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Unintentional Overdoses: Understanding the Fentanyl Landscape and Reducing Harm

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Structured Abstract:

Purpose of review: Adolescent and young adult overdoses and overdose fatalities continue to increase despite reductions in self-reported substance use. This review aims to explore factors contributing to this overdose epidemic, highlight signs of overdose and the role of the overdose reversal medication naloxone, and provide recommendations for practice change to support patients and decrease their risk of unintentional overdose.

Recent findings: The potent opioid fentanyl is a common contaminant in non-opioid substances, as well as in heroin and counterfeit pills, heightening risk of fatal overdose. Adolescents and young adults who die of overdose are rarely engaged in substance use disorder treatment. Medications for opioid use disorder are effective at reducing risk of fatal overdose but are underutilized, as is the opioid reversal medication naloxone.

Summary: Pediatric clinician engagement in harm reduction with adolescents and young adults, starting with screening through a confidential interview, may enhance pathways to care and reduce the risk of overdose.

Keywords

overdose; harm reduction; opioids; naloxone; adolescents

Introduction

Unintentional overdoses have steadily risen among adolescents and young adults (AYAs) in many locations internationally. The United States (US) leads high-income countries in overdose deaths per capita, with Canada, the United Kingdom, Australia, and Scandinavian countries also experiencing elevated and rising overdose mortality[1]. Given North America accounts for 60% of the world's opioid consumption, this paper will touch on international trends but primarily focus on recommendations related to clinical practice in the US.

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Policies, rules, regulations, and resources differ depending on the country and smaller area of jurisdiction, and it is wise for any clinician to look for information specific to their location of practice.

Recent Overdose Epidemiology

In the US, overdose is now the third leading cause of death among children under 20 (following firearm injuries and motor vehicle crashes)[*2], resulting in >1,100 deaths among adolescents aged 10-19 in 2021 alone[**3], Mortality including young adults up to age 24 is even higher, with fatal overdose rates five times higher than that of adolescents alone[4]. Morbidity from non-fatal overdose is also significant; AYAs aged 15-24 years experienced more than 218,000 nonfatal emergency room visits for unintentional poisoning in 2020[5].

The top substances involved in overdoses among AYAs have shifted, with illicitly manufactured fentanyl overtaking heroin and prescription opioids as the drug most commonly involved[**3]. Illicitly manufactured fentanyl is a highly potent, non-pharmaceutically produced synthetic opioid often used by those manufacturing and selling illicit substances as an additive to enhance the effect and addiction potential of various illicit substances. Most overdose deaths among AYAs involve a combination of multiple substances, most commonly benzodiazepines, methamphetamine, and/or cocaine[*6].

There are significant disparities among AYAs. In the US, for example, recent increases in overdose mortality rates during the COVID-19 epidemic were highest among AYAs who were aged 15-24, male, Black, American Indian/Alaskan Native, and Hispanic [*7]. This is consistent with 2010-2019 data demonstrating a decreasing proportion of overdose deaths in non-Hispanic White adolescents[*6] and estimating 48% higher overdose mortality among US-born Black men compared to US-born white men, a finding that did not hold in non-US-born immigrant people of color, implicating locale-based structural inequities[*8].

US national surveys, including the Youth Risk Behavior Survey, Monitoring the Future, and National Survey on Drug Use and Health, all continue to document relatively high frequency of substance use, including heroin use and misuse of prescription opioids, among adolescents[9-11]. Despite decreases in overall rates of use across these surveys, overdose deaths continue to climb in the setting of an increasingly lethal fentanyl-tainted drug supply. Overdose rates may yet increase further amid rising mental health problems in the wake of the COVID-19 epidemic.

Context of AYA overdoses

In recent years, there has been a sharp rise in counterfeit or “pressed” pills in illicit drug markets in both US and international drug markets[12-14]. These counterfeit pills mimic prescription drugs, including opioids (e.g., oxycodone) or benzodiazepines (e.g., alprazolam), but contain fentanyl and have contributed to unintentional poisoning and overdose[**3]. Counterfeit pills account for at least one-quarter of all overdose deaths among AYAs aged 10-19 in the US, although this is likely an undercount since thorough testing is often not conducted at the scene of death[**3].

Fentanyl also increasingly contaminates other drug supplies, adulterating cocaine, methamphetamine and other illicit substances[15]. Adulteration of illicit substances is a constantly-changing landscape; recent years have seen additional contamination of substances such as xylazine, which may lead to severe skin ulceration when injected[16].

Recent data from the US Centers for Disease Control and Prevention provide important context around overdose among AYAs. Most AYAs aged 10-19 years overdose at home; two-thirds of the time when this happens, someone else is present in another room in the home, often unaware of the AYA's use. Two-thirds of the time, naloxone is not administered at all, and more than half have no pulse at the time of first responders' arrival to the home. Two out of every five AYAs who die of overdose have struggled with a mental health disorder such as depression or anxiety. One in every three who die from overdose has known prior opioid use, and one in seven has had a known prior overdose. Only 3% of those who die are engaged in substance use disorder treatment[**3].

Signs of Overdose

While respiratory depression is the central cause of opioid-related fatalities, an understanding of the overall physiology and associated signs of opioid-related overdose is important to ensure prompt identification and treatment (Table 1). Opioids have a strong effect on mu-opioid receptors in the brain that regulate the respiratory rate, limiting the ability of the body to respond appropriately to hypoxia and hypercarbia[17]. Because of this, overdosing individuals may have a respiratory rate as low as 4-6 breaths per minute and appear cyanotic. They may appear lethargic or to be 'nodding off' to sleep while also experiencing opioid-related euphoria. They may additionally exhibit anxiety, aggression, or depression because of inhibition of dopamine release mediated by delta-opioid receptors[17].

Some, but not all, individuals experiencing opioid overdose will have small, constricted pupils because of the miotic effect of many opioids on kappa-opioid receptors; however, opioid overdose should not be clinically ruled out if miosis is not present[17]. Since many overdoses involve polysubstance use (often including stimulants), the physiologic effects of opioid overdose may be masked by the effects of other substances, making it harder to identify and treat[17]. Additionally, when substances like benzodiazepines and gabapentin are co-involved in an overdose, mortality is made more likely by the lack of response to naloxone of the respiratory depression triggered by these substances[17].

Introduction to Harm Reduction

Harm reduction, which entails working to decrease the risk of injury or death without exclusively emphasizing abstinence, is essential for AYAs for several reasons[18, *19, *20]. AYAs report high levels of stigma around opioid use[**21] and may be uncomfortable in opioid use disorder treatment settings (e.g., detoxification or rehabilitation), which they may perceive as restrictive and isolating from their social community[22]. Developmentally, AYAs may overemphasize the perceived immediate benefit of substance use for valent social reasons, undervaluing personal risk[23]. For these reasons, AYAs may have difficulty

reducing or ceasing their substance use, and the clinician can play a critical role in keeping them safe.

Harm reduction is anchored in patient-centered tenets of respect for person[24]. Harm reduction allows clinicians to develop longitudinal relationships with AYAs who use drugs and facilitate their enhanced access to whole-person healthcare beyond substance use treatment. To prevent overdoses, clinicians have an imperative to meet AYAs where they are, discussing substance use openly and nonjudgmentally, and using motivational interviewing techniques to explore ambivalence around use and cessation. Even when an AYA is not ready or able to decrease their use, clinicians can reduce harm by discussing strategies to reduce overdose, including access to overdose reversal medication (i.e., naloxone) and education on its use.

Behavioral Harm Reduction Strategies

When AYAs disclose their substance use, clinicians can then tailor a discussion of harm reduction strategies that are specific, targeted, and skills-based. To support this disclosure in the first place, we recommend conducting a private, confidential interview with AYAs. Although the age of consent for substance use treatment in many parts of the US is lower than the age of majority (18 years) and in other countries the age of consent may be lower for all medical treatments, AYA may be unaware of their ability to consent to confidential treatment without the knowledge and consent of their caregivers[25-27]. AYA may fear forced disclosure to family, school, or legal authorities[25]. They may also be unaware of confidential access to harm reduction supplies for minors in their area.

We recommend that clinicians clearly explain the local age at which adolescents can consent to treatment and any local limitations to their ability to conduct a confidential interview. In the US, when the risk of ‘harm to self’ is high for an adolescent under 18 years of age, it is the clinician’s obligation to inform a parent or guardian. Most substance use does not constitute ‘harm to self,’ and thus does not require disclosure to parents or guardians. Clinicians should clearly state that if they feel the risk of overdose is high enough to constitute risk of harm to self that this might be grounds for breaking confidentiality and explain parameters that they themselves would consider harm to self. They should be clear that this would be done only after having a conversation with the adolescent about the best way to go about sharing this information. As every clinician’s comfort level with risk of harm to self is different, AYA may have heard of peers’ negative experiences with mere disclosure of substance use. As such, they may be fearful to disclose and work toward harm reduction in the absence of clear clinician-specific parameters of their disclosure threshold for harm to self.

After assuring confidentiality, the clinician should proceed asking nonjudgmental, straightforward questions about prior and current use patterns and the AYA’s current readiness to cease or decrease their substance use. Even when an AYA is not ready to reduce their use or abstain, there are many behavioral strategies that clinicians can emphasize to reduce the risk of overdose (Table 2).

Advising AYAs not to use opioids and other substances that could be opioid-laced alone and encouraging them to take turns using with a peer promotes the possibility that someone could reverse an overdose and call emergency services to assist. Asking AYAs whether they use alone can also help clinicians identify triggers for substance use (e.g., stress, loneliness) and potentially reduce their use. Clinicians can counsel AYAs who typically use alone to have someone check in on them every 3-5 minutes or use an overdose prevention hotline (e.g., “Never Use Alone” in the US at https://neverusealone.com/ or in Scotland at https://neverusealonescotland.co.uk/), through which someone will stay on the line when an AYA uses substances and call emergency services if they become unresponsive in order to decrease risk of incidental harm to self.

Clinicians can counsel AYAs to try only a small amount of a new drug purchase at first to assess its potency, especially given varying amounts of fentanyl in heroin and counterfeit pills, as well as fentanyl contamination of other drugs such as cocaine. They can recommend that AYA obtain and utilize fentanyl test strips to check for fentanyl within other substances. They can also encourage AYAs to minimize polysubstance use (i.e., combining multiple substances)—in particular, sedating substances such as benzodiazepines, ethanol, alpha-adrenergic agonists, and gabapentinoids.

For any AYA who injects drugs, clinicians can recommend using syringe exchange programs and supervised injection facilities, which are increasingly present in many countries. AYAs who inject drugs should also receive screening and treatment for human immunodeficiency virus (HIV) and hepatitis B/C viruses[28] and may be eligible for HIV pre-exposure prophylaxis (PrEP)[29].

Overdose Reversal Medication

Clinicians should liberally prescribe naloxone, the opioid overdose reversal medication widely available in an easy-to-administer nasal spray (Table 3). They can offer the prescription to AYAs and/or family members (if confidentiality is not a concern), as well as brief education on its use. If an AYA is concerned about a parent or others becoming aware of their use, clinicians can direct them to mail distribution programs (e.g., NEXT Distro in the US, https://nextdistro.org/ or through a site involved with the Take Home Naloxone program in Australia[31]), which offer confidential access.

It is important to emphasize that AYAs and family members should still immediately call emergency services after administering naloxone to ensure medical support since overdose reversal may be unsuccessful or recur after naloxone wears off. Given the potency of fentanyl, multiple administrations of naloxone are sometimes needed. Clinicians should become familiar with their local Good Samaritan laws (if any), which exist across Canada and in many areas across the US and prevent people who use substances from some drug-related prosecution when law enforcement responds to an emergency call[32].

Naloxone comes in different concentrations and forms of administration. Administering intranasal naloxone is straightforward and easily taught through direct clinician counseling, local training programs, or web-based training resources[30]. The standard initial dose of

intranasal naloxone is 4 mg per actuation. Many intranasal naloxone kits contain two spray devices, and the individual responding to the overdose should administer a spray to one nostril at a time every 2-3 minutes until respiratory depression is reversed. (As outlined above, in the interim, they or another respondent should call emergency services.)

There are virtually no side effects to naloxone; there are, however, two additional considerations to its use. First, administering naloxone can cause uncomfortable symptoms of opioid withdrawal in a person with chronic, heavy opioid use. Such symptoms are uncomfortable but not life-threatening, however. Second, an overdose can resume 30-90 minutes after naloxone administration when it wears off, thus highlighting the importance of ongoing care.

Overdose reversal medications available to the lay public are currently limited to addressing opioid overdose (i.e., naloxone). For other substances that may be involved in overdoses (e.g., stimulants or other sedatives including alcohol), care is largely supportive. Overdose reversal medications, including, for example, flumazenil for benzodiazepine overdose, are limited to use in clinical settings.

Addiction Treatment as Overdose Prevention

Beyond recommending patient behavioral strategies and increasing access to reversal medications, when an AYA wants to reduce their use, connecting them to timely, evidence-based addiction treatment can dramatically reduce their future risk of overdose. Medications for opioid use disorder include buprenorphine, methadone, and naltrexone, but, internationally, AYAs experience limited access to these medications[33].

There is currently considerable room to grow in terms of clinician prescription of both medications for opioid use disorder, as well as naloxone prescription, across all ages. Among individuals who visited US emergency rooms for nonfatal overdose between 2019-2021, only 1 in 13 received naloxone and 1 in 12 received buprenorphine (despite both being considered standard of care for individuals experiencing opioid overdose)[*34]. Pediatric clinicians are poised to address this treatment gap among AYAs; some of this care in the US may be off-label, as the FDA has approved buprenorphine for individuals 16 or older but naltrexone and methadone only in adults.

Among individuals at risk for opioid overdose, buprenorphine and methadone are associated with reductions in all-cause mortality[35], withdrawal symptoms, and cravings, and with increased engagement and retention in addiction treatment[36]. The American Academy of Pediatrics recommends that pediatricians offer medications for opioid use disorder to AYAs[37], and the Society for Adolescent Health and Medicine recommends offering medications to adolescents even in the absence of their desire to engage in behavioral therapy[38]. There are multiple evidence-based outpatient behavioral treatments for AYAs with substance use disorders[39], but local provider access may be limited, and patients and families may face other barriers to accessing behavioral healthcare not collocated in their primary care office.

Conclusion: Strengthening the Pediatric Workforce

Overdose prevention and addiction treatment have not traditionally been viewed as the province of pediatric clinicians. However, pediatricians and other clinicians working with AYAs have a critical role to play by delivering evidence-based strategies in their own clinics and communities. In addition to directly supporting AYAs and families through their clinical care, pediatric clinicians can support local public health interventions, such as naloxone distribution.

Pediatric clinicians can also work to reduce stigma against AYAs who use substances to enhance the likelihood AYAs will disclose their use and consider treatment; simple strategies include promoting the use of non-stigmatizing language in their own clinical settings[*40]. Clinicians can increase their knowledge of addiction treatment and overdose prevention strategies through free educational resources such as those available through the Providers Clinical Support System (https://pcssnow.org). Through such strategies, pediatric clinicians are poised to help end the rising epidemic of overdoses among AYAs.

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Abbreviations

AYAs	Adolescents and young adults
US	United States

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Key Points

- Overdoses continue to rise among adolescents and young adults despite reductions in self-reported use of opioids and other substances.
- The current substance use landscape includes a heightened risk of overdose given contamination and substitution with potent fentanyl.
- Pediatric clinicians can reduce the risk of overdose by engaging in harm reduction strategies with patients, including counseling on overdose prevention.
- Connecting adolescents and young adults with substance use treatment including evidence-based medication can reduce their risk of fatal overdose.

Table 1 –

Signs and Symptoms of Opioid-Related Overdose

General	Looks very pale Feels clammy to the touch
Respiratory	Very slow or no breathing Gurgling noises in throat Blue or purple fingernails or lips
Cardiac	Very slow or no heart rate
Gastrointestinal	Vomiting
Psychiatric	Limp body, can’t be awakened Can’t speak Falling asleep Euphoria Anxiety Aggression Depression
Ocular	Small pupils (not absolute)

Table 2 –

Behavioral Risk Reduction Strategies for Providers to Recommend to Youth

- Don’t use alone
  - Take turns using so someone could give naloxone in the event of an overdose
  - Have a friend call or text you every 3-5 minutes or call the Never Use Alone line at 800-484-3731 if you are alone
- Don’t mix substances, especially things that can make you sleepy such as alcohol or benzodiazepines
- Try a little bit of a new purchase to check how strong it is before you take your normal amount
- Consider using take-home test strips to test for the presence of fentanyl in pills, heroin, cocaine, or other drugs before you try them
- Have overdose reversal medication (naloxone) on hand, and make sure those around you know how to use it
- Call emergency services (e.g., 911) in the event of an overdose, including if naloxone is given
  - *Counsel youth on the presence of so-called “Good Samaritan Laws” in some jurisdictions, which allow individuals to call emergency services in the event of an overdose and not be charged with drug possession*
  - *Explain that given the short action of duration of naloxone, an overdose can recur 30-90 minutes when naloxone wears off; thus, calling emergency services is critical even after naloxone is given*
- Use safe syringe access and medically supervised drug-use facilities if available

Table 3 –

How to Administer Intranasal Naloxone to an Unresponsive Person Concerning for Opioid Overdose

1. Take the single-dose device out of the packaging and peel off any tab or label.
2. Put your thumb on the bottom of the plunger. Put your first and middle fingers on each side of the nozzle.
3. With the patient lying on their back, support their neck and allow their head to tilt back.
4. Insert the nozzle of the medication into the patient's nostril until your fingers meet the bottom of their nose.
5. Press the plunger once firmly, then remove the single-dose device from the patient's nose.
6. Place the patient on their side in a recovery position and call emergency services.
7. Alternating nostrils, give an additional dose (if available) every 2-3 minutes until they are responsive. [30]

Stay with the patient while they await the arrival of emergency services. Be familiar with any local Good Samaritan laws.