

Opioid analgesics

Mu-opioid receptor agonists that remain the most effective agents for severe pain and, by the same mechanism, carry the respiratory-depression and addiction risk that now dominates their regulation.

Online guide: <https://www.medguideglobal.com/pharmacology/analgesia-and-anaesthesia/opioid-analgesics>

Content updated: 2026-08-24

Quick revision

One Liner: Opioids relieve pain by activating the mu-opioid receptor presynaptically and postsynaptically; the same receptor activation that blunts pain also depresses respiratory drive, which is why every serious risk in this class traces back to one mechanism.

1. Mechanism: presynaptic mu-receptor activation blocks calcium channels and reduces release of substance P and glutamate; postsynaptically it opens potassium channels and hyperpolarises the neuron. [1]
2. Mu, kappa and delta receptors all contribute to analgesia at spinal and supraspinal sites, but the mu-1 receptor carries most of the clinical analgesic and dependence effect. [2]
3. Every opioid carries an FDA boxed warning for addiction, abuse and misuse, and for life-threatening respiratory depression. [5]
4. The 2022 CDC guideline prefers nonopioid therapy for subacute and chronic pain and directs clinicians to the lowest effective dose when an opioid is used at all. [4]
5. Concomitant benzodiazepines or other CNS depressants, including alcohol, raise the risk of profound sedation, respiratory depression, coma and death. [5][4]
6. Codeine is contraindicated under age 12 and after tonsillectomy/adenoidectomy under age 18, because CYP2D6 ultra-rapid metabolisers convert it to morphine dangerously fast. [7]
7. Methadone carries an additional boxed warning for QT prolongation and torsades de pointes, distinct from the class-wide respiratory-depression warning. [6]
8. Naloxone is a pure competitive mu-antagonist that reverses overdose within minutes but lasts only 30 to 60 minutes, so a long-acting opioid overdose can need repeated doses. [1]
9. Once physical dependence is established, opioid therapy should not be stopped abruptly or tapered rapidly except for a life-threatening indication; a clinician manages any taper. [4]

Overview

1. Opioid analgesics act on mu, kappa and delta opioid receptors distributed spinally and supraspinally, with the mu-1 receptor responsible for most clinically significant analgesia. The class spans natural opium derivatives (morphine, codeine), semisynthetic agents (oxycodone, hydromorphone, buprenorphine) and fully synthetic agents (fentanyl, methadone, tramadol), and it remains the most effective option available for severe acute and cancer-related pain. [1][2]
2. Every opioid on the US market carries an FDA boxed warning for addiction, abuse and misuse; for life-threatening respiratory depression; for neonatal opioid withdrawal syndrome after prolonged use in pregnancy; and for the danger of combining an opioid with benzodiazepines or other CNS depressants. These are not theoretical cautions attached for legal reasons - they describe the mechanism directly, since the receptor activity that relieves pain is the same activity that suppresses brainstem respiratory drive. [5]
3. Prescribing practice has shifted accordingly. The 2022 CDC Clinical Practice Guideline for Prescribing Opioids for Pain prefers nonopioid therapy for subacute and chronic pain, directs clinicians toward the lowest effective dose and shortest necessary duration when an opioid is used, and asks clinicians to build in naloxone access and a plan for reassessment from the start rather than treating these as afterthoughts. [4]

Classification and drug examples

Intro: Opioids are best learned by chemical origin and by receptor activity, because both predict clinical behaviour: natural and semisynthetic full agonists behave differently from a fully synthetic phenylpiperidine, a prodrug like codeine, a partial agonist like buprenorphine, or a mixed-mechanism agent like tramadol.

1. Name: Natural and semisynthetic full mu-agonists

1. Note: The reference agents for severe pain; potency and onset vary but the mechanism and the boxed warnings are shared across the group.

1. Name: Morphine

1. Route: Oral/IV/IM/epidural

1. Note: A naturally occurring opium alkaloid and the reference opioid against which other agents' potency is typically compared. [5]

2. Name: Oxycodone

2. Route: Oral

2. Note: Semisynthetic full agonist widely used for moderate to severe pain; available alone or combined with acetaminophen. [1]

3. Name: Hydromorphone

3. Route: Oral/IV

3. Note: A potent semisynthetic agonist used when a smaller injected volume or rapid titration is needed. [1]

4. Name: Codeine

4. Route: Oral

4. Note: A naturally occurring opium alkaloid and a prodrug requiring CYP2D6 conversion to morphine for its analgesic effect; contraindicated under age 12 and after tonsillectomy/adenoidectomy under 18 because of ultra-rapid-metaboliser risk. [7] [1]

2. Name: Fully synthetic full mu-agonists (phenylpiperidines and relatives)

2. Note: Made entirely by chemical synthesis rather than derived from the opium poppy; grouped separately because that distinction, not potency alone, is what the mechanism-family classification is being tested on.

1. Name: Fentanyl

1. Route: IV/transdermal/transmucosal

1. Note: A fully synthetic phenylpiperidine, highly potent, used in anaesthesia and, transdermally, in opioid-tolerant chronic pain; a leading driver of illicit overdose deaths outside the regulated supply. [1]

2. Name: Pethidine (meperidine)

Meperidine

2. Route: IV/IM

2. Note: An older fully synthetic phenylpiperidine whose metabolite normeperidine can accumulate in renal impairment and cause seizures. [1] [1]

3. Name: Long-acting and mechanistically atypical agents

3. Note: Grouped because each carries an examinable feature beyond simple mu-agonism: methadone's cardiac risk, buprenorphine's partial agonism and ceiling effect, and tramadol's monoamine reuptake action.

1. Name: Methadone

1. Route: Oral/IV

1. Note: Long, unpredictable half-life used for chronic pain and opioid use disorder maintenance; carries an additional boxed warning for QT prolongation and torsades de pointes. [6]

2. Name: Buprenorphine

2. Route: Sublingual/transdermal/IV

2. Note: A partial mu-agonist with a ceiling effect on respiratory depression, used for both pain and opioid use disorder treatment; can precipitate withdrawal if given too soon after a full agonist. [1]

3. Name: Tramadol

3. Route: Oral

3. Note: A weak mu-agonist that also inhibits serotonin and norepinephrine reuptake, which is why it carries both a seizure risk and a serotonin syndrome risk distinct from typical opioids. [1]

4. Name: Tapentadol

4. Route: Oral

4. Note: Combines mu-agonism with norepinephrine reuptake inhibition, similar in concept to tramadol but structurally distinct. [1] [1]

4. Name: Opioid antagonists

4. Note: Not analgesics - included because they reverse or block the class and are essential to safe opioid prescribing.

1. Name: Naloxone

1. Route: IV/IM/intranasal

1. Note: Pure competitive mu-antagonist used to reverse opioid overdose; its 30-to-60-minute duration can be shorter than the opioid it is reversing. [1]

2. Name: Naltrexone

2. Route: Oral/IM depot

2. Note: Longer-acting antagonist used for relapse prevention in opioid use disorder once a supervised washout period has passed. [3] [3]

Mechanism of action

Summary: Opioids activate G-protein-coupled mu-opioid receptors, acting presynaptically to reduce neurotransmitter release and postsynaptically to hyperpolarise the neuron. The same receptor family, expressed in the brainstem, is what produces the class's defining harm: dose-dependent respiratory depression.

Target: Mu-opioid receptor (with kappa and delta contributions), a Gi-coupled GPCR

Cidal Static: Not applicable - this class relieves pain rather than treating an infectious organism.

Kill Kinetics: Effect tracks receptor occupancy and plasma concentration; unlike an antimicrobial, more drug produces more analgesia and more respiratory depression together, not a categorically different killing behaviour.

1. Step: 1

1. Title: Presynaptic calcium channel blockade

1. Detail: Opioids block calcium channels on nociceptive afferent nerves, which inhibits release of pain-signalling neurotransmitters such as substance P and glutamate before the signal ever reaches the next neuron. [1]

2. Step: 2

2. Title: Postsynaptic potassium channel opening

2. Detail: On the postsynaptic side, opioid receptor activation opens potassium channels, hyperpolarising the cell membrane and making the neuron less likely to fire. [1]

3. Step: 3

3. Title: Gi-protein signalling reduces cAMP

3. Detail: As G-protein-coupled receptors, opioid receptors activate inhibitory Gi proteins on binding, which suppresses adenylate cyclase and lowers intracellular cAMP, reinforcing the inhibitory signal that produces both effects above. [2]

4. Step: 4

4. Title: Analgesia at spinal and supraspinal sites

4. Detail: Mu, kappa and delta receptors together mediate analgesia both in the spinal cord dorsal horn and at supraspinal sites, including descending pain-inhibition pathways from the brainstem. [2]

5. Step: 5

5. Title: The same mechanism depresses brainstem respiratory drive

5. Detail: Mu-2 receptor activation in the brainstem respiratory centres produces the dose-dependent respiratory depression that is the class's principal life-threatening risk - a direct consequence of the analgesic mechanism, not a

separate off-target effect. [2][5]

Major clinical uses

1. Drug: Morphine

1. Indication: Moderate to severe acute pain, cancer pain, and pain in palliative care

1. Line: first-line for severe pain

1. Note: Dosing and route depend on the clinical setting and are set by the treating clinician against a current prescribing reference. [1]

2. Drug: Fentanyl

2. Indication: Intraoperative and procedural analgesia; transdermal use in opioid-tolerant chronic cancer pain

2. Line: targeted

2. Note: Its potency and rapid onset make it central to anaesthesia but also central to illicit-supply overdose risk. [1]

3. Drug: Oxycodone

3. Indication: Moderate to severe acute or chronic pain not adequately controlled by nonopioid therapy

3. Line: second-line, after nonopioid options

3. Note: The CDC guideline directs immediate-release formulations at the lowest effective dose when starting therapy. [4]

4. Drug: Methadone

4. Indication: Chronic pain in selected patients, and maintenance treatment for opioid use disorder

4. Line: specialist-directed

4. Note: Requires cardiac risk assessment because of its QT-prolongation boxed warning. [6]

5. Drug: Buprenorphine

5. Indication: Moderate to severe chronic pain and medication treatment for opioid use disorder

5. Line: specialist-directed

5. Note: Its partial-agonist ceiling effect on respiratory depression is a distinct safety property within the class. [1]

6. Drug: Naloxone

6. Indication: Reversal of suspected or confirmed opioid overdose

6. Line: emergency reversal agent

6. Note: The CDC guideline directs clinicians to offer naloxone as part of routine risk mitigation whenever opioids are prescribed. [4][1]

Pharmacokinetics

1. Drug: Morphine

1. Route: Oral/IV/IM/epidural

1. Absorption: Variable oral bioavailability due to first-pass hepatic metabolism

1. Csf Penetration: Crosses into CNS to act at central mu-receptors; also used epidurally/intratheally

1. Metabolism: Hepatic glucuronidation to active (morphine-6-glucuronide) and inactive metabolites

1. Elimination: Renal; active metabolite can accumulate in renal impairment

1. Half Life: See prescribing reference; varies by formulation

1. Dose Adjust: Renal impairment; hepatic impairment; monitor for accumulation of active metabolite [1]

2. Drug: Codeine

2. Route: Oral

2. Absorption: Well absorbed orally; a prodrug requiring CYP2D6 activation

2. Csf Penetration: Crosses to CNS after conversion to morphine

2. Metabolism: CYP2D6-mediated O-demethylation to morphine; CYP2D6 activity varies genetically (poor to ultra-rapid metaboliser)

2. Elimination: Renal

- 2. Half Life: See prescribing reference
- 2. Dose Adjust: Contraindicated under age 12 and post-tonsillectomy/adenoidectomy under 18; CYP2D6 genotype materially changes exposure [7]
- 3. Drug: Methadone
- 3. Route: Oral/IV
- 3. Absorption: High oral bioavailability
- 3. Csf Penetration: Crosses to CNS
- 3. Metabolism: Hepatic, chiefly CYP3A4, 2B6, 2C19 and 2C9; plasma concentration can rise sharply if an inducer of these enzymes is stopped
- 3. Elimination: Hepatic/biliary with a long and variable half-life
- 3. Half Life: Long and highly variable between patients; accumulation risk on titration
- 3. Dose Adjust: Cardiac monitoring for QT prolongation; caution with CYP450-interacting drugs [6]
- 1. This page gives no dose regimens by design. Opioid dosing depends on the indication, prior opioid exposure, renal and hepatic function, and concurrent medications, and must come from a current prescribing reference and the treating clinician.
- 2. Discontinuation of a cytochrome P450 inducer in a patient on methadone can raise methadone plasma concentration and precipitate life-threatening respiratory depression, illustrating why opioid interactions are not limited to other sedatives. [6]

Adverse effects

- 1. Effect: Constipation
 - 1. Detail: Opioid-induced reduction in gastrointestinal motility is near-universal with regular use and does not reliably resolve with tolerance the way sedation does. [1]
- 2. Effect: Sedation, nausea, pruritus and miosis
 - 2. Detail: Common dose-related effects reported across the class, alongside dysphoria or euphoria depending on the individual and the agent. [1]
- 1. Effect: Life-threatening respiratory depression
 - 1. Detail: Serious, life-threatening or fatal respiratory depression can occur with any opioid, most often at initiation or after a dose increase.
 - 1. Action: Monitor closely at initiation and after any dose increase; have naloxone available. [5]
- 2. Effect: Addiction, abuse and misuse
 - 2. Detail: Every opioid exposes patients to the risk of addiction, abuse and misuse, which can lead to overdose and death, independent of whether the drug is used exactly as prescribed.
 - 2. Action: Assess risk before starting, discuss it with the patient, and reassess at follow-up. [5][4]
- 3. Effect: Neonatal opioid withdrawal syndrome
 - 3. Detail: Prolonged opioid use during pregnancy can cause neonatal opioid withdrawal syndrome, which can be life-threatening if not recognised and treated.
 - 3. Action: Anticipate and monitor for withdrawal in neonates exposed to opioids in utero. [5]
- 4. Effect: Accidental fatal ingestion
 - 4. Detail: A single accidentally ingested dose, particularly by a child, can be fatal.
 - 4. Action: Secure storage and disposal counselling. [5]
- 1. Drug: Methadone
 - 1. Effect: QT interval prolongation and torsades de pointes, reported more often at doses above 200 mg/day. [6]
- 2. Drug: Codeine
 - 2. Effect: Life-threatening or fatal respiratory depression in children who are CYP2D6 ultra-rapid metabolisers, even at labelled doses. [7]
- 3. Drug: Tramadol

3. Effect: Seizure risk and serotonin syndrome risk beyond typical opioid effects, from its added serotonin and norepinephrine reuptake inhibition. [1]
4. Drug: Pethidine (meperidine)
4. Effect: Its metabolite normeperidine can accumulate in renal impairment and cause seizures, a risk not shared by most other opioids. [1]

Contraindications, precautions and interactions

1. Significant respiratory depression, or acute/severe bronchial asthma in an unmonitored setting without resuscitative equipment. [5]
2. Known or suspected gastrointestinal obstruction, including paralytic ileus. [5]
3. Concurrent use of monoamine oxidase inhibitors, or use within the preceding 14 days. [5]
4. Codeine specifically: children younger than 12 years, and patients younger than 18 years after tonsillectomy and/or adenoidectomy. [7]
1. Hepatic or renal impairment, which can alter clearance of the parent drug or an active metabolite. [1]
2. Pregnancy, because of neonatal opioid withdrawal syndrome risk with prolonged use. [5]
3. A personal or family history of substance use disorder, mental health condition, or other opioid-misuse risk factors, which should be discussed rather than treated as an automatic bar to appropriate pain treatment. [1]
1. With: Benzodiazepines and other CNS depressants, including alcohol
1. Effect: Profound sedation, respiratory depression, coma and death. [5][4]
2. With: Serotonergic drugs, with tramadol or methadone
2. Effect: Raised risk of serotonin syndrome. [1]
3. With: CYP450 inducers or inhibitors, with methadone
3. Effect: Stopping an inducer can raise methadone concentration and precipitate life-threatening respiratory depression; enzyme interactions affect several opioids metabolised through CYP pathways. [6]

Comparison tables

Title: What sets each major opioid apart

Caption: The features most often tested beyond the shared mu-agonist mechanism. A prescribing reference and the treating clinician govern actual therapy.

1. Key: drug
1. Label: Drug
1. Is Row Header: true
2. Key: feature
2. Label: Distinguishing feature
3. Key: risk
3. Label: Risk this creates
1. Drug: Codeine
1. Feature: Prodrug requiring CYP2D6 conversion to morphine
1. Risk: Ultra-rapid metabolisers, especially children, risk fatal respiratory depression [7]
2. Drug: Methadone
2. Feature: Long, variable half-life and CYP450-dependent kinetics
2. Risk: QT prolongation/torsades de pointes; accumulation on titration [6]
3. Drug: Buprenorphine
3. Feature: Partial mu-agonist with a ceiling effect
3. Risk: Can precipitate withdrawal if given too soon after a full agonist [1]
4. Drug: Tramadol
4. Feature: Weak mu-agonism plus serotonin/norepinephrine reuptake inhibition

- 4. Risk: Seizure and serotonin syndrome risk beyond typical opioid effects [1]
- 5. Drug: Pethidine (meperidine)
- 5. Feature: Active metabolite normeperidine
- 5. Risk: Seizures with accumulation in renal impairment or prolonged use [1]

High-yield exam pearls

- 1. Pearl: One receptor explains both the benefit and the danger.
 - 1. Why: Mu-receptor activation produces analgesia and, through the same postsynaptic potassium-channel hyperpolarisation acting on brainstem respiratory centres, produces respiratory depression - the class's defining trade-off rather than a separate side effect. [1][2]
- 2. Pearl: Guidelines now start with what is not an opioid.
 - 2. Why: The 2022 CDC guideline states nonopioid therapies are preferred for subacute and chronic pain and are at least as effective as opioids for many common types of acute pain - a reversal of decades of practice that is a common exam trap. [4]
- 3. Pearl: Codeine is a prodrug, and that is exactly its danger in children.
 - 3. Why: Codeine itself is a weak mu-agonist; its analgesic effect depends on CYP2D6 converting it to morphine. Ultra-rapid metabolisers make that conversion abnormally fast and complete, producing morphine levels high enough to kill a child after a standard dose. [7]
- 4. Pearl: Methadone's danger is not only respiratory.
 - 4. Why: Unlike most opioids, methadone has a boxed warning for QT prolongation and torsades de pointes, reported more often at doses above 200 mg/day and demanding cardiac monitoring on initiation and dose change. [6]
- 5. Pearl: Naloxone can run out before the opioid does.
 - 5. Why: Naloxone's action lasts only 30 to 60 minutes. A long-acting opioid or one taken in large quantity can outlast a single naloxone dose, so repeated dosing and monitoring for re-sedation are standard after reversal. [1]
- 6. Pearl: Detoxification alone is not treatment for opioid use disorder.
 - 6. Why: The CDC guideline explicitly states detoxification on its own, without medications for opioid use disorder, is not recommended because of overdose risk after the drug is withdrawn and tolerance is lost. [4]

Common exam traps

- 1. Trap: "Opioids and benzodiazepines are fine to combine as long as doses are moderate."
 - 1. Correction: Both the FDA boxed warning and the CDC guideline single out this combination: concurrent CNS depressants, including alcohol, raise the risk of profound sedation, respiratory depression, coma and death, and the guideline directs particular caution before co-prescribing. [5][4]
- 2. Trap: "Codeine is safe in children because it is a weaker opioid."
 - 2. Correction: Codeine is contraindicated in children younger than 12 and, after tonsillectomy or adenoidectomy, in those younger than 18. Its danger comes from CYP2D6 ultra-rapid metabolism to morphine, not from its own potency. [7]
- 3. Trap: "An opioid taper can be stopped abruptly whenever a clinician judges it best."
 - 3. Correction: The CDC guideline states that unless there is a life-threatening issue, opioid therapy should not be discontinued abruptly and dosage should not be rapidly reduced from higher doses - abrupt cessation itself carries withdrawal and safety risk. [4]
- 4. Trap: "All opioids carry the same cardiac risk profile."
 - 4. Correction: Methadone is distinguished by its own boxed warning for QT prolongation and torsades de pointes; this is not a class-wide property of morphine, fentanyl or oxycodone. [6]

Self-test questions

1. Question: By what dual mechanism do opioids produce analgesia at the mu receptor?

1. They block postsynaptic sodium channels and open presynaptic chloride channels
2. They block presynaptic calcium channels, reducing neurotransmitter release, and open postsynaptic potassium channels, hyperpolarising the neuron
3. They act purely postsynaptically by blocking NMDA receptors
4. They inhibit cyclooxygenase presynaptically to reduce prostaglandin release

1. Explanation: Opioids act presynaptically by blocking calcium channels on nociceptive afferents, reducing release of substance P and glutamate, and postsynaptically by opening potassium channels, which hyperpolarises the cell membrane. Both actions reduce pain signal transmission. [1]

2. Question: Why is codeine contraindicated in children younger than 12 years?

1. Codeine is not absorbed orally in children
2. Codeine directly damages the paediatric respiratory centre regardless of metabolism
3. CYP2D6 ultra-rapid metabolisers convert codeine to morphine unusually fast and completely, producing life-threatening or fatal respiratory depression
4. Children lack mu-opioid receptors until puberty

2. Explanation: Codeine's analgesic effect depends on CYP2D6 converting it to morphine. Ultra-rapid metabolisers - whose prevalence varies by ethnicity - produce abnormally high morphine levels even at labelled doses, which is why the FDA label contraindicates codeine under 12 and after tonsillectomy/adenoidectomy under 18. [7]

3. Question: According to the 2022 CDC opioid prescribing guideline, what is the preferred first approach to subacute and chronic pain?

1. Immediate-release opioids at the lowest dose for the shortest duration
2. Maximising nonpharmacologic and nonopioid pharmacologic therapies, since these are preferred for subacute and chronic pain
3. Extended-release/long-acting opioids started early to prevent dose escalation
4. Routine co-prescription of benzodiazepines to manage anxiety around chronic pain

3. Explanation: The guideline states nonopioid therapies are preferred for subacute and chronic pain, and clinicians should maximise nonpharmacologic and nonopioid pharmacologic therapies before or alongside any opioid use. [4]

4. Question: What distinguishes methadone's boxed warning from that of most other opioids?

1. Methadone alone carries a warning for gastrointestinal perforation
2. Methadone alone carries a warning for life-threatening QT prolongation and torsades de pointes, in addition to the class-wide respiratory depression warning
3. Methadone is the only opioid with no addiction potential
4. Methadone alone requires no monitoring for respiratory depression

4. Explanation: Methadone's label adds a specific boxed warning for QT interval prolongation and torsades de pointes, reported more often with doses above 200 mg/day, on top of the respiratory depression and addiction warnings shared with the rest of the class. [6]

5. Question: A patient is reversed from an apparent long-acting opioid overdose with naloxone and initially wakes. Why does the care team keep monitoring rather than discharge the patient?

1. Naloxone permanently blocks the mu receptor for 24 hours, so no further risk exists
2. Naloxone's effect lasts only about 30 to 60 minutes, so a long-acting or large-quantity opioid can outlast a single dose and re-sedation can follow
3. Naloxone itself causes delayed respiratory depression
4. Monitoring is required only for children, never for adults

5. Explanation: Naloxone is a short-acting competitive mu-antagonist. Because its action lasts only 30 to 60 minutes, an opioid with a longer duration of action can re-assert its effect once naloxone wears off, so repeated dosing and

observation are standard practice. [1]

6. Question: Why does the CDC guideline advise against detoxification alone for opioid use disorder?

1. Detoxification alone is more expensive than medication treatment
2. Detoxification alone removes tolerance without treating the underlying disorder, raising the risk of fatal overdose on relapse
3. Detoxification alone is illegal in the United States
4. Detoxification alone works only for methadone, not other opioids

6. Explanation: The guideline recommends offering or arranging evidence-based medication treatment for opioid use disorder and states that detoxification on its own, without medications, is not recommended because of the overdose risk it carries. [4]

7. Question: Which statement about concurrent benzodiazepine and opioid use is correct?

1. It is safe as long as the benzodiazepine is short-acting
2. It carries an FDA boxed warning and CDC guidance urging particular caution, because of profound sedation, respiratory depression, coma and death
3. It is only dangerous in patients over 65
4. It is recommended as standard practice for anxious patients starting opioid therapy

7. Explanation: Both the opioid boxed warning and the CDC guideline flag concurrent benzodiazepine and opioid (or other CNS depressant) use as a specific, serious risk requiring particular caution and a documented risk-benefit discussion, not routine co-prescribing. [5][4]

Frequently asked questions

1. Question: Why do opioids cause both pain relief and breathing problems?

1. Answer: Both effects come from the same mu-opioid receptor mechanism. Activation in pain-processing pathways relieves pain; the same receptor family in brainstem respiratory centres suppresses the drive to breathe. It is one mechanism producing two effects, not two separate actions. [2][5]

2. Question: Why are nonopioid treatments now recommended before opioids for chronic pain?

2. Answer: The 2022 CDC guideline found nonopioid therapies are preferred for subacute and chronic pain and at least as effective as opioids for many common types of acute pain, while opioids carry addiction and overdose risks that nonopioid options do not. [4]

3. Question: Is it ever safe to stop a prescribed opioid on your own?

3. Answer: No. Any change to opioid therapy, including stopping it, should be made with the prescribing clinician. Abrupt discontinuation or rapid dose reduction from a higher dose carries its own risks and should only happen under medical guidance, except in a genuine emergency. [4]

4. Question: What should someone do if they suspect an opioid overdose?

4. Answer: Call emergency services immediately. Naloxone can reverse an opioid overdose if available, but its effect lasts only 30 to 60 minutes, so continued monitoring and repeat dosing may be needed even after the person appears to wake up. [1]

5. Question: Why is codeine treated differently from other opioids in children?

5. Answer: Codeine only works after the body converts it to morphine via the CYP2D6 enzyme. Children who are genetically ultra-rapid metabolisers can generate morphine levels high enough to cause fatal respiratory depression even at a standard dose, which is why the FDA label contraindicates codeine under 12 and after tonsillectomy/adenoidectomy under 18. [7]

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