<table>
<thead>
<tr>
<th>Substance Use Disorder (SUD)</th>
<th>• History of SUD is the strongest risk factor for developing opioid misuse or OUD</th>
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| Bipolar Disorder or Schizophrenia | • Patients with mental health disorders are more likely to be at risk for drug overdose  
• Bipolar disorder may cause manic episodes to occur, **reducing your impulse control** and leading to excessive consumption of your prescription opioids  
• Concurrent use of opioids and sedating psychotherapeutic medications **increases the risk of CNS and respiratory depression** |
| Cerebrovascular Disease | • Opioids may worsen cognitive impairment, confusion or cause hallucinations  
• Risk of overdose is greatest during first 3 to 7 days after starting an opioid or increasing its dose |
| Chronic Kidney Disease with Renal Impairment | • Renal impairment slows down the rate at which opioids are excreted from the body thus creating a higher risk for OD  
• Risk for overdose **greatest during opioid initiation and dose escalation**  
• **65+ Patients:** Lower dose, use caution when initiating opioids due to age-related renal changes |
| Heart Failure | • Certain opioids and their metabolites may have decreased clearance (increases risk of oversedation, hypotension, bradycardia, respiratory depression)  
• Cognitive impairment is common and can increase the risk for overdose  
• **Older Patients:** Increased risk for opioid-induced respiratory depression due to comorbidities (i.e CHD, COPD, stroke in addition to heart failure) |
| Non-malignant Pancreatic Disease | • Chronic pancreatitis opioid-treated patients have high prevalence of strong risk factors for opioid overdose  
• Pancreatic disease may result in accelerated gastric emptying/malabsorption, causing a decrease in drug absorption and resulting in patients taking higher opioid doses |
| Chronic Pulmonary Disease | • **Patients with COPD and sleep apnea:** Higher risk for opioid-related toxicity/overdose and overdose-related death  
• **60+ Patients:** Increased risk of respiratory depression  
• **60+ Patients with COPD and co-occurring CHD, heart failure, OSA, asthma, or stroke:** Increased risk of opioid-induced respiratory depression |
| Chronic Headache | • **Frequent headache patients:** Underuse of prophylactic migraine medications may lead to overuse of opioid analgesic overuse to handle recurrent migraines  
• **Medication-overuse headache (MOH):** If opioids are used more than 10 times a month for migraines. patient can become dependent  
• **Patients with co-occurring mental health disorder(s) and recurrent headache:** Higher risk for developing opioid use disorder and high risk of opioid-related overdose |

**If the patient concomitantly is on the following drugs:**

Concurrent use of CNS depressants and Opioids can result in sedation, respiratory depression, coma, & death

| Fentanyl | • Fentanyl is **substantially more potent than morphine** and is associated with an increased risk for overdose  
• **Patients with Renal Impairment:** Fentanyl has reduced clearance and may cause increased fentanyl plasma levels, leading to respiratory depression and over-sedation  
• **18+ Patients with Cancer:** Rapid-onset, short acting fentanyl dosage forms used for management of breakthrough pain |
| **Morphine** | • Morphine use (ER/LA) is associated with an increased risk for serious opioid-induced respiratory depression  
• *Patients with Renal Impairment:* Accumulation of morphine metabolite may lead to oversedation, respiratory depression, and neuro-excitatory effects |
| **Methadone** | • *Risk of overdose increases for these patients:* At the initiation of therapy and following dose increase, on complex medication regimens, with severely impaired renal or hepatic function  
• *Patients with high degree of opioid tolerance:* Fatal methadone overdose has happened during changing to methadone or start of methadone treatment  
• Concurrent use of methadone with amitriptyline, fluvoxamine, biaxin, ciprofloxacin, fluconazole, or voriconazole can inhibit its metabolism. This may cause an increase in plasma levels and the risk of unintentional overdose |
| **Hydromorphone** | • Hydromorphone is associated with a greater risk for serious opioid-induced respiratory depression  
• *Patients with Renal Impairment:* Clearance of hydromorphone and its metabolites is reduced, and accumulation may lead to respiratory depression, neuroexcitatory effects, and oversedation  
• *Patients with Severe Hepatic Impairment:* Hydromorphone should be avoided  
• Concurrent use of hydromorphone and other CNS depressants can result in sedation, respiratory depression, coma, and death |
| **ER/LA formulation of any prescription opioid** | • Patients treated with ER/LA opioid formulations have a greater risk for unintentional overdose and death opposed to those taking immediate release or short acting opioid formulations  
• **Chronic, non-cancer pain in opioid-naive patients:** Risk of overdose is considerably high during the first 2 to 4 weeks after start of ER/LA opioid therapy  
• Risk for overdose greatest during start of an ER/LA opioid and after each dosage increase |
| **A prescription benzodiazepine** | • Concurrent use of a benzodiazepine and opioid has been alarmingly identified in prescription drug overdose deaths  
• Benzodiazepine withdrawal holds more risk compared to opioid withdrawal, as serious issues can occur such as seizures, delirium, anxiety, or insomnia  
• Recommendation: Taper benzodiazepines slowly over months to avoid harmful consequences from happening to patient  
• **Patients with Insomnia:** Avoid using benzodiazepines |
| **A prescription antidepressant** | • Certain antidepressants are more sedating than others and can increase the risk of respiratory depression and/or oversedation when used with opioids  
• Increased opioid plasma levels may occur in pharmacokinetic interactions between certain antidepressants and opioids, increasing the risk of opioid toxicity  
• *Patients with an active, unstable mental health disorder or uncontrolled suicide risk:* Heightened risk for drug overdose  
• *Patients treated with concurrent opioids and antidepressants:* Risk for overdose greatest during first 3 to 7 days after starting an opioid or increasing its dosage |
| **Is the patient’s current maximum prescribed opioid dose ≥ 100 MME/day** | • Risk for serious opioid-related toxicity, such as overdose and death, steadily increase with the average daily opioid dose  
• Opioid doses >= 100 MME/day substantially increase the risk of overdose compared to lower doses, such as <20 MME/day  
• *Patients taking high doses for Chronic Non-Cancer Pain (≥ 90 MME/day):* Tapering opioid dosage should be based on assessment of benefits versus risks. Consider tapering opioid therapy to reduced dose or discontinuation if pain or benefits are small or risks are high |