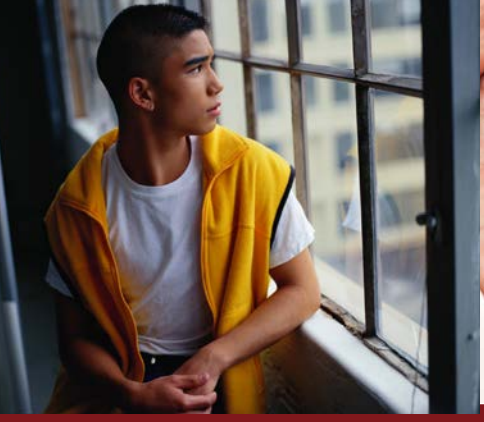

CAPT Decision-Support Tools

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

Updated May 2016

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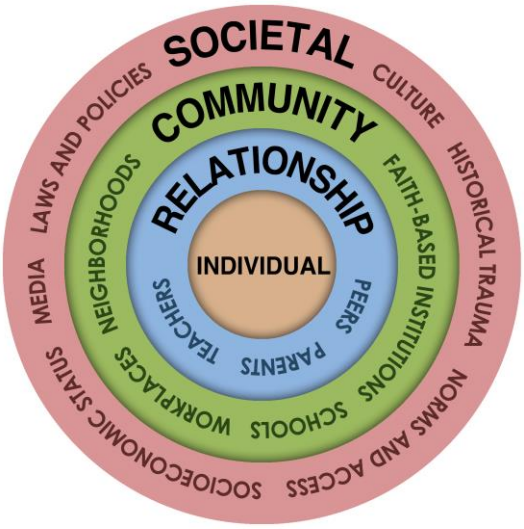
INTRODUCTION

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. Conversly, 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

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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 outcomes[5] 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.

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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

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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.

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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.

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[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.

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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] anxiety[13]), **acute and chronic pain** (i.e., having a current painful physical disorder,[14] chronic pain,[15] past-year back pain[16]), **physical health problems** (i.e., fatigue,[17] headaches[18]), and **heightened physiological reactions** to certain types of drugs (i.e., having a greater subjective euphoric reaction[19]). 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 drugs[22] and who are prescribed opioids at a large dosage[23] or have multiple prescriptions[24] 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, Schrager, 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 Model[31] 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

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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		• 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, Kecojevic, & Lankenau, 2013
Having a history of depression		• 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		• 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		• Prescription opioid misuse	NSDUH[36] respondents (age range = 12–17)	Ford & Rigg, 2015
		• 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
		• Prescription opioid misuse	Outpatient clinic patients (average age = 72.8)	Park & Lavin, 2010

[36] National Survey on Drug Use and Health

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Having a current depression diagnosis (cont.)		• Risk for opioid misuse	Individuals with cancer receiving services from a pain center	Koyyalagunta et al., 2013
Having a current mental health disorder		• 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		• Opioid abuse • Opioid dependence	Medicaid and private insurance network enrollees who were prescribed at least 90 days of opioids	Edlund et al., 2010
		• Opioid use disorder	Private insurance network enrollees with a cancer diagnosis	Edlund et al., 2014
		• 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		• 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	• Risk for opioid misuse	Individuals with cancer receiving services from a pain center	Koyyalagunta et al., 2013
Having high attentional impulsivity		• Risk for prescription opioid misuse	Individuals receiving opioid therapy for chronic low-back pain (average age = 47.5)	Marino et al., 2013

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Having suicidal ideation		• Prescription drug misuse	Homeless youth (average age = 21.5)	Rhoades, Winetrobe, & Rice, 2014
Past 30-day anxiety		• Risk for opioid misuse	Individuals with cancer receiving services from a pain center	Koyyalagunta et al., 2013
Past-year anxiety diagnosis		• Prescription opioid misuse	NSDUH respondents (age range = 18–25)	Mowbray & Quinn, 2015
Past-year posttraumatic stress disorder diagnosis		• 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		• 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		• 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		• 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

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
"Catastrophizing" current pain severity (cont.)		• 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		• Prescription opioid misuse	Medicaid and private insurance network enrollees who used opioids for at least 90 days	Sullivan et al., 2010
		• 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		• 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
		• Risk for opioid misuse	Individuals with cancer receiving services from a pain center	Koyyalagunta et al., 2013
		• Opioid addiction	Individuals who received 4+ opioid prescriptions (age range = 18 or older)	Boscarino et al., 2010
		• Prescription opioid misuse	Outpatient clinic patients (average age = 72.8)	Park & Lavin, 2010
Having chronic pain		• Prescription opioid abuse	Individuals with opioid dependence receiving methadone (average age = 35)	Rosenblum et al., 2007

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Having an increased perception of pain negative effects (anxiety about pain)		• 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		• Opioid use disorder	Private insurance network enrollees with a cancer diagnosis	Edlund et al., 2014
Having greater pain sensitivity		• Opioid misuse	Individuals being treated for spinal pain	Edwards et al., 2011
		• 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		• Opioid misuse	Individuals being treated for spinal pain	Edwards et al., 2011
Having more painful withdrawal symptoms		• Prescription opioid abuse	Individuals with opioid dependence receiving methadone (average age = 35)	Rosenblum et al., 2007
Back pain diagnosis		• 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
		• Prescription opioid misuse	Medicaid and private insurance network enrollees who used opioids for at least 90 days	Sullivan et al., 2010
		• Opioid abuse • Opioid dependence	Private insurance network enrollees who were prescribed at least 90 days of opioids	Edlund et al., 2010

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Reporting chronic pain as reason for methadone treatment		• 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		• 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		• Risk for opioid misuse	Individuals with cancer receiving services from a pain center	Koyyalagunta et al., 2013
Having 12 or more physical health care visits in one year		• 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		• Risk for opioid misuse	Individuals with cancer receiving services from a pain center	Koyyalagunta et al., 2013
Having one or more limitations on activities of daily living		• Exposure to prescription drugs with abuse potential	Medicare respondents (age range = 65 or older)	Simoni-Wastila, Zuckerman, Singhal, Briesacher, & Hsu, 2005
Having “poor” health		• Opioid addiction	Individuals who received 4+ opioid prescriptions (age range = 18 or older)	Boscarino et al., 2010

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Having "poor" health (cont.)		• Prescription opioid abuse • Prescription stimulant abuse	NSDUH respondents (12 or older)	Arkes & Iguchi, 2008
		• Exposure to prescription drugs with abuse potential	Medicare respondents (age range = 65 or older)	Simoni-Wastila, Zuckerman, Singhal, Briesacher, & Hsu, 2005
		• Prescription opioid misuse	NSDUH respondents (age ranges = 18–25 and 35–49)	Mowbray & Quinn, 2015
Headache diagnosis		• Opioid abuse • Opioid dependence	Private insurance network enrollees who were prescribed at least 90 days of opioids	Edlund et al., 2010
		• 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		• 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

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
	Increased severity of physical disability[37]	• Prescription opioid misuse	Outpatient clinic patients (average age = 72.8)	Park & Lavin, 2010
Injury during deployment		• 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		• 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		• 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		• 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		• Prescription stimulant use	University students who were non-dependent cocaine users or prescription stimulant misusers	Harlé et al., 2014
Having stronger drug cravings		• 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).

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Substance Use or Misuse				
Being a current cigarette smoker		• Prescription opioid abuse • Prescription stimulant abuse	NSDUH respondents (12 and older)	Arkes & Iguchi, 2008
		• Opioid misuse	Cancer treatment patients (average age = 54.8)	Novy et al., 2012
Co-occurring use of prescription opioids and benzodiazepines		• 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		• 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, Kecojevic, & Lankenau, 2013
Ever non-orally ingesting a prescription drug		• 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, Kecojevic, & Lankenau, 2013
Having a current non-opioid substance use disorder		• 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		• Opioid addiction	Individuals who received 4+ opioid prescriptions (age range = 18 or older)	Boscarino et al., 2010

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Having a history of psychotropic drug use		• Opioid addiction	Individuals who received 4+ opioid prescriptions (age range = 18 or older)	Boscarino et al., 2010
Having a history of severe opioid abuse		• Opioid addiction	Individuals who received 4+ opioid prescriptions (age range = 18 or older)	Boscarino et al., 2010
Having a substance use disorder diagnosis		• Opioid abuse • Opioid dependence	Medicaid and private insurance network enrollees who were prescribed at least 90 days of opioids	Edlund et al., 2010
		• Opioid use disorder	Private insurance network enrollees with a cancer diagnosis	Edlund et al., 2014
Having baseline prescription drug misuse		• 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		• Prescription opioid abuse	Individuals with opioid dependence receiving methadone (average age = 35)	Rosenblum et al., 2007
Having no previous history of methadone treatment		• Prescription opioid abuse	Individuals with opioid dependence receiving methadone (average age = 35)	Rosenblum et al., 2007
Heavy alcohol use		• 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		• 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

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Initiation of prescription drug misuse before age 13 (vs. after age 21)		• 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		• 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		• Prescription drug misuse	Dependent or problem drinkers who entered a treatment program for any chemical dependency	Matzger & Weisner, 2007
		• 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, Kecojevic, & Lankenau, 2013
Lifetime marijuana use		• 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		• Prescription drug misuse	Dependent or problem drinkers who entered a treatment program for any chemical dependency	Matzger & Weisner, 2007

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Other illicit substance use		• 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
		• Prescription drug misuse	Homeless youth (average age = 21.5)	Rhoades, Winetrobe, & Rice, 2014
Other substance use disorder diagnosis		• 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		• Prescription opioid misuse	Private insurance network enrollees who used opioids for at least 90 days	Sullivan et al., 2010
Past 30-day alcohol use		• 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		• Prescription opioid abuse • Prescription stimulant abuse	NSDUH respondents (12 years or older)	Arkes & Iguchi, 2008
Past 30-day other substance use		• Prescription opioid misuse	NSDUH respondents (age range = 12–17)	Ford & Rigg, 2015
Past 30-day substance use disorder		• Prescription opioid misuse	Medicaid and private insurance network enrollees who used opioids for at least 90 days	Sullivan et al., 2010

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Past 90-day benzodiazepine use		• 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		• 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, Kecojevic, & Lankenau, 2013
Past 90-day prescription opioid misuse		• 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, Kecojevic, & Lankenau, 2013
Past 90-day prescription stimulant misuse		• 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, Kecojevic, & Lankenau, 2013
Past 90-day prescription tranquilizer misuse		• 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, Kecojevic, & Lankenau, 2013
Past-year alcohol misuse		• Prescription opioid abuse • Prescription stimulant abuse	NSDUH respondents (12 and older)	Arkes & Iguchi, 2008
		• Prescription opioid misuse	NSDUH respondents (age ranges: 12–17, 18–25, 35–49)	Mowbray & Quinn, 2015

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Past-year marijuana use		• Prescription opioid abuse • Prescription stimulant abuse	NSDUH respondents (12 and older)	Arkes & Iguchi, 2008
Past-year non-opioid prescription abuse		• 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		• Prescription opioid abuse • Prescription stimulant abuse	NSDUH respondents (12 and older)	Arkes & Iguchi, 2008
Past-year other substance use		• Prescription opioid misuse	NSDUH respondents (age ranges: 12–17, 18–25, 26–34, 35–49, 50+)	Mowbray & Quinn, 2015
Younger age of first prescription		• Initiation into opioid, stimulant and tranquilizer misuse	Prescription drug misusers (age range = 16–25; average age = 21)	Kecojevic et al., 2012
Younger age of substance use initiation		• Prescription opioid misuse	NSDUH respondents (age ranges: 12–17 and 18–25)	Mowbray & Quinn, 2015
Behavior				
Ever being incarcerated		• 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, Kecojevic, & Lankenau, 2013
Having a history of doctor shopping behavior		• Drug-related death	Residents dispensed at least one controlled prescription drug (average age = 49)	Peirce, Smith, Abate, & Halverson, 2012

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Having a history of pharmacy shopping behavior		• Drug-related death	Residents dispensed at least one controlled prescription drug (average age = 49)	Peirce, Smith, Abate, & Halverson, 2012
Participation in organized sports		• 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		• 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		• Prescription opioid misuse	NSDUH respondents (age range = 12–17)	Ford & Rigg, 2015
Prescription Access				
Concurrent use of multiple prescribed opioids		• 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		• 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		• Drug-related death	Residents dispensed at least one controlled prescription drug (average age = 49)	Peirce, Smith, Abate, & Halverson, 2012

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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

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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		• 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		• 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, Kecojevic, & Lankenau, 2013
		• Opioid use disorder	Private insurance network enrollees with a cancer diagnosis	Edlund et al., 2014
Having a prescription for pain relievers		• 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	• 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		• Opioid abuse • Opioid dependence	Medicaid and private insurance network enrollees who were prescribed at least 90 days of opioids	Edlund et al., 2010

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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, Schrager, 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, Schrager, 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).

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Obtaining four or more filled prescriptions		• 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	• Prescription opioid abuse	Individuals in pharmaceutical coverage claims databases who were prescribed either tapentadol IR or oxycodone IR	Cepeda, Fife, Kihm, Mastrogiovanni, & Yuan, 2014
		• 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		• Opioid addiction	Individuals who received 4+ opioid prescriptions (age range = 18 or older)	Boscarino et al., 2010
Education				
	Attending a prevention class	• Prescription opioid misuse	NSDUH respondents (age range = 12–17)	Ford & Rigg, 2015
	Being a current student	• Prescription opioid abuse • Prescription stimulant abuse	NSDUH respondents (12 and older)	Arkes & Iguchi, 2008
	Having a high school diploma	• Prescription opioid abuse • Prescription stimulant abuse	NSDUH respondents (12 and older)	Arkes & Iguchi, 2008

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Having a college degree[40]		• 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	• Prescription opioid abuse • Prescription stimulant abuse	NSDUH respondents (12 and older)	Arkes & Iguchi, 2008
	Having a higher commitment to doing well in school	• Prescription drug misuse	Students in grades 5, 7, 9, and 11 in one Tennessee county	Collins, Abadi, Johnson, Shamblen, & Thompson, 2011
Employment				
	Being employed	• Prescription opioid abuse	NSDUH respondents (age range = 35–49)	Arkes & Iguchi, 2008
Being employed		• Prescription opioid abuse	Individuals with opioid dependence receiving methadone (average age = 35)	Rosenblum et al., 2007
		• Prescription opioid misuse	NSDUH respondents (age range = 18–25)	Mowbray & Quinn, 2015
Being unemployed[41]		• 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.

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
	Being unemployed[42]	• Prescription stimulant abuse	NSDUH respondents (age range = 26–34)	Arkes & Iguchi, 2008
Health Insurance				
Having health insurance[43]		• Prescription stimulant abuse	NSDUH respondents (age range = 18–25)	Arkes & Iguchi, 2008
	Having health insurance	• Prescription opioid abuse • Prescription stimulant abuse	NSDUH respondents (age range = 35 or older)	Arkes & Iguchi, 2008
Religiosity				
Having decreased religiosity		• Prescription opioid misuse	NSDUH respondents (age range = 12–17)	Ford & Rigg, 2015
Spiritual beliefs influence decision-making		• 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	• Prescription opioid misuse	NSDUH respondents (age range = 12–17)	Ford & Rigg, 2015
Having the perception that stimulant misuse is necessary to complete tasks		• 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).

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INDIVIDUAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Perceive drug test as easy to predict		• 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		• 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		• 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		• 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, Kecojevic, & Lankenau, 2013

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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 use[44] 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, Schrager, 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

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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		• Prescription opioid abuse • Prescription stimulant abuse	NSDUH respondents (age range = 12–50+; modal age range = 18–25)	Arkes & Iguchi, 2008
Being married[52]		• Prescription stimulant abuse	NSDUH respondents (age range = 26–34)	Arkes & Iguchi, 2008
	Being married	• Prescription stimulant abuse	NSDUH respondents (age range = 18–25)	Arkes & Iguchi, 2008
		• Exposure to prescription drugs with abuse potential	Medicare respondents (age range = 65 or older)	Simoni-Wastila, Zuckerman, Singhal, Briesacher, & Hsu, 2005
		• Prescription sedative misuse • Prescription stimulant misuse	Active duty service members (average age = 28.5)	Jeffery, Babeu, Nelson, Kloc, & Klette, 2013
Having unprotected sex		• 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).

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RELATIONSHIP-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Not being married		• 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		• Initiation of tranquilizer misuse	Prescription drug misusers (age range = 16–25; average age = 21)	Kecojevic et al., 2012
Experiencing a larger number of negative life events[53]		• Prescription drug misuse	NSDUH respondents (age range = 12–17; average age = 14.6)	Schroeder & Ford, 2012
Greater parental favorable attitudes towards substance abuse		• Prescription opioid misuse	NSDUH respondents (age range = 12–17)	Ford & Rigg, 2015
	Greater parental disapproval towards prescription drug misuse	• 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	• Prescription drug misuse	NSDUH respondents (age range = 12–17; average age = 14.6)	Schroeder & Ford, 2012
	Having previously been in foster care[54]	• Prescription drug misuse	Homeless youth (average age = 21.5)	Rhoades, Winetrobe, & Rice, 2014
Household being the source of first misused stimulant		• Initiation of stimulant misuse	Prescription drug misusers (age range = 16–25; average age = 21)	Kecojevic 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.

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RELATIONSHIP-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Lifetime witnessing a family member overdose		• 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, Kecojevic, & Lankenau, 2013
Household Income				
	Having a higher household income	• Prescription opioid misuse	NSDUH respondents (age range = 12–17)	Ford & Rigg, 2015
Having a lower household income (18–25; 50+)		• Prescription opioid misuse	NSDUH respondents (age ranges = 18–25 and 50 or older)	Mowbray & Quinn, 2015
Peers				
Greater peer prescription drug misuse		• 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		• Prescription opioid misuse	NSDUH respondents (age range = 12–17)	Ford & Rigg, 2015
Greater peer substance abuse or use		• Prescription opioid misuse	NSDUH respondents (age range = 12–17)	Ford & Rigg, 2015
		• Prescription drug misuse	NSDUH respondents (age range = 12–17; average age = 14.6)	Schroeder & Ford, 2012
Having a “Greek” organization affiliation		• Prescription stimulant misuse	University students (average age = 19.6)	Gallucci, Martin, Beaujean, & Usdan, 2015
Living with non-spousal other(s)		• Exposure to prescription drugs with abuse potential	Medicare respondents (age range = 65 or older)	Simoni-Wastila, Zuckerman, Singhal, Briesacher, & Hsu, 2005

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RELATIONSHIP-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Social Networks				
Alcohol misuse or illicit substance use among social networks		• Prescription drug misuse	Dependent or problem drinkers who entered treatment for any chemical dependence	Matzger & Weisner, 2007
Having weaker social bonds		• Prescription opioid misuse	NSDUH respondents (age range = 12–17)	Ford & Rigg, 2015
Past 30-day experiences of discriminatory behavior in routine interactions		• Prescription drug misuse	Filipino-American respondents (average age = 41.6)	Gee, Delva, & Takeuchi, 2007

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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 experiences[56] 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

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COMMUNITY-LEVEL FACTORS
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COMMUNITY-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Living Arrangements				
Living in a rural area		• Prescription opioid abuse	Individuals with opioid dependence receiving methadone (average age = 35)	Rosenblum et al., 2007
Living in an urban environment		• Prescription opioid misuse	NSDUH respondents (age range = 12–17)	Ford & Rigg, 2015
Moving three or more times in the past year		• Prescription opioid misuse	NSDUH respondents (age range = 12–17)	Ford & Rigg, 2015
Residing in the borough of Manhattan		• 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		• 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

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COMMUNITY-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome(s)**	**Population**	**Citation**
Workplace				
Absence of random drug testing program		• 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	• 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	• 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

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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

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SOCIETAL-LEVEL FACTORS
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SOCIETAL-LEVEL FACTORS				
Risk Factor	**Protective Factor**	**Outcome**	**Population**	**Citation**
Discrimination				
Past-year experiences of discriminatory events		• 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		• 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		• 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, Kecojevic, & Lankenau, 2013

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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	• 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)	• 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).

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INDIVIDUAL-LEVEL FACTORS					
Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Bieber et al., 2008	• 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	• Prescription opioid addiction
Bohnert et al., 2011	• 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	• Unintentional fatal prescription opioid overdose

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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	• 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	• Opioid addiction
Cepeda, Fife, Kihm, Mastrogiovanni, & Yuan, 2014	• Paying for prescriptions with cash (1,2)	• 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	(1) Prescription opioid abuse (2) Doctor shopping

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INDIVIDUAL-LEVEL FACTORS					
Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Cepeda, Fife, Kihm, Mastrogiovanni, & Yuan, 2014 (cont.)	• 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

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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	• Perception that prescription drugs are readily available • Perception that prescription drug misuse is acceptable and safe	• 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	• Prescription drug misuse
Edlund et al., 2010	• Having a mental health disorder diagnosis • Having another substance use disorder diagnosis • Having a back pain diagnosis (private enrollees only)	• 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	• Opioid abuse • Opioid dependence

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INDIVIDUAL-LEVEL FACTORS					
Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Edlund et al., 2010 (cont.)	• Having a headache diagnosis (private enrollees only) • Having a prescription for sedatives or hypnotics	• Having a prescription for Schedule III or IV opioids	• 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	• Having a prescription for opioids • Having a larger prescribed dosage of opioids • Having a mental health disorder diagnosis • Having a substance use disorder diagnosis		Sample of HealthCore private insurance network enrollees (n = 568,640) who met study eligibility criteria: • 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	• Opioid use disorder

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INDIVIDUAL-LEVEL FACTORS					
Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Edlund et al., 2014 (cont.)	• Having four or more non-tracer pain diagnoses		• No opioid use or diagnosis of opioid dependence in the six months prior to the new diagnosis		
Edlund, Steffick, Hudson, Harris, & Sullivan, 2007	• 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): • 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	• Prescription opioid abuse
Edwards et al., 2011	• 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	• Opioid misuse

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INDIVIDUAL-LEVEL FACTORS					
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	• 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	• Prescription opioid misuse
Ford & Rigg, 2015	• Having a current depression diagnosis • Having decreased religiosity • School delinquency • Past 30-day other substance use	• 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	• Prescription opioid misuse

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INDIVIDUAL-LEVEL FACTORS					
Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Gallucci, Martin, Beaujean, & Usdan, 2015	• Having the perception that stimulant misuse is necessary to complete tasks	• 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	• Prescription stimulant misuse
Gelernter et al., 2014	• 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	• Opioid dependence
Grattan, Sullivan, Saunders, Campbell, & Von Korff, 2012	• 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	• Prescription opioid misuse

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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	• 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	• Prescription opioid overdose

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INDIVIDUAL-LEVEL FACTORS					
Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Harlé et al., 2014	• 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	• Prescription stimulant use
Huffman et al., 2015	• 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	• Prescription opioid addiction
Jeffery, Babeu, Nelson, Kloc, & Klette, 2013	• 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	(1) Prescription pain reliever misuse (2) Prescription tranquilizer misuse (3) Prescription sedative misuse

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Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Jeffery, Babeu, Nelson, Kloc, & Klette, 2013 (cont.)	• 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
Kecojevic et al., 2012	• 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

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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)		
Koyyalagunta et al., 2013	• 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	• 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	• Risk for opioid misuse
Mackesy-Amiti, Donenberg, & Ouellet, 2015	• 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	(1) Past-year prescription opioid misuse (2) Past-year prescription opioid abuse (3) Past-year prescription opioid dependence

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Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Mackesy-Amiti, Donenberg, & Ouellet, 2015 (cont.)	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	• 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	• Risk for prescription opioid misuse
Martel, Wasan, Jamison, & Edwards, 2013	• "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	• Risk for prescription opioid misuse

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INDIVIDUAL-LEVEL FACTORS					
Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Martel, Wasan, Jamison, & Edwards, 2013 (cont.)	• 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	• 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	• Prescription drug misuse
McCabe, West, Morales, Cranford, & Boyd, 2007	• 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	• Prescription drug abuse • Prescription drug dependence

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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	• "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	• Risk for prescription opioid misuse
Mowbray & Quinn, 2015	• 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	• Prescription opioid misuse

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INDIVIDUAL-LEVEL FACTORS					
Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Mowbray & Quinn, 2015 (cont.)	• 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	• 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	• Opioid misuse

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Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Novy et al., 2012 (cont.)			members were current smokers.		
Park & Lavin, 2010	• Having a higher level of reported pain • Having a current depression diagnosis	• 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	• Prescription opioid misuse
Peirce, Smith, Abate, & Halverson, 2012	• 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	• Drug-related death

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Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Peirce, Smith, Abate, & Halverson, 2012 (cont.)	controlled substances • Excessive exposure to prescription opioids or benzodiazepines		49; mean subset population age = 40.6)		
Rhoades, Winetrobe, & Rice, 2014	• 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	• Prescription drug misuse
Rosenblum et al., 2007	• 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	• 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.

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Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Rosenblum et al., 2007 (cont.)	• Having more painful withdrawal symptoms				
Siegler, Tuazon,O'Brien, & Paone, 2014	• 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	(1) Unintentional fatal opioid overdose in a home (2) Unintentional fatal opioid overdose in other environments
Silva, Schrager, Kecojevic, & Lankenau, 2013	• 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	• 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	• Non-fatal prescription drug overdose

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Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Silva, Schrager, Kecojevic, & Lankenau, 2013 (cont.)	• 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	• 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	• Exposure to prescription drugs with abuse potential
Sullivan et al., 2010	• Past 30-day back pain • Other pain conditions • Past 30-day substance use	• 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	• Prescription opioid misuse

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Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Sullivan et al., 2010 (cont.)	disorder (self-reported) • 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: • 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	

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Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Veliz et al., 2014	• 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	• Medical use of prescription opioids • Accidental misuse of prescription opioids • Intentional misuse of prescription opioids

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RELATIONSHIP-LEVEL FACTORS					
Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Arkes & Iguchi, 2008	• Being married (for ages 26-34) (2) • Being divorced (1,2)	• 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	(1) Prescription opioid abuse (2) Prescription stimulant abuse
Collins, Abadi, Johnson, Shamblen, & Thompson, 2011	• Greater peer prescription drug misuse	• 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	• Prescription drug misuse
Edlund, Steffick, Hudson, Harris, & Sullivan, 2007	• 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: • 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	• Prescription opioid abuse

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Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Edlund, Steffick, Hudson, Harris, & Sullivan, 2007 (cont.)			• Never having a cancer diagnosis • Not having an opioid dependence diagnosis in 2000, 2001, or 2002		
Ford & Rigg, 2015	• Having weaker social bonds • Greater peer substance abuse • Greater peer favorable attitudes towards substance abuse • Greater parental favorable attitudes towards substance abuse	• 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	• Prescription opioid misuse
Gallucci, Martin, Beaujean, & Usdan, 2015	• 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	• Prescription stimulant misuse

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RELATIONSHIP-LEVEL FACTORS					
Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Gee, Delva, & Takeuchi, 2007	• 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	• Prescription drug misuse
Jeffery, Babeu, Nelson, Kloc, & Klette, 2013		• 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	• Prescription sedative misuse • Prescription stimulant misuse
Kecojevic et al., 2012	• 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	(1) Initiation of tranquilizer misuse (2) Initiation of stimulant misuse

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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	• 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	• Prescription drug misuse
Mowbray & Quinn, 2015	• 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	• Prescription opioid misuse
Rhoades, Winetrobe, & Rice, 2014	• Having unprotected sex	• 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	• Prescription drug misuse

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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	• Greater peer substance use • Experiencing a larger number of negative life events [64]	• 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	• Prescription drug misuse
Silva, Schrager, Kecojevic, & Lankenau, 2013	• 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	• 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.

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RELATIONSHIP-LEVEL FACTORS					
Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Simoni-Wastila, Zuckerman, Singhal, Briesacher, & Hsu, 2005	• Living with non-spousal other(s)	• 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	• Exposure to prescription drugs with abuse potential

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COMMUNITY-LEVEL FACTORS					
Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Collins, Abadi, Johnson, Shamblen, & Thompson, 2011		• 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	• Prescription drug misuse
Ford & Rigg, 2015	• 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	• Prescription opioid misuse

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COMMUNITY-LEVEL FACTORS					
Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Heck et al., 2014		• 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	• Prescription opioid misuse • Prescription ADHD medication misuse
Jeffery, Babeu, Nelson, Kloc, & Klette, 2013	• 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	• Prescription pain reliever misuse • Prescription tranquilizer misuse • Prescription sedative misuse • Prescription stimulant misuse

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COMMUNITY-LEVEL FACTORS					
Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Rosenblum et al., 2007	• 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	• Prescription opioid abuse
Siegler, Tuazon, O'Brien, & Paone, 2014	• 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	(1) Unintentional fatal opioid overdose in a home (2) Unintentional fatal opioid overdose in other environments

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SOCIETAL-LEVEL FACTORS					
Citation	**Risk Factor(s)**	**Protective Factor(s)**	**Population**	**Design & Analysis**	**Outcome(s)**
Gee, Delva, & Takeuchi, 2007	• 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	• Prescription drug misuse
Schroeder & Ford, 2012	• 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	• Prescription drug misuse
Silva, Schrager, Kecojevic, & Lankenau, 2013	• 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	• Non-fatal prescription drug overdose

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