals who received 4+ opioid prescriptions (age range = 18 or older) | Boscarino et al., 2010 |
| Having a current anti-social personality disorder diagnosis | | <ul style="list-style-type: none"> • Past-year prescription opioid misuse | Individuals who inject drugs (age range = 18–25; average age = 22.2) | Mackesy-Amiti, Donenberg, & Ouellet, 2015 |
| Having a current depression diagnosis | | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH ³⁶ respondents (age range = 12–17) | Ford & Rigg, 2015 |
| | | <ul style="list-style-type: none"> • Prescription opioid misuse | Individuals receiving chronic opioid therapy with no history of substance abuse (age range = 21–80) | Grattan, Sullivan, Saunders, Campbell, & Von Korff, 2012 |
| | | <ul style="list-style-type: none"> • Prescription opioid misuse | Outpatient clinic patients (average age = 72.8) | Park & Lavin, 2010 |

³⁶ National Survey on Drug Use and Health

| INDIVIDUAL-LEVEL FACTORS | | | | |
|---|----------------------------|---|--|--|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Having a current depression diagnosis (cont.) | | <ul style="list-style-type: none"> • Risk for opioid misuse | Individuals with cancer receiving services from a pain center | Koyyalagunta et al., 2013 |
| Having a current mental health disorder | | <ul style="list-style-type: none"> • Prescription opioid abuse | Veterans who were being prescribed 91-day or more supply of opioids, never had a cancer diagnosis, and have not had an opioid dependence diagnosis | Edlund, Steffick, Hudson, Harris, & Sullivan, 2007 |
| Having a mental health disorder diagnosis | | <ul style="list-style-type: none"> • Opioid abuse • Opioid dependence | Medicaid and private insurance network enrollees who were prescribed at least 90 days of opioids | Edlund et al., 2010 |
| | | <ul style="list-style-type: none"> • Opioid use disorder | Private insurance network enrollees with a cancer diagnosis | Edlund et al., 2014 |
| | | <ul style="list-style-type: none"> • Prescription opioid misuse | Medicaid and private insurance network enrollees who used opioids for at least 90 days | Sullivan et al., 2010 |
| Having ever been diagnosed with posttraumatic stress disorder | | <ul style="list-style-type: none"> • Past-year prescription opioid misuse • Past-year prescription opioid abuse • Past-year prescription opioid dependence | Men who inject drugs (age range = 18–25; average age = 22.2) | Mackesy-Amiti, Donenberg, & Ouellet, 2015 |
| | Having positive well-being | <ul style="list-style-type: none"> • Risk for opioid misuse | Individuals with cancer receiving services from a pain center | Koyyalagunta et al., 2013 |
| Having high attentional impulsivity | | <ul style="list-style-type: none"> • Risk for prescription opioid misuse | Individuals receiving opioid therapy for chronic low-back pain (average age = 47.5) | Marino et al., 2013 |

| INDIVIDUAL-LEVEL FACTORS | | | | |
|--|-------------------|---|---|--|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Having suicidal ideation | | <ul style="list-style-type: none"> • Prescription drug misuse | Homeless youth (average age = 21.5) | Rhoades, Winetrobe, & Rice, 2014 |
| Past 30-day anxiety | | <ul style="list-style-type: none"> • Risk for opioid misuse | Individuals with cancer receiving services from a pain center | Koyalagunta et al., 2013 |
| Past-year anxiety diagnosis | | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age range = 18–25) | Mowbray & Quinn, 2015 |
| Past-year posttraumatic stress disorder diagnosis | | <ul style="list-style-type: none"> • Past-year prescription opioid abuse • Past-year prescription opioid dependence | Men who inject drugs (age range = 18–25; average age = 22.2) | Mackesy-Amiti, Donenberg, & Ouellet, 2015 |
| Past-year substance-induced major depression diagnosis | | <ul style="list-style-type: none"> • Past-year prescription opioid misuse | Individuals who inject drugs (age range = 18–25; average age = 22.2) | Mackesy-Amiti, Donenberg, & Ouellet, 2015 |
| Past-year mood disorders | | <ul style="list-style-type: none"> • Prescription opioid abuse • Doctor shopping | Individuals in pharmaceutical coverage claims databases who were prescribed either tapentadol Immediate Release (IR) or oxycodone IR | Cepeda, Fife, Kihm, Mastrogiovanni, & Yuan, 2014 |
| Experiencing Pain | | | | |
| “Catastrophizing” current pain severity | | <ul style="list-style-type: none"> • Risk for prescription opioid misuse | Veterans who have a current or previous substance use disorder and received an opioid prescription in the last 90 days (average age = 55) | Morasco, Turk, Donovan, & Dobscha, 2013 |

| INDIVIDUAL-LEVEL FACTORS | | | | |
|---|-------------------|---|--|--|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| "Catastrophizing" current pain severity (cont.) | | <ul style="list-style-type: none"> Risk for prescription opioid misuse | Individuals being treated for chronic musculoskeletal pain who do not have a current substance use disorder (average age = 47.3) | Martel, Wasan, Jamison, & Edwards, 2013 |
| Having a current painful physical disorder | | <ul style="list-style-type: none"> Prescription opioid misuse | Medicaid and private insurance network enrollees who used opioids for at least 90 days | Sullivan et al., 2010 |
| | | <ul style="list-style-type: none"> Prescription opioid abuse | Veterans who were being prescribed a 91-day or more supply of opioids, never had a cancer diagnosis, and have not had an opioid dependence diagnosis | Edlund, Steffick, Hudson, Harris, & Sullivan, 2007 |
| Having a high level of pain | | <ul style="list-style-type: none"> Risk for prescription opioid misuse | Individuals being treated for chronic musculoskeletal pain who do not have a current substance use disorder (average age = 47.3) | Martel, Wasan, Jamison, & Edwards, 2013 |
| | | <ul style="list-style-type: none"> Risk for opioid misuse | Individuals with cancer receiving services from a pain center | Koyyalagunta et al., 2013 |
| | | <ul style="list-style-type: none"> Opioid addiction | Individuals who received 4+ opioid prescriptions (age range = 18 or older) | Boscarino et al., 2010 |
| | | <ul style="list-style-type: none"> Prescription opioid misuse | Outpatient clinic patients (average age = 72.8) | Park & Lavin, 2010 |
| Having chronic pain | | <ul style="list-style-type: none"> Prescription opioid abuse | Individuals with opioid dependence receiving methadone (average age = 35) | Rosenblum et al., 2007 |

| INDIVIDUAL-LEVEL FACTORS | | | | |
|--|-------------------|--|--|--|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Having an increased perception of pain negative effects (anxiety about pain) | | <ul style="list-style-type: none"> Risk for prescription opioid misuse | Individuals being treated for chronic musculoskeletal pain who do not have a current substance use disorder (average age = 47.3) | Martel, Wasan, Jamison, & Edwards, 2013 |
| Having four or more non-tracer pain diagnoses | | <ul style="list-style-type: none"> Opioid use disorder | Private insurance network enrollees with a cancer diagnosis | Edlund et al., 2014 |
| Having greater pain sensitivity | | <ul style="list-style-type: none"> Opioid misuse | Individuals being treated for spinal pain | Edwards et al., 2011 |
| | | <ul style="list-style-type: none"> Risk for prescription opioid misuse | Individuals being treated for chronic musculoskeletal pain who do not have a current substance use disorder (average age = 47.3) | Martel, Wasan, Jamison, & Edwards, 2013 |
| Having lower pain tolerance | | <ul style="list-style-type: none"> Opioid misuse | Individuals being treated for spinal pain | Edwards et al., 2011 |
| Having more painful withdrawal symptoms | | <ul style="list-style-type: none"> Prescription opioid abuse | Individuals with opioid dependence receiving methadone (average age = 35) | Rosenblum et al., 2007 |
| Back pain diagnosis | | <ul style="list-style-type: none"> Prescription opioid abuse Doctor shopping | Individuals in pharmaceutical coverage claims databases who were prescribed either tapentadol Immediate Release (IR) or oxycodone IR | Cepeda, Fife, Kihm, Mastrogiovanni, & Yuan, 2014 |
| | | <ul style="list-style-type: none"> Prescription opioid misuse | Medicaid and private insurance network enrollees who used opioids for at least 90 days | Sullivan et al., 2010 |
| | | <ul style="list-style-type: none"> Opioid abuse Opioid dependence | Private insurance network enrollees who were prescribed at least 90 days of opioids | Edlund et al., 2010 |

| INDIVIDUAL-LEVEL FACTORS | | | | |
|--|-------------------|---|--|---|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Reporting chronic pain as reason for methadone treatment | | <ul style="list-style-type: none"> • Prescription opioid abuse | Individuals with opioid dependence receiving methadone (average age = 35) | Rosenblum et al., 2007 |
| Physical Health | | | | |
| Having ever been hospitalized for a medical issue | | <ul style="list-style-type: none"> • Past-year prescription opioid misuse • Past-year prescription opioid abuse • Past-year prescription opioid dependence | Individuals who inject drugs (age range = 18–25; average age = 22.2) | Mackesy-Amiti, Donenberg, & Ouellet, 2015 |
| Having high levels of fatigue | | <ul style="list-style-type: none"> • Risk for opioid misuse | Individuals with cancer receiving services from a pain center | Koyalagunta et al., 2013 |
| Having 12 or more physical health care visits in one year | | <ul style="list-style-type: none"> • Prescription opioid abuse | Veterans who were being prescribed a 91-day or more supply of opioids, never had a cancer diagnosis, and have not had an opioid dependence diagnosis | Edlund, Steffick, Hudson, Harris, & Sullivan, 2007 |
| Having a poor appetite | | <ul style="list-style-type: none"> • Risk for opioid misuse | Individuals with cancer receiving services from a pain center | Koyalagunta et al., 2013 |
| Having one or more limitations on activities of daily living | | <ul style="list-style-type: none"> • Exposure to prescription drugs with abuse potential | Medicare respondents (age range = 65 or older) | Simoni-Wastila, Zuckerman, Singhal, Briesacher, & Hsu, 2005 |
| Having “poor” health | | <ul style="list-style-type: none"> • Opioid addiction | Individuals who received 4+ opioid prescriptions (age range = 18 or older) | Boscarino et al., 2010 |

| INDIVIDUAL-LEVEL FACTORS | | | | |
|------------------------------|-------------------|--|--|---|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Having “poor” health (cont.) | | <ul style="list-style-type: none"> • Prescription opioid abuse • Prescription stimulant abuse | NSDUH respondents (12 or older) | Arkes & Iguchi, 2008 |
| | | <ul style="list-style-type: none"> • Exposure to prescription drugs with abuse potential | Medicare respondents (age range = 65 or older) | Simoni-Wastila, Zuckerman, Singhal, Briesacher, & Hsu, 2005 |
| | | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age ranges = 18–25 and 35–49) | Mowbray & Quinn, 2015 |
| Headache diagnosis | | <ul style="list-style-type: none"> • Opioid abuse • Opioid dependence | Private insurance network enrollees who were prescribed at least 90 days of opioids | Edlund et al., 2010 |
| | | <ul style="list-style-type: none"> • Prescription pain reliever misuse • Prescription tranquilizer misuse • Prescription sedative misuse • Prescription stimulant misuse | Active duty service members (average age = 28.5) | Jeffery, Babeu, Nelson, Kloc, & Klette, 2013 |
| Illness | | <ul style="list-style-type: none"> • Prescription opioid overdose | Individuals who use prescription drugs as prescribed and prescribed misusers (age range = 18–70; average age = 35.2) | Green, Black, Serrano, Budman, & Butler, 2011 |

| INDIVIDUAL-LEVEL FACTORS | | | | |
|--|---|---|---|---|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| | Increased severity of physical disability ³⁷ | <ul style="list-style-type: none"> • Prescription opioid misuse | Outpatient clinic patients (average age = 72.8) | Park & Lavin, 2010 |
| Injury during deployment | | <ul style="list-style-type: none"> • Prescription pain reliever misuse • Prescription tranquilizer misuse | Active duty service members (average age = 28.5) | Jeffery, Babeu, Nelson, Kloc, & Klette, 2013 |
| Genetic and Physiological Reactions | | | | |
| Change in tolerance related to incarceration history | | <ul style="list-style-type: none"> • Prescription opioid overdose | Medically healthy abusers and illicit users (age range = 18–70; average age = 35.2) | Green, Black, Serrano, Budman, & Butler, 2011 |
| Genetic factors | | <ul style="list-style-type: none"> • Opioid dependence | Individuals recruited from other studies of opioid, cocaine, or alcohol dependence | Gelernter et al., 2014 |
| Having a greater subjective euphoric reaction to opioids | | <ul style="list-style-type: none"> • Prescription opioid addiction | Individuals who either had an opioid addiction diagnosis or were receiving long-term opioid therapy but did not have an addiction diagnosis | Bieber et al., 2008 |
| Having reduced response inhibition | | <ul style="list-style-type: none"> • Prescription stimulant use | University students who were non-dependent cocaine users or prescription stimulant misusers | Harlé et al., 2014 |
| Having stronger drug cravings | | <ul style="list-style-type: none"> • Prescription opioid abuse | Individuals with opioid dependence receiving methadone (average age = 35) | Rosenblum et al., 2007 |

³⁷ Authors suggest that physically disabled individuals may be less reliant on opioids for pain management because many consume multiple medications for conditions and are afraid of pharmacological adverse effects or because they are more open to considering nonpharmacological treatments than individuals who are less physically disabled (Park & Lavin, 2010).

| INDIVIDUAL-LEVEL FACTORS | | | | |
|--|-------------------|---|--|--|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Substance Use or Misuse | | | | |
| Being a current cigarette smoker | | <ul style="list-style-type: none"> • Prescription opioid abuse • Prescription stimulant abuse | NSDUH respondents (12 and older) | Arkes & Iguchi, 2008 |
| | | <ul style="list-style-type: none"> • Opioid misuse | Cancer treatment patients (average age = 54.8) | Novy et al., 2012 |
| Co-occurring use of prescription opioids and benzodiazepines | | <ul style="list-style-type: none"> • Unintentional fatal opioid overdose in a home | New York City residents who died from an unintentional opioid overdose (age range = 15–84) | Siegler, Tuazon, O'Brien, & Paone, 2014 |
| Ever injecting a tranquilizer | | <ul style="list-style-type: none"> • Non-fatal prescription drug overdose | Individuals (mostly homeless) who misused prescription drugs at least three times in the past 90 days (age range = 16–25) | Silva, Schragger, Kecojevic, & Lankenau, 2013 |
| Ever non-orally ingesting a prescription drug | | <ul style="list-style-type: none"> • Non-fatal prescription drug overdose | Individuals (mostly homeless) who misused prescription drugs at least three times in the past 90 days (age range = 16–25) | Silva, Schragger, Kecojevic, & Lankenau, 2013 |
| Having a current non-opioid substance use disorder | | <ul style="list-style-type: none"> • Prescription opioid abuse | Veterans who were being prescribed a 91-day or more supply of opioids, never had a cancer diagnosis, and have not had an opioid dependence diagnosis | Edlund, Steffick, Hudson, Harris, & Sullivan, 2007 |
| Having a history of opioid abuse | | <ul style="list-style-type: none"> • Opioid addiction | Individuals who received 4+ opioid prescriptions (age range = 18 or older) | Boscarino et al., 2010 |

| INDIVIDUAL-LEVEL FACTORS | | | | |
|---|-------------------|---|---|---|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Having a history of psychotropic drug use | | <ul style="list-style-type: none"> • Opioid addiction | Individuals who received 4+ opioid prescriptions (age range = 18 or older) | Boscarino et al., 2010 |
| Having a history of severe opioid abuse | | <ul style="list-style-type: none"> • Opioid addiction | Individuals who received 4+ opioid prescriptions (age range = 18 or older) | Boscarino et al., 2010 |
| Having a substance use disorder diagnosis | | <ul style="list-style-type: none"> • Opioid abuse • Opioid dependence | Medicaid and private insurance network enrollees who were prescribed at least 90 days of opioids | Edlund et al., 2010 |
| | | <ul style="list-style-type: none"> • Opioid use disorder | Private insurance network enrollees with a cancer diagnosis | Edlund et al., 2014 |
| Having baseline prescription drug misuse | | <ul style="list-style-type: none"> • Prescription drug misuse | Dependent or problem drinkers who entered a treatment program for any chemical dependency | Matzger & Weisner, 2007 |
| Having no history of injection drug use | | <ul style="list-style-type: none"> • Prescription opioid abuse | Individuals with opioid dependence receiving methadone (average age = 35) | Rosenblum et al., 2007 |
| Having no previous history of methadone treatment | | <ul style="list-style-type: none"> • Prescription opioid abuse | Individuals with opioid dependence receiving methadone (average age = 35) | Rosenblum et al., 2007 |
| Heavy alcohol use | | <ul style="list-style-type: none"> • Prescription opioid overdose | Medically healthy prescription drug abusers (age range = 18–70; average age = 35.2) | Green, Black, Serrano, Budman, & Butler, 2011 |
| History or recent initiation of drug use by injection | | <ul style="list-style-type: none"> • Prescription opioid overdose | Prescription drug misusers, medically healthy prescription drug abusers, illicit drug users (age range = 18–70; average age = 35.2) | Green, Black, Serrano, Budman, & Butler, 2011 |

| INDIVIDUAL-LEVEL FACTORS | | | | |
|---|-------------------|---|---|---|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Initiation of prescription drug misuse before age 13 (vs. after age 21) | | <ul style="list-style-type: none"> • Prescription drug abuse • Prescription drug dependence | National epidemiologic survey on alcohol and related conditions: respondents (age range = 18–98; modal age range = 25–44) | McCabe, West, Morales, Cranford, & Boyd, 2007 |
| Lifetime heroin use | | <ul style="list-style-type: none"> • Unintentional fatal opioid overdose in environments other than the home | New York City residents who died from an unintentional opioid overdose (age range = 15–84) | Siegler, Tuazon, O'Brien, & Paone, 2014 |
| Lifetime illicit substance use | | <ul style="list-style-type: none"> • Prescription drug misuse | Dependent or problem drinkers who entered a treatment program for any chemical dependency | Matzger & Weisner, 2007 |
| | | <ul style="list-style-type: none"> • Non-fatal prescription drug overdose | Individuals (mostly homeless) who misused prescription drugs at least three times in the past 90 days (age range = 16–25) | Silva, Schragar, Kecojevic, & Lankenau, 2013 |
| Lifetime marijuana use | | <ul style="list-style-type: none"> • Prescription drug misuse | Dependent or problem drinkers who entered a treatment program for any chemical dependency | Matzger & Weisner, 2007 |
| Lifetime previous misuse of prescription drugs | | <ul style="list-style-type: none"> • Prescription drug misuse | Dependent or problem drinkers who entered a treatment program for any chemical dependency | Matzger & Weisner, 2007 |

| INDIVIDUAL-LEVEL FACTORS | | | | |
|--|-------------------|--|--|--|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Other illicit substance use | | <ul style="list-style-type: none"> • Prescription pain reliever misuse • Prescription tranquilizer misuse • Prescription sedative misuse • Prescription stimulant misuse | Active duty service members (average age = 28.5) | Jeffery, Babeu, Nelson, Kloc, & Klette, 2013 |
| | | <ul style="list-style-type: none"> • Prescription drug misuse | Homeless youth (average age = 21.5) | Rhoades, Winetrobe, & Rice, 2014 |
| Other substance use disorder diagnosis | | <ul style="list-style-type: none"> • Prescription opioid addiction | Individuals receiving opioid therapy for chronic non-cancer pain (average age = 46.5) | Huffman et al., 2015 |
| Past 30-day alcohol misuse | | <ul style="list-style-type: none"> • Prescription opioid misuse | Private insurance network enrollees who used opioids for at least 90 days | Sullivan et al., 2010 |
| Past 30-day alcohol use | | <ul style="list-style-type: none"> • Prescription pain reliever misuse • Prescription stimulant misuse | Active duty service members (average age = 28.5) | Jeffery, Babeu, Nelson, Kloc, & Klette, 2013 |
| Past 30-day drunkenness | | <ul style="list-style-type: none"> • Prescription opioid abuse • Prescription stimulant abuse | NSDUH respondents (12 years or older) | Arkes & Iguchi, 2008 |
| Past 30-day other substance use | | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age range = 12–17) | Ford & Rigg, 2015 |
| Past 30-day substance use disorder | | <ul style="list-style-type: none"> • Prescription opioid misuse | Medicaid and private insurance network enrollees who used opioids for at least 90 days | Sullivan et al., 2010 |

| INDIVIDUAL-LEVEL FACTORS | | | | |
|--|-------------------|---|--|--|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Past 90-day benzodiazepine use | | <ul style="list-style-type: none"> • Prescription opioid abuse • Doctor shopping | Individuals in pharmaceutical coverage claims databases who were prescribed either tapentadol Immediate Release (IR) or oxycodone IR | Cepeda, Fife, Kihm, Mastrogiovanni, & Yuan, 2014 |
| Past 90-day injection drug use | | <ul style="list-style-type: none"> • Non-fatal prescription drug overdose | Individuals (mostly homeless) who misused prescription drugs at least three times in the past 90 days (age range = 16–25) | Silva, Schragger, Kecojevic, & Lankenau, 2013 |
| Past 90-day prescription opioid misuse | | <ul style="list-style-type: none"> • Non-fatal prescription drug overdose | Individuals (mostly homeless) who misused prescription drugs at least three times in the past 90 days (age range = 16–25) | Silva, Schragger, Kecojevic, & Lankenau, 2013 |
| Past 90-day prescription stimulant misuse | | <ul style="list-style-type: none"> • Non-fatal prescription drug overdose | Individuals (mostly homeless) who misused prescription drugs at least three times in the past 90 days (age range = 16–25) | Silva, Schragger, Kecojevic, & Lankenau, 2013 |
| Past 90-day prescription tranquilizer misuse | | <ul style="list-style-type: none"> • Non-fatal prescription drug overdose | Individuals (mostly homeless) who misused prescription drugs at least three times in the past 90 days (age range = 16–25) | Silva, Schragger, Kecojevic, & Lankenau, 2013 |
| Past-year alcohol misuse | | <ul style="list-style-type: none"> • Prescription opioid abuse • Prescription stimulant abuse | NSDUH respondents (12 and older) | Arkes & Iguchi, 2008 |
| | | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age ranges: 12–17, 18–25, 35–49) | Mowbray & Quinn, 2015 |

| INDIVIDUAL-LEVEL FACTORS | | | | |
|--|-------------------|---|--|--|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Past-year marijuana use | | <ul style="list-style-type: none"> • Prescription opioid abuse • Prescription stimulant abuse | NSDUH respondents (12 and older) | Arkes & Iguchi, 2008 |
| Past-year non-opioid prescription abuse | | <ul style="list-style-type: none"> • Prescription opioid abuse • Doctor shopping | Individuals in pharmaceutical coverage claims databases who were prescribed either tapentadol Immediate Release (IR) or oxycodone IR | Cepeda, Fife, Kihm, Mastrogiovanni, & Yuan, 2014 |
| Past-year other illicit substance use | | <ul style="list-style-type: none"> • Prescription opioid abuse • Prescription stimulant abuse | NSDUH respondents (12 and older) | Arkes & Iguchi, 2008 |
| Past-year other substance use | | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age ranges: 12–17, 18–25, 26–34, 35–49, 50+) | Mowbray & Quinn, 2015 |
| Younger age of first prescription | | <ul style="list-style-type: none"> • Initiation into opioid, stimulant and tranquilizer misuse | Prescription drug misusers (age range = 16–25; average age = 21) | Keckojevic et al., 2012 |
| Younger age of substance use initiation | | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age ranges: 12–17 and 18–25) | Mowbray & Quinn, 2015 |
| Behavior | | | | |
| Ever being incarcerated | | <ul style="list-style-type: none"> • Non-fatal prescription drug overdose | Individuals (mostly homeless) who misused prescription drugs at least three times in the past 90 days (age range = 16–25) | Silva, Schrage, Keckojevic, & Lankenau, 2013 |
| Having a history of doctor shopping behavior | | <ul style="list-style-type: none"> • Drug-related death | Residents dispensed at least one controlled prescription drug (average age = 49) | Peirce, Smith, Abate, & Halverson, 2012 |

| INDIVIDUAL-LEVEL FACTORS | | | | |
|---|-------------------|--|--|--|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Having a history of pharmacy shopping behavior | | <ul style="list-style-type: none"> • Drug-related death | Residents dispensed at least one controlled prescription drug (average age = 49) | Peirce, Smith, Abate, & Halverson, 2012 |
| Participation in organized sports | | <ul style="list-style-type: none"> • Medical use of prescription opioids • Accidental misuse of prescription opioids • Intentional misuse of prescription opioids | Male students living in Michigan (age range = 11–17; average age = 14) | Veliz et al., 2014 |
| Paying for prescriptions with cash | | <ul style="list-style-type: none"> • Prescription opioid abuse • Doctor shopping | Individuals in pharmaceutical coverage claims databases who were prescribed either tapentadol Immediate Release (IR) or oxycodone IR | Cepeda, Fife, Kihm, Mastrogiovanni, & Yuan, 2014 |
| School delinquency | | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age range = 12–17) | Ford & Rigg, 2015 |
| Prescription Access | | | | |
| Concurrent use of multiple prescribed opioids | | <ul style="list-style-type: none"> • Prescription opioid misuse | Individuals being treated with opioid prescriptions for cancer or blood diseases (age range = 12–28) | Ehrentraut et al., 2014 |
| Co-prescribed psychiatric sedative medications | | <ul style="list-style-type: none"> • Prescription opioid overdose | Prescription drug misusers, medically healthy prescription drug abusers, illicit drug users (age range = 18–70; average age = 35.2) | Green, Black, Serrano, Budman, & Butler, 2011 |
| Excessive exposure to prescription opioids or benzodiazepines | | <ul style="list-style-type: none"> • Drug-related death | Residents dispensed at least one controlled prescription drug (average age = 49) | Peirce, Smith, Abate, & Halverson, 2012 |

| INDIVIDUAL-LEVEL FACTORS | | | | |
|---|---|---|--|--|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Having a larger prescribed dosage of opioids | | • Opioid use disorder | Private insurance network enrollees with a cancer diagnosis | Edlund et al., 2014 |
| | | • Prescription opioid addiction | Individuals receiving opioid therapy for chronic non-cancer pain (average age = 46.5) | Huffman et al., 2015 |
| | Having a long-acting opioid prescription only | • Prescription opioid misuse | Medicaid and private insurance network enrollees who used opioids for at least 90 days | Sullivan et al., 2010 |
| | Having a lower prescribed dosage of opioids | • Opioid abuse • Opioid dependence | Medicaid and private insurance network enrollees who were prescribed at least 90 days of opioids | Edlund et al., 2010 |
| | Having a lower prescribed supply of opioids | • Opioid abuse • Opioid dependence | Private insurance network enrollees who were prescribed at least 90 days of opioids | Edlund et al., 2010 |
| Having a maximum prescribed daily opioid dosage greater than 100 milligrams | | • Unintentional fatal prescription opioid overdose | Individuals being treated with opioid pain management therapy (age range = 18–70+ years; modal sample age 50–59) | Bohnert et al., 2011 |
| Having a prescription for anxiety/depression | | • Prescription pain reliever misuse • Prescription tranquilizer misuse • Prescription sedative misuse | Active duty service members (average age = 28.5) | Jeffery, Babeu, Nelson, Kloc, & Klette, 2013 |
| Having a prescription for high-dosage morphine | | • Risk for opioid misuse | Individuals with cancer receiving services from a pain center | Koyyalagunta et al., 2013 |

| INDIVIDUAL-LEVEL FACTORS | | | | |
|---|--|--|--|--|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Having a prescription for more than a 211-day supply of opioid medication in one year | | <ul style="list-style-type: none"> • Prescription opioid abuse | Veterans who were being prescribed a 91-day or more supply of opioids, never had a cancer diagnosis, and have not had an opioid dependence diagnosis | Edlund, Steffick, Hudson, Harris, & Sullivan, 2007 |
| Having a prescription for opioids | | <ul style="list-style-type: none"> • Non-fatal prescription drug overdose | Individuals (mostly homeless) who misused prescription drugs at least three times in the past 90 days (age range = 16–25) | Silva, Schragar, Keckojevic, & Lankenau, 2013 |
| | | <ul style="list-style-type: none"> • Opioid use disorder | Private insurance network enrollees with a cancer diagnosis | Edlund et al., 2014 |
| Having a prescription for pain relievers | | <ul style="list-style-type: none"> • Prescription pain reliever misuse • Prescription tranquilizer misuse • Prescription sedative misuse • Prescription stimulant misuse | Active duty service members (average age = 28.5) | Jeffery, Babeu, Nelson, Kloc, & Klette, 2013 |
| | Having a prescription for Schedule III or IV opioids | <ul style="list-style-type: none"> • Opioid abuse • Opioid dependence | Medicaid and private insurance network enrollees who were prescribed at least 90 days of opioids | Edlund et al., 2010 |
| Having a prescription for sedatives or hypnotics | | <ul style="list-style-type: none"> • Opioid abuse • Opioid dependence | Medicaid and private insurance network enrollees who were prescribed at least 90 days of opioids | Edlund et al., 2010 |

| INDIVIDUAL-LEVEL FACTORS | | | | |
|---|---|--|---|---|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| | Having a prescription for stimulants ^{38,39} | • Non-fatal prescription drug overdose | Individuals (mostly homeless) who misused prescription drugs at least three times in the past 90 days (age range = 16–25) | Silva, Schrage, Kecojevic, & Lankenau, 2013 |
| | | • Prescription stimulant misuse | University students (average age = 19.6) | Gallucci, Martin, Beaujean, & Usdan, 2015 |
| Having a prescription for tranquilizers | | • Non-fatal prescription drug overdose | Individuals (mostly homeless) who misused prescription drugs at least three times in the past 90 days (age range = 16–25) | Silva, Schrage, Kecojevic, & Lankenau, 2013 |
| Having a short-acting opioid prescription only or in conjunction with a long-acting opioid prescription | | • Prescription opioid misuse | Medicaid and private insurance network enrollees who used opioids for at least 90 days | Sullivan et al., 2010 |
| Having a prescription for a high-dosage opioid | | • Prescription opioid misuse | Medicaid and private insurance network enrollees who used opioids for at least 90 days | Sullivan et al., 2010 |
| Having unmonitored access to tranquilizers | | • Initiation of tranquilizer use | Prescription drug misusers (age range = 16–25; average age = 21) | Kecojevic et al., 2012 |
| Obtaining filled prescriptions for two or more types of controlled substances | | • Drug-related death | Residents dispensed at least one controlled prescription drug (average age = 49) | Peirce, Smith, Abate, & Halverson, 2012 |

³⁸ Individuals misusing stimulants may exhibit different drug use patterns than those misusing opioids. In this research sample, the majority of stimulants users had stable housing and did not have a history of injection drug use compared to opioid misusers, and may therefore experience less contextual stressors that many associate with an increase in overdose risk (Silva et al., 2013).

³⁹ Authors suggest that students with prescriptions may feel more in control of its use better than those without a prescription resulting in a reduction in misuse (Gallucci et al., 2015).

| INDIVIDUAL-LEVEL FACTORS | | | | |
|---|---|---|--|--|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Obtaining four or more filled prescriptions | | <ul style="list-style-type: none"> • Drug-related death | Residents dispensed at least one controlled prescription drug (average age = 49) | Peirce, Smith, Abate, & Halverson, 2012 |
| | Prescribed tapentadol Immediate Release (IR; type of opioid drug) instead of oxycodone IR | <ul style="list-style-type: none"> • Prescription opioid abuse | Individuals in pharmaceutical coverage claims databases who were prescribed either tapentadol IR or oxycodone IR | Cepeda, Fife, Kihm, Mastrogiovanni, & Yuan, 2014 |
| | | <ul style="list-style-type: none"> • Prescription opioid abuse | Individuals in pharmaceutical coverage claims databases who were prescribed either tapentadol IR or oxycodone IR | Cepeda, Fife, Ma, & Ryan, 2013 |
| Receiving opioid therapy through a specialty clinic | | <ul style="list-style-type: none"> • Opioid addiction | Individuals who received 4+ opioid prescriptions (age range = 18 or older) | Boscarino et al., 2010 |
| Education | | | | |
| | Attending a prevention class | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age range = 12–17) | Ford & Rigg, 2015 |
| | Being a current student | <ul style="list-style-type: none"> • Prescription opioid abuse • Prescription stimulant abuse | NSDUH respondents (12 and older) | Arkes & Iguchi, 2008 |
| | Having a high school diploma | <ul style="list-style-type: none"> • Prescription opioid abuse • Prescription stimulant abuse | NSDUH respondents (12 and older) | Arkes & Iguchi, 2008 |

| INDIVIDUAL-LEVEL FACTORS | | | | |
|---------------------------------------|--|---|--|---|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Having a college degree ⁴⁰ | | <ul style="list-style-type: none"> Unintentional fatal opioid overdose in a home | New York City residents who died from an unintentional opioid overdose (age range = 15–84) | Siegler, Tuazon, O'Brien, & Paone, 2014 |
| | Having a four-year college degree | <ul style="list-style-type: none"> Prescription opioid abuse Prescription stimulant abuse | NSDUH respondents (12 and older) | Arkes & Iguchi, 2008 |
| | Having a higher commitment to doing well in school | <ul style="list-style-type: none"> Prescription drug misuse | Students in grades 5, 7, 9, and 11 in one Tennessee county | Collins, Abadi, Johnson, Shamblen, & Thompson, 2011 |
| Employment | | | | |
| | Being employed | <ul style="list-style-type: none"> Prescription opioid abuse | NSDUH respondents (age range = 35–49) | Arkes & Iguchi, 2008 |
| Being employed | | <ul style="list-style-type: none"> Prescription opioid abuse | Individuals with opioid dependence receiving methadone (average age = 35) | Rosenblum et al., 2007 |
| | | <ul style="list-style-type: none"> Prescription opioid misuse | NSDUH respondents (age range = 18–25) | Mowbray & Quinn, 2015 |
| Being unemployed ⁴¹ | | <ul style="list-style-type: none"> Prescription stimulant abuse | NSDUH respondents (age range = 18–25) | Arkes & Iguchi, 2008 |

⁴⁰ The focus of the study was on exploring the demographics of those who overdosed at home versus those outside the home. The rest of the studies listed in this document explore education factors with outcomes associated with misuse or abuse. There could be something about a college educated person which propels them to misuse opioids at home rather than outside the home.

⁴¹ 18 to 25 year olds who are unemployed have higher risk than those who are out of the workforce (Arkes & Iguchi, 2008). Those out of the workforce may be current students; thus protecting them from stimulant misuse.

| INDIVIDUAL-LEVEL FACTORS | | | | |
|--|--|--|--|--|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| | Being unemployed ⁴² | <ul style="list-style-type: none"> • Prescription stimulant abuse | NSDUH respondents (age range = 26–34) | Arkes & Iguchi, 2008 |
| Health Insurance | | | | |
| Having health insurance ⁴³ | | <ul style="list-style-type: none"> • Prescription stimulant abuse | NSDUH respondents (age range = 18–25) | Arkes & Iguchi, 2008 |
| | Having health insurance | <ul style="list-style-type: none"> • Prescription opioid abuse • Prescription stimulant abuse | NSDUH respondents (age range = 35 or older) | Arkes & Iguchi, 2008 |
| Religiosity | | | | |
| Having decreased religiosity | | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age range = 12–17) | Ford & Rigg, 2015 |
| Spiritual beliefs influence decision-making | | <ul style="list-style-type: none"> • Prescription pain reliever misuse • Prescription stimulant misuse | Active duty service members (average age = 28.5) | Jeffery, Babeu, Nelson, Kloc, & Klette, 2013 |
| Perception | | | | |
| | Having greater perception of substance abuse risks | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age range = 12–17) | Ford & Rigg, 2015 |
| Having the perception that stimulant misuse is necessary to complete tasks | | <ul style="list-style-type: none"> • Prescription stimulant misuse | University students (average age = 19.6) | Gallucci, Martin, Beaujean, & Usdan, 2015 |

⁴² Being unemployed for 26 to 34 year olds is protective for stimulant abuse in comparison to those out of the workforce (Arkes & Iguchi, 2008). It could be that without employment, they have lack of health insurance and less access to prescriptions.

⁴³ Having health insurance may provide young adults (18-25 year olds) with an easier way to access a prescription for stimulants (Arkes & Iguchi, 2008).

| INDIVIDUAL-LEVEL FACTORS | | | | |
|---|-------------------|--|---|---|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Perceive drug test as easy to predict | | <ul style="list-style-type: none"> • Prescription pain reliever misuse | Active duty service members (average age = 28.5) | Jeffery, Babeu, Nelson, Kloc, & Klette, 2013 |
| Perception that prescription drug misuse is acceptable and safe | | <ul style="list-style-type: none"> • Prescription drug misuse | Students in grades 5, 7, 9, and 11 in one Tennessee county | Collins, Abadi, Johnson, Shamblen, & Thompson, 2011 |
| Perception that prescription drugs are readily available | | <ul style="list-style-type: none"> • Prescription drug misuse | Students in grades 5, 7, 9, and 11 in one Tennessee county | Collins, Abadi, Johnson, Shamblen, & Thompson, 2011 |
| Negative Life Events | | | | |
| Past 90-day homelessness | | <ul style="list-style-type: none"> • Non-fatal prescription drug overdose | Individuals (mostly homeless) who misused prescription drugs at least three times in the past 90 days (age range = 16–25) | Silva, Schrager, Keckojevic, & Lankenau, 2013 |

RELATIONSHIP-LEVEL FACTORS

At the relationship level, our inner circle of family and friends, with whom we are in direct contact and communicate most frequently, influence our attitudes and behaviors. Family, especially parents, can influence NMUPD among children both positively and negatively. For example, adolescent children whose **parents express disapproval** of substance use⁴⁴ or who have a **strong bond with their parents**⁴⁵ are less likely to misuse prescription drugs; adolescent children whose parents express favorable attitudes toward substance use, however, are more likely to misuse prescription drugs.⁴⁶

Youth exposure to prescription drug use in the household environment can also influence their future drug use. For example, youth who have **witnessed a family member overdose** are more likely to overdose on prescription drugs themselves,⁴⁷ and youth who have accessed stimulants for the first time in their homes initiated NMUPD at a relatively early age.⁴⁸ Peer attitudes and behaviors also may be strongly associated with individuals' NMUPD. Young people who associate with a large number of friends that misuse prescription drugs are more likely to do the same compared to their counterparts.⁴⁹ Certain social networks and situations also trigger misuse. For example, compared to their counterparts, college students involved with fraternities and sororities were more likely to misuse stimulants,⁵⁰ and Filipino-American respondents who experienced discrimination in their routine interactions were more likely to misuse prescription drugs.⁵¹

⁴⁴ Collins, Abadi, Johnson, Shamblen, & Thompson, 2011

⁴⁵ Schroeder & Ford, 2012

⁴⁶ Ford & Rigg, 2015

⁴⁷ Silva, Schragger, Kecojevic, & Lankenau, 2013

⁴⁸ Kecojevic et al., 2012

⁴⁹ Collins, Abadi, Johnson, Shamblen, & Thompson, 2011; Ford & Rigg, 2015; Schroeder & Ford, 2012

⁵⁰ Gallucci, Martin, Beaujean, & Usdan, 2015

⁵¹ Gee, Delva, & Takeuchi, 2007

RELATIONSHIP-LEVEL FACTORS

How to read this table: “Factor is associated with Outcome among Population(s) of Interest.”

RELATIONSHIP-LEVEL FACTORS

| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
|--------------------------------------|-------------------|---|---|---|
| Intimate Partner Relationship | | | | |
| Being divorced | | <ul style="list-style-type: none"> • Prescription opioid abuse • Prescription stimulant abuse | NSDUH respondents (age range = 12–50+; modal age range = 18–25) | Arkes & Iguchi, 2008 |
| Being married ⁵² | | <ul style="list-style-type: none"> • Prescription stimulant abuse | NSDUH respondents (age range = 26–34) | Arkes & Iguchi, 2008 |
| | Being married | <ul style="list-style-type: none"> • Prescription stimulant abuse | NSDUH respondents (age range = 18–25) | Arkes & Iguchi, 2008 |
| | | <ul style="list-style-type: none"> • Exposure to prescription drugs with abuse potential | Medicare respondents (age range = 65 or older) | Simoni-Wastila, Zuckerman, Singhal, Briesacher, & Hsu, 2005 |
| | | <ul style="list-style-type: none"> • Prescription sedative misuse • Prescription stimulant misuse | Active duty service members (average age = 28.5) | Jeffery, Babeu, Nelson, Kloc, & Klette, 2013 |
| Having unprotected sex | | <ul style="list-style-type: none"> • Prescription drug misuse | Homeless youth (average age = 21.5) | Rhoades, Winetrobe, & Rice, 2014 |

⁵² Authors suggest that 26 to 34 year olds who are married may experience more stress related to family and children than those who have never been married; thus increasing risk for stimulant abuse (Arkes & Iguchi, 2008).

| RELATIONSHIP-LEVEL FACTORS | | | | |
|--|---|---|---|---|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Not being married | | <ul style="list-style-type: none"> • Prescription opioid abuse | Military veterans who have been prescribed a 91-day or more supply of opioids | Edlund, Steffick, Hudson, Harris, & Sullivan, 2007 |
| Parents & Family | | | | |
| Experienced childhood sexual abuse | | <ul style="list-style-type: none"> • Initiation of tranquilizer misuse | Prescription drug misusers (age range = 16–25; average age = 21) | Keckojevic et al., 2012 |
| Experiencing a larger number of negative life events ⁵³ | | <ul style="list-style-type: none"> • Prescription drug misuse | NSDUH respondents (age range = 12–17; average age = 14.6) | Schroeder & Ford, 2012 |
| Greater parental favorable attitudes towards substance abuse | | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age range = 12–17) | Ford & Rigg, 2015 |
| | Greater parental disapproval towards prescription drug misuse | <ul style="list-style-type: none"> • Prescription drug misuse | Students in grades 5, 7, 9, and 11 in one Tennessee county | Collins, Abadi, Johnson, Shamblen, & Thompson, 2011 |
| | Having a stronger parental bond | <ul style="list-style-type: none"> • Prescription drug misuse | NSDUH respondents (age range = 12–17; average age = 14.6) | Schroeder & Ford, 2012 |
| | Having previously been in foster care ⁵⁴ | <ul style="list-style-type: none"> • Prescription drug misuse | Homeless youth (average age = 21.5) | Rhoades, Winetrobe, & Rice, 2014 |
| Household being the source of first misused stimulant | | <ul style="list-style-type: none"> • Initiation of stimulant misuse | Prescription drug misusers (age range = 16–25; average age = 21) | Keckojevic et al., 2012 |

⁵³ Negative life events were measured through an index of answers to six major life events (1) fighting with parents, (2) low grades in school, (3) not residing with biological parents, (4) not having health insurance, (5) participating in a government-assistance program, and (6) having fair or overall poor health.

⁵⁴ The participants in this study were homeless youth and those who experienced foster care were less likely to misuse (Rhoades et al., 2014). It could be that these youth had access to resources or experiences that the other homeless youth did not; thus making them less likely to misuse.

| RELATIONSHIP-LEVEL FACTORS | | | | |
|--|----------------------------------|---|---|---|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Lifetime witnessing a family member overdose | | <ul style="list-style-type: none"> • Non-fatal prescription drug overdose | Individuals (mostly homeless) who misused prescription drugs at least three times in the past 90 days (age range = 16–25) | Silva, Schragger, Kecojevic, & Lankenau, 2013 |
| Household Income | | | | |
| | Having a higher household income | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age range = 12–17) | Ford & Rigg, 2015 |
| Having a lower household income (18–25; 50+) | | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age ranges = 18–25 and 50 or older) | Mowbray & Quinn, 2015 |
| Peers | | | | |
| Greater peer prescription drug misuse | | <ul style="list-style-type: none"> • Prescription drug misuse | Students in grades 5, 7, 9, and 11 in one Tennessee county | Collins, Abadi, Johnson, Shamblen, & Thompson, 2011 |
| Greater peer favorable attitudes towards substance abuse | | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age range = 12–17) | Ford & Rigg, 2015 |
| Greater peer substance abuse or use | | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age range = 12–17) | Ford & Rigg, 2015 |
| | | <ul style="list-style-type: none"> • Prescription drug misuse | NSDUH respondents (age range = 12–17; average age = 14.6) | Schroeder & Ford, 2012 |
| Having a “Greek” organization affiliation | | <ul style="list-style-type: none"> • Prescription stimulant misuse | University students (average age = 19.6) | Gallucci, Martin, Beaujean, & Usdan, 2015 |
| Living with non-spousal other(s) | | <ul style="list-style-type: none"> • Exposure to prescription drugs with abuse potential | Medicare respondents (age range = 65 or older) | Simoni-Wastila, Zuckerman, Singhal, Briesacher, & Hsu, 2005 |

| RELATIONSHIP-LEVEL FACTORS | | | | |
|--|-------------------|--|---|--|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Social Networks | | | | |
| Alcohol misuse or illicit substance use among social networks | | <ul style="list-style-type: none"> • Prescription drug misuse | Dependent or problem drinkers who entered treatment for any chemical dependence | Matzger & Weisner, 2007 |
| Having weaker social bonds | | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age range = 12–17) | Ford & Rigg, 2015 |
| Past 30-day experiences of discriminatory behavior in routine interactions | | <ul style="list-style-type: none"> • Prescription drug misuse | Filipino-American respondents (average age = 41.6) | Gee, Delva, & Takeuchi, 2007 |

COMMUNITY-LEVEL FACTORS

At the community level, the settings where we live and work can influence the decisions we make and our subsequent behaviors. Research demonstrates that aspects of our neighborhoods where we live can influence misuse of prescription drugs. For youth ages 12 to 17, **moving three or more times in the past year** and/or living in an **urban environment** can increase the likelihood of misusing opioids.⁵⁵ In general, residential mobility or instability is associated with adverse childhood experiences⁵⁶ and can put a child at risk for developmental and social problems. Frequent mobility often disrupts routines and breaks social ties. When youth move, social capital shifts—they can lose social support and access to resources that can help them navigate developmental challenges.⁵⁷ In addition, research suggests that having a **Gay-Straight Alliance** (GSA) in schools is protective for sexual and gender minority students in high school, and helps protect against prescription opioid and ADHD medication misuse.⁵⁸ **Community norms** that disapprove of NMUPD also protect against NMUPD: if the community as a whole disapproves of use (or if young people think that their community frowns upon NMUPD), young people in that community will be less likely to misuse prescription drugs.⁵⁹

⁵⁵ Ford & Rigg, 2015

⁵⁶ Dong et al., 2005

⁵⁷ Anderson, Leventhal, Newman, & Dupéré, 2014

⁵⁸ Heck et al., 2014

⁵⁹ Collins, Abadi, Johnson, Shamblen, & Thompson, 2011

COMMUNITY-LEVEL FACTORS

How to read this table: “Factor is associated with Outcome among Population(s) of Interest.”

| COMMUNITY-LEVEL FACTORS | | | | |
|---|-------------------|---|--|---|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Living Arrangements | | | | |
| Living in a rural area | | <ul style="list-style-type: none"> • Prescription opioid abuse | Individuals with opioid dependence receiving methadone (average age = 35) | Rosenblum et al., 2007 |
| Living in an urban environment | | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age range = 12–17) | Ford & Rigg, 2015 |
| Moving three or more times in the past year | | <ul style="list-style-type: none"> • Prescription opioid misuse | NSDUH respondents (age range = 12–17) | Ford & Rigg, 2015 |
| Residing in the borough of Manhattan | | <ul style="list-style-type: none"> • Unintentional fatal opioid overdose in environments other than the home | New York City residents who died from an unintentional opioid overdose (age range = 15–84) | Siegler, Tuazon, O’Brien, & Paone, 2014 |
| Residing in the borough of Staten Island | | <ul style="list-style-type: none"> • Unintentional fatal opioid overdose in a home | New York City residents who died from an unintentional opioid overdose (age range = 15–84) | Siegler, Tuazon, O’Brien, & Paone, 2014 |

| COMMUNITY-LEVEL FACTORS | | | | |
|--|---|--|---|---|
| Risk Factor | Protective Factor | Outcome(s) | Population | Citation |
| Workplace | | | | |
| Absence of random drug testing program | | <ul style="list-style-type: none"> • Prescription pain reliever misuse • Prescription tranquilizer misuse • Prescription sedative misuse • Prescription stimulant misuse | Active duty service members (average age = 28.5) | Jeffery, Babeu, Nelson, Kloc, & Klette, 2013 |
| School | | | | |
| | Presence of Gay-Straight Alliance (GSA) in school | <ul style="list-style-type: none"> • Prescription opioid misuse • Prescription ADHD medication misuse | LGBT ⁶⁰ high school students (age range = 16 or older; average age = 17) | Heck et al., 2014 |
| Community Norms | | | | |
| | Community norms against use | <ul style="list-style-type: none"> • Prescription drug misuse | Students in grades 5, 7, 9, and 11 in one Tennessee county | Collins, Abadi, Johnson, Shamblen, & Thompson, 2011 |

⁶⁰ Lesbian, Gay, Bisexual, Transgender

SOCIETAL-LEVEL FACTORS

Societal-level factors, at the outermost level of the socio-ecological model, encompass elements of the broader culture and policy context. Out of all the socio-ecological levels, we were able to find the fewest societal-level factors related to NMUPD, primarily because the research in this area is limited. The few factors we did find, however, reveal that some individuals may turn to substances to cope with environmental stressors. One stressor associated with increased likelihood of NMUPD is **discriminatory practices** directed toward individuals who are traditionally underrepresented or marginalized. Discriminatory events (i.e., “treated unfairly or badly” because of racial or ethnic status, speaking a different language, or speaking with an accent) and unfair treatment based on social status (i.e., being treated with less courtesy or respect than others; experiencing worse service at restaurants or stores; people acting “afraid of you,” like “you are dishonest,” or they are “better than you”; being called names or insulted; and being threatened or harassed) permeate society and can place individuals, relationships, social networks, and communities on the receiving end at risk for prescription drug misuse.⁶¹

⁶¹ Gee, Delva, & Takeuchi, 2007

SOCIETAL-LEVEL FACTORS

How to read this table: “Factor is associated with Outcome among Population(s) of Interest.”

| SOCIETAL-LEVEL FACTORS | | | | |
|--|-------------------|--|---|---|
| Risk Factor | Protective Factor | Outcome | Population | Citation |
| Discrimination | | | | |
| Past-year experiences of discriminatory events | | <ul style="list-style-type: none"> • Prescription drug misuse | Filipino-American respondents (average age = 41.6) | Gee, Delva, & Takeuchi, 2007 |
| Social Perception & Media | | | | |
| Societally influenced perception of risks of substance use | | <ul style="list-style-type: none"> • Prescription drug misuse | NSDUH respondents (age range = 12–17; average age = 14.6) | Schroeder & Ford, 2012 |
| Socioeconomic Status | | | | |
| Belonging to a lower social class during adolescence | | <ul style="list-style-type: none"> • Non-fatal prescription drug overdose | Individuals (mostly homeless) who misused prescription drugs at least three times in the past 90 days (age range = 16–25) | Silva, Schragger, Kecojevic, & Lankenau, 2013 |

SECTION 2. RISK AND PROTECTIVE FACTORS, ORGANIZED BY STUDY

This section provides detailed information on the research studies that identified the risk and protective factors for NMUPD from Section 1 above. Within each level of influence, we list relevant articles, the factors they identify, and details on participant characteristics, analyses, and any outcomes significantly associated with the identified factors.

Please note: For studies with more than one outcome of interest, the outcomes are numbered, and the numbers are listed (in parentheses) next to the risk and/or protective factors with which they are significantly associated.

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|--|--|--|--|---|---|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Arkes & Iguchi, 2008 | <ul style="list-style-type: none"> • Past 30-day cigarette use (1,2)⁶² • Past 30-day drunkenness (1,2) • Past-year marijuana use (1,2) • Past-year alcohol misuse (1,2) • Past-year other illicit substance use (1,2) • Having “poor” health (1,2) • Having health insurance (for ages 18-25) (2) • Being unemployed (for ages 18-25) (2) | <ul style="list-style-type: none"> • Having a high school diploma (1,2) • Having a four-year college degree (1,2) • Being a current student (1,2) • Being employed (for ages 35-49) (1) • Being unemployed (for-ages 26-34) (2) • Having health insurance (for ages 35 and over) (1,2) | Random sample of National Survey on Drug Use and Health (NSDUH) respondents nationwide (n = 164,870; 50.8% female) from 2001 to 2003 (age range = 12–over 50; modal age range = 18–25) | Retrospective, pooled cross-sectional study using multivariate analysis of data from three survey years | (1) Prescription opioid abuse (2) Prescription stimulant abuse |

⁶² Risk factors may vary by age group depending on outcome (i.e., opioid or stimulant abuse).

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|--------------------------------------|---|----------------------|--|---|--|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Bieber et al., 2008 | <ul style="list-style-type: none"> Having a greater subjective euphoric reaction to opioids | | Convenience samples of individuals being treated at McLean Hospital in Belmont, MA, in 2008, who either had an opioid addiction diagnosis (n = 20; 50% female) or were receiving long-term opioid therapy but did not have an addiction diagnosis (n = 20; 45% female) (age range = 19–70; average age = 44) | Retrospective, cross-sectional study using bivariate analysis | <ul style="list-style-type: none"> Prescription opioid addiction |
| Bohnert et al., 2011 | <ul style="list-style-type: none"> Having a maximum prescribed daily opioid dosage greater than 100 milligrams | | Random sample of individuals being treated with opioid pain management therapy through the Veterans Health Administration (VHA) system (n = 154,684; 6.7% female) in FY2004 or FY2005 and a subgroup of that sample who had an unintentional fatal prescription opioid overdose (n = 740; 6.7% | Retrospective, cross-sectional study using bivariate analysis | <ul style="list-style-type: none"> Unintentional fatal prescription opioid overdose |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|--|--|---|--|---|--|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Bohnert et al., 2011 (cont.) | | | female) between FY2004 and FY2008 (age range = 18–over 70; modal sample age range = 50–59; modal population age range = 40–49) | | |
| Boscarino et al., 2010 | <ul style="list-style-type: none"> • Receiving opioid therapy through a specialty clinic • Having “poor” health (self-reported) • Having a high level of pain (self-reported) • Having a history of opioid abuse • Having a history of severe opioid abuse • Having a history of depression • Having a history of psychotropic drug use | | Random sample of individuals who received four or more opioid prescriptions from Geisinger Clinic prescribers serving northeastern Pennsylvania counties (n = 705) in 2006 or 2007 (age range = 18 or older) | Retrospective, cross-sectional study using multivariate and bivariate analyses | <ul style="list-style-type: none"> • Opioid addiction |
| Cepeda, Fife, Kihm, Mastrogiovanni, & Yuan, 2014 | <ul style="list-style-type: none"> • Paying for prescriptions with cash (1,2) | <ul style="list-style-type: none"> • Prescribed tapentadol Immediate Release (IR; type of opioid | National sample of individuals in the IMS LRx or the IMS Dx prescription claims databases who were | Retrospective, longitudinal study using multivariate analysis of data from baseline | <ul style="list-style-type: none"> (1) Prescription opioid abuse (2) Doctor shopping |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|--|---|---|--|--|-----------------------------|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Cepeda, Fife, Kihm, Mastrogiovanni, & Yuan, 2014 (cont.) | <ul style="list-style-type: none"> • Past-year non-opioid prescription abuse (1, 2) • Past-year mood disorders (1,2) • Past-year back pain (1,2) • Past 90-day benzodiazepine use (1,2) | drug) instead of oxycodone IR (1) | prescribed either tapentadol IR or oxycodone IR (n = 277,401; 60.3% female) in 2010 or 2011 and followed for one year (average age = 53.1) | through the ensuing year | |
| Cepeda, Fife, Ma, & Ryan, 2013 | | • Prescribed tapentadol Immediate Release (IR; type of opioid drug) instead of oxycodone IR | Random sample of individuals nationwide in the Optum or MarketScan pharmaceutical coverage claims databases who were prescribed either tapentadol IR or oxycodone IR (n = 39,367; 55.5% female) in 2010 and followed for one year. Individuals with any recent opioid exposure prior to this prescription were excluded. The average age of individuals in | Retrospective, longitudinal study using multivariate analysis of data from baseline through the ensuing year | • Prescription opioid abuse |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|---|---|---|---|---|---|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Cepeda, Fife, Ma, & Ryan, 2013 (cont.) | | | Optum was 43.8 for those prescribed oxycodone IR and 47.5 for those prescribed tapentadol IR. The average age of individuals in MarketScan was 42.1 for those prescribed oxycodone IR and 46.1 for those prescribed tapentadol. | | |
| Collins, Abadi, Johnson, Shamblen, & Thompson, 2011 | <ul style="list-style-type: none"> • Perception that prescription drugs are readily available • Perception that prescription drug misuse is acceptable and safe | <ul style="list-style-type: none"> • Having a higher commitment to doing well in school | Convenience sample of students in grades 5, 7, 9, and 11 in one Tennessee county (n = 1,105; 57% female) in 2009. Most (53%) were over the age of 13. | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> • Prescription drug misuse |
| Edlund et al., 2010 | <ul style="list-style-type: none"> • Having a mental health disorder diagnosis • Having another substance use disorder diagnosis • Having a back pain diagnosis (private enrollees only) | <ul style="list-style-type: none"> • Having a lower prescribed supply of opioids (private enrollees only) • Having a lower prescribed dosage of opioids | Populations of Arkansas Medicaid (n = 9,651; 71.6% female) and HealthCore private insurance network enrollees (n = 36,605; 59% female) who met study eligibility criteria: | Retrospective, longitudinal study using multivariate and time sensitivity analyses of data from 12 months pre-baseline to up to 54 months post-baseline | <ul style="list-style-type: none"> • Opioid abuse • Opioid dependence |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|---|---|--|--|--|---|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Edlund et al., 2010 (cont.) | <ul style="list-style-type: none"> • Having a headache diagnosis (private enrollees only) • Having a prescription for sedatives or hypnotics | <ul style="list-style-type: none"> • Having a prescription for Schedule III or IV opioids | <ul style="list-style-type: none"> • Having at least 90 days of prescribed opioid use within a six-month period between January 2001 and December 2004 • Being continuously enrolled in coverage for at least 12 months before and after that period • Cancer-free • Living in their communities | | |
| Edlund et al., 2014 | <ul style="list-style-type: none"> • Having a prescription for opioids • Having a larger prescribed dosage of opioids • Having a mental health disorder diagnosis • Having a substance use disorder diagnosis | | <p>Sample of HealthCore private insurance network enrollees (n = 568,640) who met study eligibility criteria:</p> <ul style="list-style-type: none"> • The development of at least one new chronic non-cancer pain diagnosis between 2000 and 2005 | Retrospective, longitudinal study using multivariate analyses of data from 12 months pre-baseline to 12 months post-baseline | <ul style="list-style-type: none"> • Opioid use disorder |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|--|---|----------------------|---|--|---|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Edlund et al., 2014 (cont.) | <ul style="list-style-type: none"> • Having four or more non-tracer pain diagnoses | | <ul style="list-style-type: none"> • No opioid use or diagnosis of opioid dependence in the six months prior to the new diagnosis | | |
| Edlund, Steffick, Hudson, Harris, & Sullivan, 2007 | <ul style="list-style-type: none"> • Having a current non-opioid substance use disorder • Having a current mental health disorder • Having a current painful physical disorder • Having a prescription for more than a 211-day supply of opioid medication in one year • Having 12 or more physical health care visits in one year | | Population of veterans with data in the South Central Veterans Affairs Health Care Network who met study criteria (n = 15,160; 5.1% female): <ul style="list-style-type: none"> • Being prescribed a 91-day or more supply of opioids in 2002 • Never having a cancer diagnosis • Not having an opioid dependence diagnosis in 2000, 2001, or 2002 | Retrospective, longitudinal study using multivariate analysis | <ul style="list-style-type: none"> • Prescription opioid abuse |
| Edwards et al., 2011 | <ul style="list-style-type: none"> • Having greater pain sensitivity (self-reported) • Having lower pain tolerance (self-reported) | | Convenience sample of individuals being treated at the Pain Management Center at Brigham & Women's Hospital in Boston, MA | Prospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> • Opioid misuse |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
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| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Edwards et al., 2011 (cont.) | | | for spinal pain (n = 276; 61.2% female) in 2011. | | |
| Ehrentraut et al., 2014 | <ul style="list-style-type: none"> • Concurrent use of multiple prescribed opioids | | Convenience sample of individuals being treated at St. Jude Children’s Research Hospital in Tennessee for cancer or blood disease with opioid prescriptions (n = 94; 45.7% female) in 2012 and 2013 (age range = 12–28; average age = 16.3) | Retrospective, cross-sectional study using bivariate analysis | <ul style="list-style-type: none"> • Prescription opioid misuse |
| Ford & Rigg, 2015 | <ul style="list-style-type: none"> • Having a current depression diagnosis • Having decreased religiosity • School delinquency • Past 30-day other substance use | <ul style="list-style-type: none"> • Having greater perception of substance abuse risks • Attending a prevention class | Random sample of NSDUH respondents nationwide (n = 15,648; 49.6% female) in 2012 (age range = 12–17; average age = 14.7). 5.3% of sample members reported having a history of prescription opioid misuse. | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> • Prescription opioid misuse |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
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| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Gallucci, Martin, Beaujean, & Usdan, 2015 | <ul style="list-style-type: none"> Having the perception that stimulant misuse is necessary to complete tasks | <ul style="list-style-type: none"> Having a prescription for stimulants | Cluster sample of students at a large public university in the southeast United States (n = 978; 67.8% female) in the 2010 fall semester (average age = 19.6) | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> Prescription stimulant misuse |
| Gelernter et al., 2014 | <ul style="list-style-type: none"> Genetic factors | | Cluster sample of individuals recruited from other studies of opioid, cocaine, or alcohol dependence in Connecticut, Massachusetts, Pennsylvania, or South Carolina (n = 5,697). A secondary cross-sectional cluster sample of similar individuals (n = 2,549) was used for replication purposes. | Retrospective, cross-sectional case-control study | <ul style="list-style-type: none"> Opioid dependence |
| Grattan, Sullivan, Saunders, Campbell, & Von Korff, 2012 | <ul style="list-style-type: none"> Having a current depression diagnosis | | Stratified convenience sample of individuals receiving chronic opioid therapy from Group Health Cooperative or Kaiser Permanente in California (n = 1,334; | Retrospective, cross-sectional study using multivariate analysis of survey data | <ul style="list-style-type: none"> Prescription opioid misuse |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|--|---|----------------------|---|--|--|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Grattan, Sullivan, Saunders, Campbell, & Von Korff, 2012 (cont.) | | | 69% female) in 2008 and 2009 (age range = 21–80) | | |
| Green, Black, Serrano, Budman, & Butler, 2011 | <ul style="list-style-type: none"> • Change in tolerance related to incarceration history (among medically healthy abusers and illicit users) • Illness (among those who use as prescribed and prescribed misusers) • Heavy alcohol use (among medically healthy abusers) • Co-prescribed psychiatric sedative medications (among prescribed misusers, medically healthy abusers, illicit users) • History or recent initiation of drug use by injection (among prescribed misusers, medically healthy abusers, illicit users) | | Convenience sample of population of Addiction Severity Index-Multimedia Version (ASI-MV) respondents (n = 26,314; 43.6% female) between 2005 and 2009 (age range = 18–70; average age = 35.2) | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> • Prescription opioid overdose |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
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| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Harlé et al., 2014 | <ul style="list-style-type: none"> • Having reduced response inhibition | | Convenience sample of individuals recruited from universities in California who were non-dependent cocaine users or prescription stimulant misusers (n = 158; 39.2% female) or control individuals (n = 47; 55.3% female) over a five-year period | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> • Prescription stimulant use |
| Huffman et al., 2015 | <ul style="list-style-type: none"> • Other substance use disorder diagnosis • Having a larger prescribed opioid dosage (significance found for each 50-milligram increase) | | Convenience sample of individuals receiving opioid therapy for chronic non-cancer pain in Ohio (n = 199; 60.8% female) in 2010–2011 (average age = 46.5). Individuals who had ever previously misused prescription opioids were ineligible for the study. | Retrospective, cross-sectional study using bivariate analysis | <ul style="list-style-type: none"> • Prescription opioid addiction |
| Jeffery, Babeu, Nelson, Kloc, & Klette, 2013 | <ul style="list-style-type: none"> • Received prescription for pain relief in the past month (1,2,3,4) | | Population of all active duty service members (ADSM) who completed the U.S. Department of Defense’s Health | Retrospective, cross-sectional study using multivariate analysis | <ol style="list-style-type: none"> (1) Prescription pain reliever misuse (2) Prescription tranquilizer misuse (3) Prescription sedative misuse |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|--|--|----------------------|--|--|--|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Jeffery, Babeu, Nelson, Kloc, & Klette, 2013 (cont.) | <ul style="list-style-type: none"> • Received prescription for pain relief in the past year (1,2,3,4) • Received prescription for anxiety/depression in the past month or more than a year ago (1,2,3) • Headache post-deployment (1,2,3,4) • Spiritual beliefs influence decision-making (1,4) • History of illicit drug use (1,2,3,4) • Past 30-day alcohol use (1,4) • Perceive drug test as easy to predict (1) • Injury during deployment (1,2) | | Related Behaviors Survey of Active Duty Military Personal (n = 28,546; 14.2% female) in 2008. The survey was voluntary and available to all current ADSM (average age = 28.5). | | (4) Prescription stimulant misuse |
| Keckojevic et al., 2012 | <ul style="list-style-type: none"> • Younger age of first prescription (1) • Having unmonitored access to tranquilizers (2) | | Random sample of New York and Los Angeles residents who participated in a previous study on prescription drug | Retrospective, cross-sectional study using multivariate analysis | (1) Initiation into opioid, tranquilizer, and stimulant misuse (2) Initiation of tranquilizer use |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|---|---|--|--|---|---|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Kecojevic et al., 2012 (cont.) | | | misuse (n = 596; 31.9% female) that was published in 2012 (age range = 16–25; average age = 21) | | |
| Koyalagunta et al., 2013 | <ul style="list-style-type: none"> • Having high pain status (self-reported) • Having a prescription for high-dosage morphine • Having high levels of fatigue • Having a poor appetite • Having current diagnosis of depression • Past 30-day anxiety | <ul style="list-style-type: none"> • Having positive well-being (self-reported) | Convenience sample of individuals with cancer who received services from a Texas pain center (n = 522; 52.1% female) between January and June 2009 | Prospective, longitudinal study using multivariate analysis of survey data and clinical records at baseline, one-month follow-up, and six-to-nine month follow-up | <ul style="list-style-type: none"> • Risk for opioid misuse |
| Mackesy-Amiti, Donenberg, & Ouellet, 2015 | <ul style="list-style-type: none"> • Having ever been hospitalized for a medical issue (1, 2, 3) • Having a current anti-social personality disorder diagnosis (1) • Having ever been diagnosed with posttraumatic stress | | Convenience sample of individuals who inject drugs who were recruited from Chicago, IL neighborhoods (n = 570; 38.1% female) (age range = 18–25; average age = 22.2) | Retrospective, cross-sectional study using multivariate analysis | <ol style="list-style-type: none"> (1) Past-year prescription opioid misuse (2) Past-year prescription opioid abuse (3) Past-year prescription opioid dependence |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|---|--|----------------------|--|--|---|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Mackesy-Amiti, Donenberg, & Ouellet, 2015 (cont.) | <ul style="list-style-type: none"> disorder (1, 2, 3; men only) Past-year posttraumatic stress disorder diagnosis (2, 3; men only) Past-year substance-induced major depression diagnosis (1) | | | | |
| Marino et al., 2013 | <ul style="list-style-type: none"> Having high attentional impulsivity | | Convenience sample of individuals receiving opioid therapy for chronic low-back pain in Texas who were already enrolled in a larger study about prescription opioid misuse (n = 42; 54.8% female). The study was published in 2013 (average age = 47.5). | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> Risk for prescription opioid misuse |
| Martel, Wasan, Jamison, & Edwards, 2013 | <ul style="list-style-type: none"> “Catastrophizing” current pain status Having greater pain sensitivity (self-reported) | | Convenience sample of individuals being treated for chronic musculoskeletal pain at Brigham and Women’s Hospital in | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> Risk for prescription opioid misuse |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|---|--|----------------------|--|--|---|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Martel, Wasan, Jamison, & Edwards, 2013 (cont.) | <ul style="list-style-type: none"> • Having an increased perception of pain negative effects (anxiety about pain) • Demonstrating increased pain sensitivity | | Massachusetts (n = 115; 58.3% female) (average age = 47.3) | | |
| Matzger & Weisner, 2007 | <ul style="list-style-type: none"> • Lifetime marijuana use • Lifetime other illicit substance use • Lifetime previous misuse of prescription drugs • Having baseline prescription drug misuse | | Convenience sample (n = 926) and random sample (n = 672) from a northern California county contacted in 1995 or 1996. All members of both samples were dependent or problem drinkers. The convenience sample was of individuals who entered a treatment program for any chemical dependency. | Prospective, longitudinal study using multivariate analysis of data from baseline, and post-1, 3, 5, and 7 years | <ul style="list-style-type: none"> • Prescription drug misuse |
| McCabe, West, Morales, Cranford, & Boyd, 2007 | <ul style="list-style-type: none"> • Initiation of prescription drug misuse before age 13 (vs. after age 21) | | Random sample of National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) respondents nationwide (n = 43,093; | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> • Prescription drug abuse • Prescription drug dependence |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|---|---|----------------------|--|--|---|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| McCabe, West, Morales, Cranford, & Boyd, 2007 (cont.) | | | 52% female) in 2001–2002 (age range = 18–98; modal age range = 25–44) | | |
| Morasco, Turk, Donovan, & Dobscha, 2013 | <ul style="list-style-type: none"> • “Catastrophizing” current pain severity | | Convenience sample from a larger convenience sample study (n = 284) of chronic pain in individuals receiving service from a VA medical center (n = 80; 8.7% female) between March 2009 and August 2011 (average age = 55). Inclusion in this study required individuals to also have a current or previous substance use disorder and receipt of an opioid prescription in the past 90 days. | Retrospective, cross-sectional study using multivariate analysis of survey data and clinical records | <ul style="list-style-type: none"> • Risk for prescription opioid misuse |
| Mowbray & Quinn, 2015 | <ul style="list-style-type: none"> • Past-year other substance use (ages: 12–17; 18–25; 26–34; 35–49; 50+) | | Random sample of NSDUH respondents nationwide (n = 113,665) in 2011 and 2012 (modal age range = 18–25) | Retrospective, cross-sectional study using multivariate analysis of survey data | <ul style="list-style-type: none"> • Prescription opioid misuse |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|---|--|----------------------|--|--|---|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Mowbray & Quinn, 2015 (cont.) | <ul style="list-style-type: none"> • Past-year alcohol misuse (ages: 12–17; 18–25; 35–49) • Past-year anxiety diagnosis (ages: 18–25) • “Poor” health status (self-reported) (ages: 18–25; 35–49) • Younger age of substance use initiation (ages: 12–17; 18–25) • Being employed (ages: 18–25) | | | | |
| Novy et al., 2012 | <ul style="list-style-type: none"> • Being a current cigarette smoker | | Convenience sample of every consecutive new cancer treatment patient at the Pain Management Center of the University of Texas MD Anderson Cancer Center (n = 486; 51.8% female) from January through June 2009 (average age = 54.8). 19.3% of sample | Retrospective, longitudinal study using multivariate analysis of data at baseline, 2–6 weeks post-baseline, and 6–9 months post-baseline | <ul style="list-style-type: none"> • Opioid misuse |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|---|--|---|--|---|--|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Novy et al., 2012 (cont.) | | | members were current smokers. | | |
| Park & Lavin, 2010 | <ul style="list-style-type: none"> • Having a higher level of reported pain • Having a current depression diagnosis | <ul style="list-style-type: none"> • Increased severity of physical disability | Cluster convenience sample of individuals who received care from outpatient clinics affiliated with the Baltimore Veterans Affairs Medical Center and the University of Maryland Medical System (n = 163; 31.3% female) in 2008–2009 (age range = 65–90; average age = 72.8) | Retrospective, cross-sectional study using multivariate analysis of survey data | <ul style="list-style-type: none"> • Prescription opioid misuse |
| Peirce, Smith, Abate, & Halverson, 2012 | <ul style="list-style-type: none"> • Having a history of doctor shopping behavior • Having a history of pharmacy shopping behavior • Obtaining four or more filled prescriptions • Obtaining filled prescriptions for two or more types of | | Sample of West Virginia residents dispensed at least one controlled prescription drug (n = 1,049,903) between July 2005 and December 2007, and a subset population of such residents deceased due to a drug-related overdose (n = 698) (mean population age = | Retrospective, longitudinal study using bivariate analyses of data looking backward from baseline through the previous six months | <ul style="list-style-type: none"> • Drug-related death |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|---|--|----------------------|---|--|---|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Peirce, Smith, Abate, & Halverson, 2012 (cont.) | <ul style="list-style-type: none"> controlled substances Excessive exposure to prescription opioids or benzodiazepines | | 49; mean subset population age = 40.6) | | |
| Rhoades, Winetrobe, & Rice, 2014 | <ul style="list-style-type: none"> Other illicit substance use Having suicidal ideation | | Convenience sample of homeless youth receiving services from Los Angeles drop-in centers (n = 435; 31% female) in 2012–2013 (average age = 21.5) | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> Prescription drug misuse |
| Rosenblum et al., 2007 | <ul style="list-style-type: none"> Being employed Having chronic pain Reporting chronic pain as reason for methadone treatment Having no previous history of methadone treatment Having no history of injection drug use Having stronger drug cravings | | Cluster convenience sample of individuals with opioid dependence receiving methadone treatment at 72 clinics in 33 states (n = 5,663; 36.6% female) in 2005 (average age = 35 ⁶³) | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> Prescription opioid abuse |

⁶³ The study compared individuals who abused prescription drugs to individuals who abused heroin only. As such, some of these risk factors may only be significant in that comparison and not when comparing to the general public.

| INDIVIDUAL-LEVEL FACTORS | | | | | |
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| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Rosenblum et al., 2007 (cont.) | <ul style="list-style-type: none"> • Having more painful withdrawal symptoms | | | | |
| Siegler, Tuazon, O'Brien, & Paone, 2014 | <ul style="list-style-type: none"> • Having a college degree (1) • Co-occurring use of prescription opioids and benzodiazepines (1) • Lifetime heroin use (2) | | Population of New York City residents who died from an unintentional opioid overdose as defined by the ICD-10 (n = 2,649; 26.2% female) between January 2005 and December 2010 (age range = 15–84) | Retrospective, cross-sectional study using multivariate and bivariate analyses | <ul style="list-style-type: none"> (1) Unintentional fatal opioid overdose in a home (2) Unintentional fatal opioid overdose in other environments |
| Silva, Schragar, Kecojevic, & Lankenau, 2013 | <ul style="list-style-type: none"> • Ever being admitted to a psychiatric hospital • Ever being incarcerated • Lifetime illicit substance use • Ever ingesting a prescription drug non-orally • Ever injecting a tranquilizer • Past 90-day injection drug use | <ul style="list-style-type: none"> • Having a prescription for stimulants | Stratified sample of individuals in New York City and Los Angeles who misused prescription drugs at least three times in the past 90 days (n = 596; 32.4% female) between October 2009 and March 2011 (age range = 16–25; average age = 21). Most (59.6%) of the participants were homeless. | Retrospective study using multivariate analysis | <ul style="list-style-type: none"> • Non-fatal prescription drug overdose |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
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| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Silva, Schrager, Kecojevic, & Lankenau, 2013 (cont.) | <ul style="list-style-type: none"> • Past 90-day prescription tranquilizer misuse • Past 90-day prescription opioid misuse • Past 90-day prescription stimulant misuse • Past 90-day homelessness • Having a prescription for tranquilizers • Having a prescription for opioids | | | | |
| Simoni-Wastila, Zuckerman, Singhal, Briesacher, & Hsu, 2005 | <ul style="list-style-type: none"> • Having “fair” or “poor” general health (self-reported) • Having one or more limitations on activities of daily living | | Random sample of Medicare enrollee respondents nationwide to the Medicare Current Beneficiary Survey (n = over 12,000) in 1999 (age range = 65 or older) | Retrospective, longitudinal study using multivariate analysis of data collected at three time points | <ul style="list-style-type: none"> • Exposure to prescription drugs with abuse potential |
| Sullivan et al., 2010 | <ul style="list-style-type: none"> • Past 30-day back pain • Other pain conditions • Past 30-day substance use | <ul style="list-style-type: none"> • Having a long-acting opioid prescription only | Population of Arkansas Medicaid and HealthCore private insurance network enrollees who met | Retrospective, longitudinal study using multivariate analysis of claims data from | <ul style="list-style-type: none"> • Prescription opioid misuse |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
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| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Sullivan et al., 2010 (cont.) | disorder (self-reported) <ul style="list-style-type: none"> • Past 30-day mental health disorder • Past 30-day alcohol misuse (for private insurance enrollees) • Having a prescription for a high-dosage opioid • Having a short-acting opioid prescription only or in conjunction with a long-acting opioid prescription | | study eligibility criteria (n = 32,024) between 2000 and 2005. Eligibility criteria: <ul style="list-style-type: none"> • At least 90 days of opioid use within a six-month period between 2000 and 2005, with no gap in use longer than 32 days • Continuous enrollment in coverage plan from 12 months before any 90-day period of use to 12 months after any 90-day period use • Cancer free • Living in the community | baseline through the ensuing 12 months | |

| INDIVIDUAL-LEVEL FACTORS | | | | | |
|---|--|-----------------------------|---|--|--|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| <u>Veliz et al., 2014</u> | <ul style="list-style-type: none"> • Participation in organized sports (men only) | | Subsample (n = 1,540; 48.8% female) of larger random sample (n = 4,511) Secondary Student Life Survey respondents in southeast Michigan from the 2009–10 through 2011–12 school years (age range at baseline = 11–17; average age = 14) | Prospective, longitudinal study using multivariate analysis of data at baseline and one- and two-years post-baseline | <ul style="list-style-type: none"> • Medical use of prescription opioids • Accidental misuse of prescription opioids • Intentional misuse of prescription opioids |

| RELATIONSHIP-LEVEL FACTORS | | | | | |
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| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Arkes & Iguchi, 2008 | <ul style="list-style-type: none"> • Being married (for ages 26-34) (2) • Being divorced (1,2) | <ul style="list-style-type: none"> • Being married (for ages 18-25) (2) | Random sample of NSDUH respondents nationwide (n = 164,870; 50.8% female) from 2001 to 2003 (age range = 12–over 50; modal age range = 18–25) | Retrospective, pooled cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> (1) Prescription opioid abuse (2) Prescription stimulant abuse |
| Collins, Abadi, Johnson, Shamblen, & Thompson, 2011 | <ul style="list-style-type: none"> • Greater peer prescription drug misuse | <ul style="list-style-type: none"> • Greater parental disapproval towards prescription drug misuse | Convenience sample of students in grades 5, 7, 9, and 11 in one Tennessee county (n = 1,105; 57% female) in 2009. Most (53%) were over age 13. | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> • Prescription drug misuse |
| Edlund, Steffick, Hudson, Harris, & Sullivan, 2007 | <ul style="list-style-type: none"> • Not being married | | Population of veterans with data in the South Central Veterans Affairs Health Care Network who met study criteria (n = 15,160; 5.1% female) in 2002. Study eligibility criteria included: <ul style="list-style-type: none"> • Being prescribed a 91-day or more supply of opioids in 2002 | Retrospective, longitudinal study using multivariate analysis of data from 2003 through 2005; descriptive analysis of 2002 pharmacy records and 2000–2002 clinical records were used to determine population size | <ul style="list-style-type: none"> • Prescription opioid abuse |

| RELATIONSHIP-LEVEL FACTORS | | | | | |
|--|--|--|---|--|---|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Edlund, Steffick, Hudson, Harris, & Sullivan, 2007 (cont.) | | | <ul style="list-style-type: none"> • Never having a cancer diagnosis • Not having an opioid dependence diagnosis in 2000, 2001, or 2002 | | |
| Ford & Rigg, 2015 | <ul style="list-style-type: none"> • Having weaker social bonds • Greater peer substance abuse • Greater peer favorable attitudes towards substance abuse • Greater parental favorable attitudes towards substance abuse | <ul style="list-style-type: none"> • Having a higher household income | Random sample of NSDUH respondents nationwide (n = 15,648; 49.6% female) in 2012 (age range = 12–17; average age = 14.7). 5.3% of sample members reported having a history of prescription opioid misuse. | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> • Prescription opioid misuse |
| Gallucci, Martin, Beaujean, & Usdan, 2015 | <ul style="list-style-type: none"> • Having a “Greek” organization affiliation | | Cluster sample of students at a large public university in the southeast United States (n = 978; 67.8% female) in the 2010 fall semester (average age = 19.6) | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> • Prescription stimulant misuse |

| RELATIONSHIP-LEVEL FACTORS | | | | | |
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| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Gee, Delva, & Takeuchi, 2007 | <ul style="list-style-type: none"> Past 30-day experiences of discriminatory behavior in routine interactions | | Random sample of Filipino-American Community Epidemiological Study respondents nationwide (n = 2,217; 50.7% female) in 1998 to 1999 (average age = 41.6) | Retrospective, cross-sectional study using bivariate and multivariate analysis of survey data | <ul style="list-style-type: none"> Prescription drug misuse |
| Jeffery, Babeu, Nelson, Kloc, & Klette, 2013 | | <ul style="list-style-type: none"> Being married | Population of all active duty service members (ADSM) who completed the U.S. Department of Defense's Health Related Behaviors Survey of Active Duty Military Personal (n = 28,546; 14.2% female) in 2008. The survey was voluntary and available to all current ADSM (average age = 28.5). | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> Prescription sedative misuse Prescription stimulant misuse |
| Keckojevic et al., 2012 | <ul style="list-style-type: none"> Household being the source of first misused stimulant (2) Experienced childhood sexual abuse (1) | | Random sample of New York and Los Angeles residents who participated in a previous study on prescription drug misuse (n = 596; 31.9% female) that was | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> (1) Initiation of tranquilizer misuse (2) Initiation of stimulant misuse |

| RELATIONSHIP-LEVEL FACTORS | | | | | |
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| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Kecojevic et al., 2012 (cont.) | | | published in 2012 (age range = 16–25; average age = 21) | | |
| Matzger & Weisner, 2007 | <ul style="list-style-type: none"> Alcohol misuse or illicit substance use among social network (combined measure) | | Convenience sample (n = 926) and random sample (n = 672) from a northern California county contacted in 1995 or 1996. All members of both samples were dependent or problem drinkers. The convenience sample was of individuals who entered a treatment program for any chemical dependency. | Prospective, longitudinal study using multivariate analysis of data from baseline, and post-1, 3, 5, and 7 years | <ul style="list-style-type: none"> Prescription drug misuse |
| Mowbray & Quinn, 2015 | <ul style="list-style-type: none"> Having a lower household income (18–25; 50+) | | Random sample of NSDUH respondents nationwide (n = 113,665) in 2011 and 2012 (modal age range = 18–25) | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> Prescription opioid misuse |
| Rhoades, Winetrobe, & Rice, 2014 | <ul style="list-style-type: none"> Having unprotected sex | <ul style="list-style-type: none"> Having previously been in foster care | Convenience sample of homeless youth receiving services from Los Angeles drop-in | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> Prescription drug misuse |

| RELATIONSHIP-LEVEL FACTORS | | | | | |
|--|---|---|--|--|--|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Rhoades, Winetrobe, & Rice, 2014 (cont.) | | | centers (n = 435; 31% female) in 2012-2013 (average age = 21.5) | | |
| Schroeder & Ford, 2012 | <ul style="list-style-type: none"> • Greater peer substance use • Experiencing a larger number of negative life events⁶⁴ | <ul style="list-style-type: none"> • Having a stronger parental bond | Random sample of younger NSDUH respondents nationwide (n = 17,705; 49% female) in 2009 (age range = 12–17; average age = 14.6) | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> • Prescription drug misuse |
| Silva, Schrager, Kecojevic, & Lankenau, 2013 | <ul style="list-style-type: none"> • Lifetime witnessing a family member overdose | | Stratified sample of individuals in New York City and Los Angeles who misused prescription drugs at least three times in the past 90 days (n = 596; 32.4% female) between October 2009 and March 2011 (age range = 16–25; average age = 21). Most (59.6%) of the participants were homeless. | Retrospective study using multivariate analysis | <ul style="list-style-type: none"> • Non-fatal prescription drug overdose |

⁶⁴ Negative life events were measured through an index of answers to six major life events (1) fighting with parent, (2) low grades in school, (3) not residing with biological parents, (4) not having health insurance, (5) participating in a government-assistance program, and (6) having fair or overall poor health.

| RELATIONSHIP-LEVEL FACTORS | | | | | |
|---|--|---|---|--|---|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Simoni-Wastila, Zuckerman, Singhal, Briesacher, & Hsu, 2005 | <ul style="list-style-type: none"> Living with non-spousal other(s) | <ul style="list-style-type: none"> Being married | Random sample of Medicare enrollee respondents nationwide to the Medicare Current Beneficiary Survey (n = over 12,000) in 1999 (age range = 65 or older). All respondents resided in the community. | Retrospective, longitudinal study using multivariate analysis of data collected at three time points | <ul style="list-style-type: none"> Exposure to prescription drugs with abuse potential |

| COMMUNITY-LEVEL FACTORS | | | | | |
|---|---|---|--|--|--|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Collins, Abadi, Johnson, Shamblen, & Thompson, 2011 | | <ul style="list-style-type: none"> Community norms against use | Convenience sample of students in grades 5, 7, 9, and 11 in one Tennessee county (n = 1,105; 57% female) in 2009. Most (53%) were over age 13. Lifetime prescription drug misuse was self-reported by 35% of the sample members. | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> Prescription drug misuse |
| Ford & Rigg, 2015 | <ul style="list-style-type: none"> Living in an urban environment Moving three or more times in the past year | | Random sample of NSDUH respondents nationwide (n = 15,648; 49.6% female) in 2012 (age range = 12–17; average age = 14.7). 5.3% of sample members reported having a history of prescription opioid misuse. | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> Prescription opioid misuse |

| COMMUNITY-LEVEL FACTORS | | | | | |
|--|--|--|---|--|--|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Heck et al., 2014 | | <ul style="list-style-type: none"> • Presence of Gay-Straight Alliance (GSA) in school (LGBTQIA only) | Convenience sample of self-identifying LGBT respondents nationwide to an online survey (n = 475; 54.1% female) between September 2011 and April 2012 (age range = 16 or older; average age = 17). All respondents were high school students. | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> • Prescription opioid misuse • Prescription ADHD medication misuse |
| Jeffery, Babeu, Nelson, Kloc, & Klette, 2013 | <ul style="list-style-type: none"> • Absence of random drug testing program | | Population of all active duty service members (ADSM) who completed the U.S. Department of Defense's Health Related Behaviors Survey of Active Duty Military Personal (n = 28,546; 14.2% female) in 2008. The survey was voluntary and available to all current ADSM (average age = 28.5). | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> • Prescription pain reliever misuse • Prescription tranquilizer misuse • Prescription sedative misuse • Prescription stimulant misuse |

| COMMUNITY-LEVEL FACTORS | | | | | |
|---|--|----------------------|--|--|--|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Rosenblum et al., 2007 | <ul style="list-style-type: none"> • Living in a rural area | | Cluster convenience sample of individuals with opioid dependence receiving methadone treatment at 72 clinics in 33 states (n = 5,663; 36.6% female) in 2005 (average age = 35) | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> • Prescription opioid abuse |
| Siegler, Tuazon, O'Brien, & Paone, 2014 | <ul style="list-style-type: none"> • Residing in the borough of Staten Island (1) • Residing in the borough of Manhattan (2) | | Population of New York City residents who died from an unintentional opioid overdose as defined by the ICD-10 (n = 2,649; 26.2% female) between January 2005 and December 2010 (age range = 15–84) | Retrospective, cross-sectional study using multivariate and bivariate analyses | <ul style="list-style-type: none"> (1) Unintentional fatal opioid overdose in a home (2) Unintentional fatal opioid overdose in other environments |

| SOCIETAL-LEVEL FACTORS | | | | | |
|---|--|----------------------|--|--|--|
| Citation | Risk Factor(s) | Protective Factor(s) | Population | Design & Analysis | Outcome(s) |
| Gee, Delva, & Takeuchi, 2007 | <ul style="list-style-type: none"> Past-year experiences of discriminatory events | | Random sample of Filipino-American Community Epidemiological Study respondents (n = 2,217; 50.7% female) in 1998 to 1999 (average age = 41.6) | Retrospective, cross-sectional study using bivariate and multivariate analyses | <ul style="list-style-type: none"> Prescription drug misuse |
| Schroeder & Ford, 2012 | <ul style="list-style-type: none"> Societally influenced perception of risks of substance use | | Random sample of younger NSDUH respondents nationwide (n = 17,705; 49% female) in 2009 (age range = 12–17; average age = 14.6) | Retrospective, cross-sectional study using multivariate analysis | <ul style="list-style-type: none"> Prescription drug misuse |
| Silva, Schragger, Kecojevic, & Lankenau, 2013 | <ul style="list-style-type: none"> Belonging to a lower social class during adolescence | | Stratified sample of individuals in New York City and Los Angeles who misused prescription drugs at least three times in the past 90-days (n = 596; 32.4% female) between October 2009 and March 2011 (age range = 16–25; average age = 21). Most (59.6%) of the participants were homeless. | Retrospective study using multivariate analysis | <ul style="list-style-type: none"> Non-fatal prescription drug overdose |

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