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RHODE  ISLAND  
MEDICAL JOURNAL

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## Drug Overdose, Addiction and Binge Drinking: Medical Problems with Public Health Consequences

DAVID C. LEWIS, MD  
GUEST EDITOR

The inexorable link between the practice of medicine and the fostering of public health is especially clear when dealing with severe drug and alcohol problems. Therefore, this focus section of the *Rhode Island Medical Journal* (RIMJ) addresses both clinical concerns like pain management and addiction treatment and also the ways in which the medical profession is joining with public health specialists and the community.

This is not the first issue of the RIMJ to deal with opioids. RI Health Director, Dr. Michael Fine, the leader in combating the current overdose epidemic, coordinated a special section of the RIMJ issue of November 2013 (Vol. 96, No. 11) which examined opioid prescribing. It is an excellent complement to this issue. (See <http://rimed.org/rimedical-journal/2013/11/2013-11-17-integrity+opioids.pdf>)

The ways in which Rhode Island has approached the overdose epidemic exemplifies the benefits of the medicine-public health connection. Public health authorities, community groups and the medical profession have reached out proactively to those in need of treatment and support. Projects were launched to make naloxone widely available. For example, the Rhode Island Medical Society successfully



advocated for the passage of the Good Samaritan Law in Rhode Island to protect anyone who calls 911 or who administers naloxone in good faith from criminal or civil liability. Implementation of the Good Samaritan law has successfully gained the necessary cooperation of EMTs and the police. Pharmacists have implemented a collaborative practice agreement with the medical profession allowing pharmacists to furnish naloxone without requiring an individual prescription. In addition, the RI Health Department has launched a new FDA-supported opioid prescriber education project. (See [http://medicine-](http://medicine-abuseproject.org/searchandrescue/ri-start)

[abuseproject.org/searchandrescue/ri-start](http://medicine-abuseproject.org/searchandrescue/ri-start))

Incorporating the diagnosis and treatment of addictive diseases into mainstream medicine has been a painfully slow process. Fortunately, that is changing. Now there is both public and medical recognition that addiction is a disease and that treatment is both necessary and effective. Both the federal parity legislation and the Affordable Care Act mandate that substance use disorders (and mental illness) are entitled to the same essential benefits as other medical and surgical conditions. This can only enhance the cooperation between medicine and public health advocates.

### GUEST EDITOR'S COMMENTARY ON THE ARTICLES

#### Medications for Addiction Treatment:

#### An Opportunity for Prescribing Clinicians to Facilitate Remission from Alcohol and Opioid Use Disorders

In spite of professional skepticism, research shows that treatment for addictive disorders is as effective as that for other chronic diseases. However, these disorders have been widely under-diagnosed and their treatment with medication underutilized. Perhaps this is because the usual interventions focused on non-medical approaches like the 12 step programs AA and NA. Now, research makes it clear that coupling medication with 12 Step or other counseling approaches results in the best outcomes.

#### Long-term Opioid Therapy for Chronic Pain and the Risk of Opioid Addiction

Using opioids to manage chronic pain is problematic, so

attention must be paid to distinguishing between the management of acute and chronic pain. The pharmacological fact that opioids can produce extraordinary degrees of tolerance and that the current overdose epidemic is related to the use of opioids for pain makes this paper a crucial component of this issue of the RIMJ.

#### Responding to Opioid Overdose in Rhode Island: Where the Medical Community Has Gone and Where We Need to Go

The opioid epidemic has triggered the new and widespread use of naloxone to save lives. The cooperation of pharmacists and the development of community-wide education have made naloxone distribution in Rhode Island one of the most effective examples of harm reduction in the nation. That Rhode Island has been a leader in this development in no small way due to the efforts of the authors of this paper.

**The Rhode Island Community Responds to Opioid Overdose Deaths**

This article documents the extraordinary breadth of response to the overdose epidemic. The way in which community leaders joined the RI Department of Health and the Department of Behavioral Health, Developmental Disabilities and Hospitals was indeed impressive. An excellent example of preventing death from overdose is the pioneering program launched by the Miriam Hospital in 2006 to distribute naloxone kits and training to opioid users and the people close to them.

**Emergency Department Naloxone Distribution: A Rhode Island Department of Health, Recovery Community, and Emergency Department Partnership to Reduce Opioid Overdose Deaths**

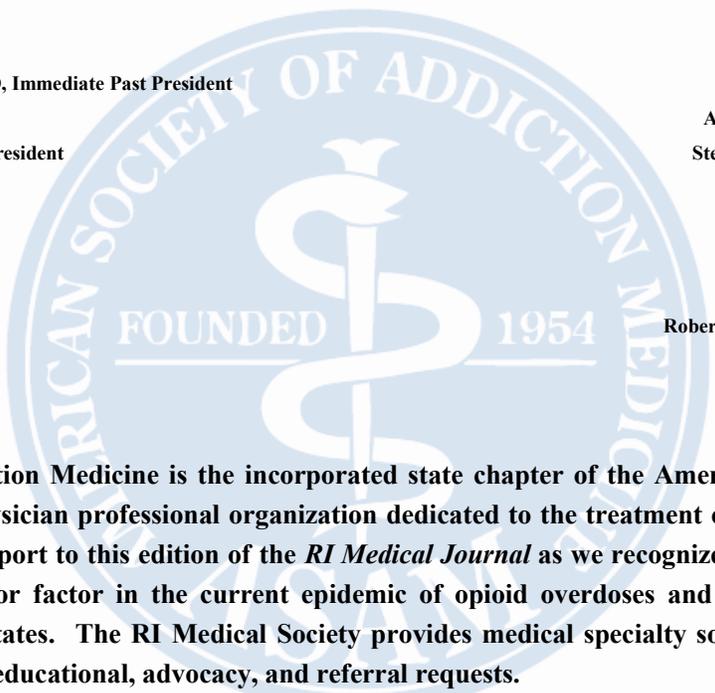
Emergency Departments usually stick to their hospital bases but this changing. The article describes the innovative way that physicians from the Emergency Department at Rhode Island Hospital have this year begun providing naloxone and education about its use to at-risk patients and also working with the Anchor Recovery Community Center to prevent deaths from overdose. This kind of alliance of hospital and community organizations will become commonplace as Accountable Care Organizations develop under the Affordable Care Act.

**Response of Colleges to Risky Drinking College Students**

Although the opioid drug epidemic makes the headlines, alcohol abuse is our most pervasive drug problem. This paper describes advances in the prevention of risky drinking by college students. The use of social media, texting and the development of apps will become even more prominent in communicating directly with individual students about the risks of their drinking behavior.

**Guest Editor**

David C. Lewis, MD, is Professor Emeritus of Community Health and Medicine; Donald G. Millar Distinguished Professor Emeritus of Alcohol and Addiction Studies, and Founder, Brown University Center for Alcohol and Addiction Studies.



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**The RI Society of Addiction Medicine is the incorporated state chapter of the American Society of Addiction Medicine, the largest physician professional organization dedicated to the treatment of addictive disorders. We are proud to provide support to this edition of the *RI Medical Journal* as we recognize that untreated substance use disorders are a major factor in the current epidemic of opioid overdoses and the largest public health problem in the United States. The RI Medical Society provides medical specialty society support services for RISAM and coordinates educational, advocacy, and referral requests.**

**For further information, please contact Megan E. Turcotte at 401-331-3207 or visit: <http://rimed.org/risam.asp>.**

# Medications for Addiction Treatment: An Opportunity for Prescribing Clinicians to Facilitate Remission from Alcohol and Opioid Use Disorders

TAE WOO PARK, MD; PETER D. FRIEDMANN, MD, MPH, FASAM, FACP

## ABSTRACT

Substance use disorders are a leading cause of morbidity and mortality in the United States. Medications for the treatment of substance use disorders are effective yet underutilized. This article reviews recent literature examining medications used for the treatment of alcohol and opioid use disorders. The neurobehavioral rationale for medication treatment and the most common ways medications work in the treatment of substance use disorders are discussed. Finally, the medications and the evidence behind their effectiveness are briefly reviewed. Physicians and other prescribing clinicians should take an active role in facilitating remission and recovery from substance use disorders by prescribing these effective medications with brief medical management counseling.

**KEYWORDS:** Substance use disorders, addiction, addiction treatment, medication

## INTRODUCTION

Substance use disorders are common cause of morbidity and mortality,<sup>1</sup> and costly to society.<sup>2</sup> Medications are effective tools in the contemporary treatment of alcohol and opioid use disorders. Despite their effectiveness, these medications are greatly underutilized, particularly for alcohol use disorders.<sup>3</sup> This article reviews the rationale for the use of medications in addiction treatment and the currently available options for clinical use.

### Neurobehavioral Rationale for Medications in Addiction Treatment

People typically misuse substances initially to activate the brain's reward centers to make themselves feel good. Abusable substances produce euphoria or other pleasurable sensations rapidly and reliably, the ideal situation for operant conditioning. With chronic use, behavioral conditioning from the reinforcing effects of these substances produce long-lasting, quasi-permanent changes in the limbic and cortical systems that manage drives, reward and motivation, learning and memory, judgment, emotion and impulse control. These neurophysiological changes preserve memory of the euphoria and a basic drive to re-experience it, leading to the learned compulsive use behavior, loss of control,

craving, and use despite adverse consequences that characterize addictive disorders. The rapid onset and short-acting nature of most substances of abuse means that dosing, and the often-antisocial behaviors associated with drug procurement, must occur multiple times per day. In addition, many substances (e.g., opioids) produce dysphoria, craving and other adverse withdrawal symptoms when the substance is absent, a form of negative reinforcement for drug cessation. Over time, the development of tolerance means that larger doses, more potent compounds or more bioavailable routes of administration (i.e., injection) must be employed to stave off withdrawal and achieve euphoria. For example, chronic opioid users commonly reach a point where they are no longer getting high and only use to prevent withdrawal and "feel normal" – a common impetus to seek treatment.

### How Medications Work In Addiction Treatment

Contemporary medication addiction treatment (MAT) generally works in one or more ways. MAT:

- (1) Attenuates the euphoria reward, helping to extinguish drug use and associated antisocial/dysfunctional behaviors;
- (2) Reduces withdrawal symptoms and thereby the negative conditioning that deters cessation of drug use; or
- (3) Produces aversive symptoms with use of the substance (i.e., punishment).

Commonly heard concerns about "substituting one addiction for another" arise from a misunderstanding of the behavioral definition of addiction. Although some medications (e.g., long-acting opioids like methadone or buprenorphine) do maintain physical dependence (i.e., tolerance and withdrawal on cessation), it should not be confused with the behavioral disorder of addiction. Most contemporary addiction medications work by attenuating the reinforcing (i.e., addicting) effects of substances. Pure antagonists like naltrexone block the positive reinforcement from euphoria, but do not address the dysphoria and other symptoms of withdrawal. The substitution of long-acting oral agonist medication like methadone reduces both the positive reinforcing euphoria of short-acting opioids like heroin or oxycodone, and withdrawal, thereby mitigating the negative reinforcement of drug use associated with its cessation. Buprenorphine works similarly, blocking the positive reinforcement and preventing withdrawal's negative reinforcement. The impact of these medications is to decrease and ultimately

**Table 1.** FDA-Approved Medications for Alcohol Use Disorders

	Action	Precautions	Adverse Reactions and Common Side Effects	Adult Dosage
<b>Oral naltrexone</b>	Blocks opioid receptors; reduces reward in response to alcohol use	Must be opioid-free 7 to 10 days. If opioid analgesia needed, larger doses required and respiratory depression deeper and prolonged. Monitor liver function.	Precipitates severe withdrawal if concurrently taking opioids; hepatotoxicity at supratherapeutic doses. Nausea, vomiting, and somnolence.	50 mg PO daily.
<b>Naltrexone depot injection</b>	Same as oral naltrexone but effects last 30 days.	Same as oral naltrexone.	Same as oral naltrexone, plus site reaction and greater somnolence.	380 mg gluteal IM injection monthly.
<b>Acamprosate</b>	Mechanism unknown but believed to reduce glutamatergic hyperexcitability.	Evaluate renal function. Moderate Kidney Disease (adjust dose for CrCl 30-50 mL/min).	Mild diarrhea.	666 mg PO TID. If creatinine clearance 30-50 mL/min: 333 mg PO TID.
<b>Disulfiram</b>	Inhibits intermediate metabolism of alcohol which can cause flushing, nausea, dizziness, and tachycardia if patient uses alcohol.	Monitor liver function. Warn patient to avoid alcohol in diet, OTC medications, toiletries. Psychosis or severe myocardial disease relatively contraindications	Disulfiram-alcohol reaction, hepatotoxicity.	250 mg PO daily (range 125 mg to 500 mg)

extinguish the compulsive and dysfunctional behaviors characteristic of addiction. Disulfiram, described below for alcohol use disorders, is the only currently available pharmacotherapy that works through punishment upon use of alcohol.

**Medications For Alcohol Use Disorder**

*Oral Naltrexone*

Naltrexone is an antagonist of the μ-opioid receptor. Opioid receptors are believed to mediate some of the rewarding effects of alcohol. By blocking the effects of endogenous opioids released by alcohol use, naltrexone is believed to reduce the rewarding effects of alcohol use. Naltrexone is generally well tolerated. Potential side effects include nausea, vomiting, somnolence and reversible elevations of liver transaminases.

The efficacy of naltrexone for alcohol use disorders has been examined in multiple large meta-analyses. The most recent meta-analyses found that naltrexone, particularly at a daily dose of 50 mg, was associated with improvements in multiple alcohol consumption outcomes, including return to any drinking, return to heavy drinking, and the number of drinking days.<sup>4</sup> The number needed to treat (NNT) to prevent one person from returning to any drinking or heavy drinking was 12, though it is important to note that most studies evaluated were short-term in duration (12 weeks). Only one long-term trial (12 months or greater) exists for naltrexone and it found no difference between naltrexone and placebo.<sup>5</sup> There is convincing evidence that the effectiveness of naltrexone is dependent on genetic factors<sup>6</sup> and adherence.<sup>7</sup>

*Naltrexone Depot Injection*

Because good adherence to oral naltrexone has been associated with improved effectiveness in treating alcohol dependent patients, an extended-release injectable form of naltrexone was developed. The rationale for this formulation was that a monthly injection would increase adherence to the medication compared to daily oral administration. Aside from a greater sedating effect and injection site reactions, the side effect profile of injectable naltrexone is comparable to oral naltrexone.

A recent meta-analysis found that injectable naltrexone was associated with a reduction in the number of heavy drinking days but was not associated with reductions in return to any drinking or heavy drinking.<sup>4</sup> In one study, among patients sober four or more days prior to the injection, injectable naltrexone tripled continuous abstinence.<sup>8</sup>

*Acamprosate*

Acamprosate’s mechanism of action is poorly understood, but it is believed to reduce the glutamatergic hyperexcitability that occurs during protracted alcohol withdrawal. By reducing this hyperexcitability, acamprosate may attenuate symptoms of protracted withdrawal such as anxiety and insomnia that negatively reinforce alcohol use. Acamprosate is generally well tolerated. The most common side effect associated with acamprosate is mild, transient diarrhea.

The efficacy of acamprosate has been examined in numerous clinical trials. A recent meta-analysis found that acamprosate was associated with improvement in the return to any drinking with a NNT of 12.<sup>4</sup> Another meta-analysis

of 22 randomized, placebo-controlled trials found that acamprosate increased abstinence days by 10% and complete abstinence almost two-fold.<sup>9</sup> Of note, earlier European trials of acamprosate showed efficacy in maintaining abstinence but subsequent trials conducted in the United States did not show a significant effect.<sup>10</sup>

**Disulfiram**

Disulfiram is used as an aversive agent and a deterrent to alcohol use. Disulfiram inhibits the enzyme aldehyde dehydrogenase. When taken with alcohol, disulfiram causes an elevation of serum acetaldehyde concentration. This buildup of acetaldehyde produces an adverse reaction characterized by flushing, increased heart rate and hypotension and may lead to nausea, vomiting, and dizziness. Disulfiram is relatively contraindicated in those with psychosis and those with severe myocardial disease. It can interact with alcohol found in everyday products like perfume and aerosols, and can cause hepatotoxicity in rare cases.

Randomized placebo-controlled clinical trials suggest that oral disulfiram has limited efficacy for alcohol use disorders. A recent meta-analysis of four well-controlled trials of disulfiram found no overall reduction in alcohol use.<sup>4</sup> Disulfiram might be more effective when medication is administered in a supervised manner. A systematic review of 11 randomized trials found improved short-term abstinence among alcohol dependent patients for whom administration of disulfiram was supervised.<sup>11</sup>

**Other Alcohol Pharmacotherapies**

Other medications have some evidence to support their off-label use for the treatment of alcohol use-disorders.

Topiramate, an anti-convulsant with GABA-ergic properties, has been found to reduce alcohol consumption in a small number of randomized clinical trials.<sup>4</sup> The opioid receptor antagonist nalmefene reduced alcohol use in a few clinical trials and may have less risk of hepatotoxicity than oral naltrexone.<sup>12</sup>

**Medications For Opioid Use Disorder**

**Methadone**

Methadone is a  $\mu$ -opioid receptor agonist with excellent oral bioavailability and a long half-life. Methadone maintenance treatment, or the daily administration of methadone to those with opioid use disorders, can reduce opioid craving, prevent symptoms of opioid withdrawal and reduce the effects of shorter-acting opioids such as heroin through cross-tolerance. These actions free patients from the need to seek illicit opioids and help normalize daily functioning. The use of methadone to treat opioid addiction is highly regulated and limited to licensed opioid treatment programs. Methadone is generally well tolerated, though overdose can occur, especially when taken in combination with sedative-hypnotics. Methadone has been linked with QTc interval prolongation but recommendations for regular screening with electrocardiogram at time of methadone initiation have been controversial.<sup>13</sup> Constipation and sweating are common side effects.

Multiple randomized clinical trials over 30 years have demonstrated that methadone maintenance treatment is highly effective in retaining patients in treatment and reducing opioid use.<sup>14</sup> Recent meta-analyses of observational studies affirm that methadone maintenance decreases mortality<sup>15</sup> and HIV transmission.<sup>16</sup> Doses of 60-100 mg/day of

**Table 2.** FDA-Approved Medications for Opioid Use Disorders

	Action	Precautions	Adverse Reactions and Common Side Effects	Adult Dosage
<b>Methadone</b>	Full opioid agonist. Long half-life allow for daily dosing which reduces need to seek illicit opioids.	Can be lethal in overdose. Has been linked with QTc interval prolongation.	Constipation and sweating.	Starting dose no more than 30 mg depending on patient tolerance to opioids. Maintenance doses of $\geq$ 60 mg daily more effective.
<b>Buprenorphine</b>	Partial opioid agonist which reduces need to seek illicit opioids. Most common formulation includes naloxone which discourages injection.	Should be opioid-free 12-24 hours prior to induction, maybe longer if using long-acting opioids. Monitor liver function.	Constipation, dizziness, nausea and vomiting	Start 4mg/1mg of sublingual buprenorphine/naloxone, total of 8 mg/2 mg in first day. Typical maintenance dose between 16-24 mg daily.
<b>Naltrexone depot injection</b>	Blocks opioid receptors and effects of opioids.	Must be opioid-free 7 to 10 days. If opioid analgesia needed, larger doses required and respiratory depression deeper and prolonged. Monitor liver function.	Precipitates severe withdrawal if concurrently taking opioids; hepatotoxicity at supratherapeutic doses. Nausea, vomiting, and somnolence, site reaction.	380 mg gluteal IM injection monthly.

methadone are more effective than lower doses in increasing treatment retention and decreasing opioid use.<sup>17</sup> Because the risk of relapse after methadone discontinuation is high, long-term treatment is necessary for many patients.

Federal law restricts the use of methadone to licensed opioid treatment programs for the treatment of opioid use disorders. Such programs are required to provide addiction counseling and directly supervise dosing such that, for example, weekly take-home dosing cannot occur among stable patients for the first nine months.

### *Buprenorphine*

Buprenorphine, a partial  $\mu$ -opioid receptor agonist, is approved for opioid maintenance treatment in office-based settings. The most common formulation is taken sublingually and includes naloxone, an opioid receptor antagonist with poor bioavailability when taken orally or sublingually. This formulation was designed to discourage misuse via injection. Buprenorphine has a long duration of action due to its high opioid receptor affinity and slow dissociation from the receptor. Buprenorphine's partial agonist properties block euphoria from other opioids, reduce craving and prevent withdrawal, while the ceiling on its agonist properties reduces the risk of respiratory depression. Because it is a partial agonist and has strong opioid receptor affinity, buprenorphine may precipitate opioid withdrawal symptoms if taken too soon after ingestion of other opioids. Possible side effects include constipation, dizziness, nausea and vomiting. It has also been linked to rare cases of hepatitis.

In randomized clinical trials buprenorphine maintenance treatment is as effective as methadone in reducing opioid use.<sup>18</sup> However, buprenorphine may be less effective than methadone in retaining patients in long-term treatment, particularly in studies that utilized dosing protocols that closely reflect clinical practice.

In order to prescribe office-based buprenorphine, physicians must have completed an approved 8-hour course and requested an amended controlled substance license from the federal Drug Enforcement Administration. Buprenorphine prescribers are limited to 30 active buprenorphine patients in the first year and 100 patients thereafter. Counseling services must be available, but are not required.

### *Naltrexone Depot Injection*

Naltrexone is a long-acting opioid antagonist that produces a dose-dependent blockage of all opiate effects. When administered orally, it effectively improves treatment retention and abstinence in patients with opioid use disorders only when adherence can be assured.<sup>19</sup> Extended-release injectable naltrexone was developed to improve adherence.

Two randomized clinical trials of injectable naltrexone for the treatment of opioid use disorders demonstrated improvement in treatment retention and the number of negative urine drug tests for opioids.<sup>20,21</sup> An ongoing effectiveness trial is testing injectable naltrexone against treatment

as usual in a group of recently released parolees with an opioid use disorder and early findings are similarly promising.<sup>22</sup>

### **Medication Management Counseling**

Much evidence suggests that pharmacotherapy and office-based medication management counseling by a doctor or nurse in generalist settings is as effective as more extensive counseling interventions.<sup>23</sup> For opioid use disorders, medications even without counseling can have substantial benefits.<sup>24</sup> Medical management counseling includes direct advice to stop substance use; monitoring and feedback of improvements in medical conditions and other consequences to enhance motivation; regular visits to monitor and encourage adherence to the pharmacotherapy; and recommending participation in mutual help groups.<sup>25</sup>

## **DISCUSSION**

A growing number of medications for alcohol and opioid use disorders have been found to be effective in reducing substance use and in some cases, mortality related to substance use. Additionally, several of these medications have been found to be cost-effective.<sup>26,27</sup> Despite these findings, medication treatments for addiction continue to be underutilized. Physicians and other prescribing clinicians can take an active role in facilitating remission and recovery among their recovering patients by prescribing these effective medications and delivering brief medical management counseling.

### **Acknowledgments**

This work was supported by 5R01DA024549 from the National Institutes on Drug Abuse (NIDA). The contents are solely the responsibility of the authors and do not necessarily represent the views of the Department of Health and Human Services, NIDA, or the Department of Veteran Affairs.

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## Disclosures

Dr. Friedmann has received grant research support from Alkermes and has participated in Orexo's speakers bureau.

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# Long-term Opioid Therapy for Chronic Pain and the Risk of Opioid Addiction

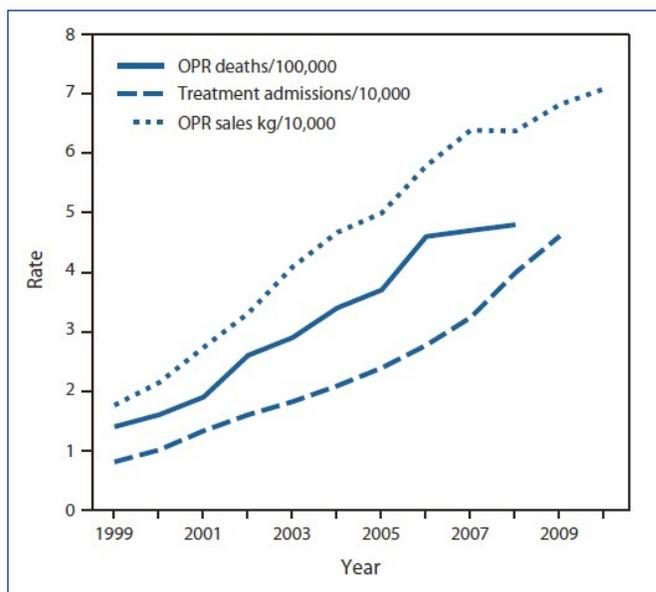
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## INTRODUCTION

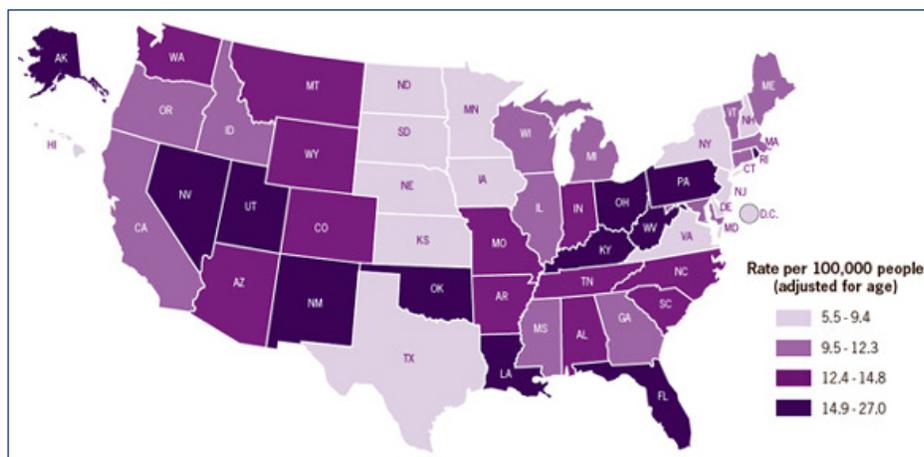
There has been a constant struggle to define the role of opioids in medical therapy, due to their potential for misuse, overuse, and addiction since pain is a completely subjective sensation, not amenable to objective measurement, and is intimately tied to emotion and the patient's psychological well-being. Thus the medical decision to administer an opioid analgesic is an attempt to balance the potential for pain relief, and the reliability of the patient's reporting, against the potential for harm. The decision-making process is less complicated when dealing with acute traumatic injury or surgical trauma. However, with many chronic pain conditions, the etiology or severity of the patient's pain is less obvious. In the majority of situations, a physician does not initiate opioid therapy with the intention of continuing it for months or years, but many patients will continue to seek opioids for relief of pain which becomes chronic.

Until 1990, chronic use of opioid analgesics was widely discouraged, with most physicians trained to taper their patients off opioid medication after an acute treatment trial. The paradigm began to shift as the movement to improve cancer pain treatment became successful with aggressive opioid prescribing. The success of aggressive opioid therapy for cancer pain treatment led to a spill over into chronic non-cancer pain treatment, spurred on by industry-supported continuing medical education programs. As high-dose opioids became more available in the community, it was accompanied by a pattern of escalating drug diversion, opioid misuse, accidental opioid overdose, and deaths that continued to climb through the past decade. (Figure 1)<sup>1</sup> Accidental opiate overdose deaths from prescription opioids began to far exceed deaths attributed to illicit drugs of abuse, such as heroin and cocaine. Nationally, accidental drug overdose deaths surpassed deaths from motor vehicle accidents, reaching a peak of 16,917 deaths from prescription opioids in 2011 (<http://www.cdc.gov/homeandrecreationalsafety/overdose/facts.html>). During the period from 2009–12, Rhode Island

**Figure 1.** Rates of opioid pain reliever (OPR) overdose death, OPR treatment admissions, and kilograms of OPR sold – United States, 1999–2010.<sup>1</sup>



**Figure 2.** Drug overdose death rate in 2008 and rate of kilograms (kg) of opioid pain relievers (OPR) sold in 2010 – United States.<sup>1</sup>

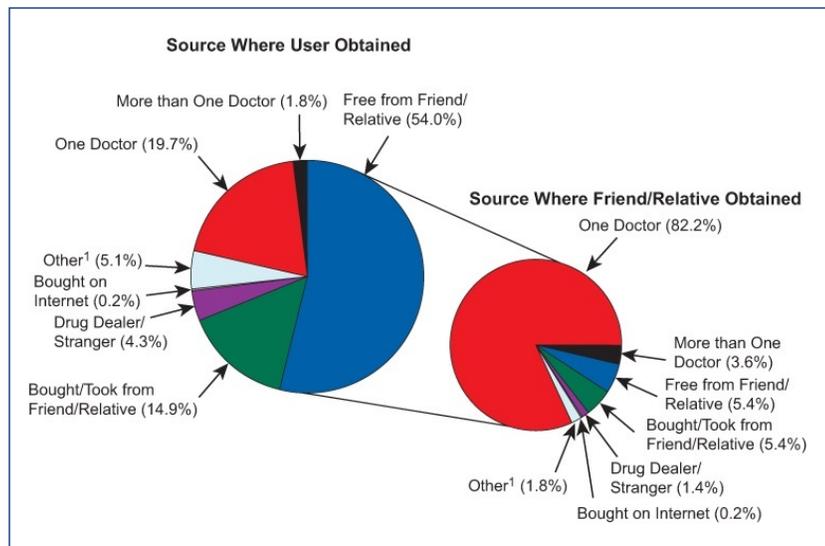


experienced 645 accidental prescription opioid deaths, and in 2008 the state's accidental opioid overdose death rate of 17.2/100,000 people ranked as the sixth highest in the nation. (Figure 2) CDC analysis of opioid prescribing rates

for the year 2012 ranked Rhode Island at 19th nationally, with 89.6 opioid prescriptions per 100 persons; however, this does not imply that 90% of the population are receiving an opioid prescription, as most are repeat prescriptions going to a small percentage of the population. Nationally, the CDC suggests that enough opioid prescriptions are dispensed annually to provide every citizen in the U.S. with a month supply of medication.

What role do prescribing physicians play in this national crisis? CDC statistics have indicated that fewer than 20% of patients dying from accidental prescription opioid overdoses have a legal prescription for the opioid medication involved in their demise. National drug surveys conducted have consistently found that the majority of nonmedical opioid users obtain access to the medication through family and friends, with only a small percentage via drug dealers or Internet sources. (Figure 3) This initially suggests that physicians are a minor source of misused medication; however, when you consider that a physician prescribed the opioids to the family and friends of the unintentional overdose victims, physicians appear to contribute an additional 60% of the misused opioid supply. Overall, physician prescribing provides more than 80% of the misused opioid supply, through their direct intent and through unintended diversion.

**Figure 3.** Opioid pain reliever sources for nonmedical use among users: 2009–2010. (www.samhsa.gov/data/NSDUH/2k10MH\_Findings/2k10MHResults.pdf)



**ARE CHRONIC PAIN PATIENTS PRESCRIBED LONG-TERM OPIOID MEDICATION AT RISK FOR ADDICTION?**

Despite their documented efficacy in treating acute and cancer pain, there is no strong evidence to support long-term prescribing of opioids for common pain problems, such as low back pain.<sup>2</sup> Recent efforts by the American Academy of Pain Medicine and the American Pain society to establish

guidelines for opioid prescribing for chronic pain found little high-level evidence of efficacy, and mostly based their recommendations on expert opinion. (http://www.americanpainsociety.org/uploads/pdfs/Opioid\_Final\_Evidence\_Report.pdf) Long-term randomized, controlled trials are difficult, if not impossible to design due to the inherent actions of the opioid class, such as obvious sedative or euphoric effects when administered, the development of tolerance, and the development of withdrawal symptoms when stopped. Even more confusing is the limited evidence of efficacy seen in open trials, where “significant” reductions in pain ratings are limited to 1–2 points on the 10- or 11-point rating scale. The self-reinforcing effects seen with opioid analgesics are often confusing to patients, who may interpret the withdrawal pattern (often manifested as pain and achiness) between doses as evidence of efficacy. Despite patient reports of subjective improvement, global measures of pain relief and improved function are modest or lacking.

Opioid-related side effects and lack of efficacy results in treatment discontinuation by as many as 30% of patients enrolled in opioid trials.<sup>3</sup> Another major reason for discontinuation of opioid therapy in clinical trials includes addiction, medication misuse, and suspicion of diversion. Definitions of aberrant drug-related behavior (ADRB) and addiction are quite varied in the literature, and are continually being redefined in the chronic pain setting. Most chronic pain patients treated with long-term opioids will develop evidence of tolerance and physical dependence, a pattern of drug-seeking behavior, craving, and even evidence of continued use despite harm (as in significant side effects). Advocates of long-term opioid treatment have argued that these parameters, typically associated with addiction, are the consequence of inadequate pain treatment and not addiction. Controversy exists over what behaviors should be classified as ADRB. Some of the more widely accepted ADRB's include: lost or stolen prescriptions, early visits without appointments seeking refills, not following the prescribed dosage pattern, seeking medications from multiple physicians, forging prescriptions, use of illicit drugs or detection of non-prescribed opioid medications with urine drug testing, and legal action related

to opioid medications.<sup>4</sup> Unfortunately, there is no uniformity in defining ADRB's or addiction in the chronic pain literature. Recognizing this difficulty, several structured evidence-based reviews have attempted to examine the risk of addiction in populations treated with long-term opioids.<sup>4,5</sup> Fishbain et al. reviewed the published literature in 2008, evaluating studies reporting on patients treated with opioids for a period ranging from 2 to 240 months, for an average exposure time of 26.2 months.<sup>5</sup> After reviewing 67

published reports, they identified 24 studies that measured abuse/addiction, involving 2,507 chronic pain patients, and found an estimated abuse/addiction rate of 3.27%. In studies that excluded patients with a history of abuse or addiction, the rate of reported abuse/addiction dropped to 0.19%. In 17 studies focusing on ADRB, the calculated ADRB incidence was 11.5%, and in patients without a prior history of abuse or addiction, the rate dropped to 0.59%.

A Cochrane Review on long-term opioid management for chronic noncancer pain published in 2010 reported similar findings, with an estimate of opioid addiction of 0.27%, leading the authors to conclude that the risk of iatrogenic opioid addiction is low.<sup>4</sup> Individual studies have estimated drug abuse/addiction to range between 0-50% of their population. This wide range is due in part to non-standardized definitions of abuse/addiction, as some included any controlled substance, not just misuse or abuse of the prescribed opioid. There is also a built in selection bias depending on the referral pattern of the treatment program. Many pain treatment programs accumulate high-risk patients with a history of substance abuse, or current abuse concerns.

One of the most consistent risk factors predicting opioid abuse/addiction, is a history of opioid abuse (odds ratio of 3.81).<sup>6</sup> Patients with a history of severe dependence or abuse had an odds ratio of 56 for developing abuse/addiction.<sup>6</sup> Weisner *et al* surveyed patients receiving long-term opioids in two large group health plans and found that patients with a history of opioid abuse had a prevalence rate of opioid use approaching 50%, compared to patients without a prior opioid abuse history of 2-3%. In their study, patients with an abuse history tended to use higher doses, averaging 100mg of morphine equivalent dose (MED), were prescribed more schedule II opioids, and were prescribed more long-acting opioids.<sup>7</sup> Gwira-Baumblatt *et al.* identified using more than 100mg MED daily had an adjusted odds ratio of 11.2 for unintentional overdose deaths.<sup>8</sup>

Recognizing the shortcomings of the current literature, and the fact that most long-term opioid trials were conducted over three months or less, it would appear that the risk of developing opioid addiction is low in a prescreened population using low to modest opioid doses. However, in patients with a history of prior substance abuse or high-dose opioid use ( $\geq 100$ mg of morphine equivalent dose), the risk of addiction/abuse is substantially higher.<sup>9</sup>

## LESSONS LEARNED

Most data dealing with the benefits and risks of long-term opioid therapy for chronic noncancer pain are based on studies of 8-12 weeks, or deal with highly selected populations. There is a general belief that there is still insufficient evidence to clearly define the safety or efficacy of long-term opioids. Tools for predicting opioid aberrancy and addiction have been studied over relatively brief periods, and are based on testing in at-risk populations, but have only modest

predictive value of treatment success or addiction/abuse when applied to more global pain populations. While some screening tools, such as SOAPP and the Opioid Risk Tool are helpful, they cannot be applied in isolation, are probably most useful as an indicator of who should be more closely monitored, and should not be used to determine who should receive long-term opioids.

Based on current evidence, the following approach to long-term opioid prescribing may be helpful. Most opioid dependent and accidental overdose patients have the following characteristics in common: 1) patients at high risk for overdose or abuse tend to be doctor shoppers, often visiting 5 or more practitioners for opioid prescriptions; 2) accidental overdose deaths are associated with prescriptions of more than 100 mg of MED daily (8.9 fold increase in risk with a 1.7% annual overdose risk); 3) male sex; 4) patients with a history of substance abuse; 5) concurrent psychiatric diagnoses; 6) use of 3 or more different pharmacies.<sup>6-11</sup> Given this, it is critical that any physician intending to prescribe long-term opioids for chronic pain review their state prescription monitoring program (for RI see: <http://www.health.ri.gov/programs/prescriptionmonitoring/>) for evidence of their patient receiving opioids from multiple prescribers or pharmacies. This program is not fool-proof, as patients accessing controlled substances across state lines can avoid scrutiny, but it demonstrates a good faith effort on the part of the physician and due diligence. Careful scrutiny and review of medical records for evidence of a past history of substance abuse will help to identify patients at risk for dependence, misuse, or addiction. A history of addiction does not necessarily preclude opioid therapy; if warranted, but definitely identifies a need for close monitoring. An opioid pain treatment agreement may also be of value, as it clearly defines the expectations for continued opioid treatment parameters, and may serve as a formal informed consent, depending on the design of the document. Finally, avoid prescribing high-dose or large quantities of opioids. The efficacy of prescribing dosages higher than 100mg of MED are associated with a greater risk of diversion, abuse, overdose, and a general lack of efficacy. Unfortunately, there are no completely reliable means to ensure success or failure. Only thoughtful prescribing with an understanding of the risks and benefits can improve treatment success and patient safety.

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# Responding to Opioid Overdose in Rhode Island: Where the Medical Community Has Gone and Where We Need to Go

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## ABSTRACT

The number of opioid overdose events in Rhode Island has increased dramatically/catastrophically in the last decade; Rhode Island now has one of the highest per capita overdose death rates in the country. Healthcare professionals have an important role to play in the reduction of unintentional opioid overdose events. This article explores the medical community's response to the local opioid overdose epidemic and proposes strategies to create a more collaborative and comprehensive response. We emphasize the need for improvements in preventing, identifying and treating opioid addiction, providing overdose education and ensuring access to the rescue medicine naloxone.

**KEYWORDS:** Opiate addiction, overdose, opioid, healthcare professionals

## INTRODUCTION

### Opioid Overdose

Over the last two decades, drug overdose has emerged as the leading cause of adult injury death in the United States (US).<sup>1</sup> In 2011, there were 41,340 deaths nation-wide resulting from drug overdose, up from 4,030 in 1999.<sup>2,3</sup> Prescription drugs were the most common drugs involved in overdose fatalities (22,810) and nearly three-quarters of these fatalities involved opioids (16,917).<sup>1</sup>

In Rhode Island drug overdose deaths outrank deaths caused by motor vehicle crashes.<sup>4</sup> With roughly four drug overdose deaths weekly, Rhode Island has the 13th highest overdose mortality rate nationally, and the highest overdose mortality rate in New England.<sup>5</sup> From 2010 to 2012, nearly all cities and towns (36/39) in the state experienced an accidental overdose death.<sup>6</sup> Although Providence reported the largest number of overdose deaths in the state (72), two towns, Central Falls and Woonsocket, reported the highest per capita rate with 77 and 73 overdose deaths per 100,000, respectively.<sup>6</sup>

From 1999 to 2010, Rhode Island mirrored national trends in overdose deaths, reporting a 182% increase in drug overdose mortality;<sup>4</sup> however, more recent trends indicate a disturbing pattern. During the spring of 2013, acetyl-fentanyl tainted heroin was linked to over a dozen unintentional

overdoses. This was followed by a doubling of the overdose mortality from November 2013 to March 2014,<sup>7</sup> this time traced to fentanyl-laced heroin and cocaine. These two "outbreaks," investigated by the Centers for Disease Control and Prevention (CDC) and other partners, suggest an increasing overlap in populations misusing prescription opioids and using illicit drugs. Whereas from 2009 to 2012, 53% of Rhode Island's 646 drug overdoses were attributed to prescription drugs and only 21% resulted from illicit drugs, an uptick in illicit drug overdoses that began in 2013 indicates a complete reversal in prior trends: overdoses attributed to illicit drugs now comprise 56% of these deaths.<sup>5,8</sup> Regardless of the cause, the death toll stands as a call to arms to the medical community to slow the death rate through prevention, treatment, reducing the stigma of addiction, and harm reduction.

### Opioid Prescribing Practices, Non-medical Use, and Treatment

Increases in both the prescribing of opioids and self-reported non-medical use of opioids are two key drivers of the rise in drug overdose fatalities nationally and at the state-level.<sup>9</sup> In 2010, there were enough pain relievers prescribed nationally to medicate every American continuously for one month.<sup>10</sup> In 2012, Rhode Island had the 19th highest number of pain-reliever prescriptions; there were 90 pain-reliever prescriptions per every 100 people in the state.<sup>9</sup>

Availability and accessibility of pain relievers are associated with their increased non-medical use.<sup>4</sup> In 2010, more than 12 million people in the US reported using prescription pain relievers non-medically.<sup>10</sup> In that same year in Rhode Island, 5.2% of adults ( $\geq 12$  years) reported nonmedical use of prescription pain relievers, amongst the highest state rates in the country.<sup>4</sup>

Despite the growing need, the availability of addiction treatment has not expanded rapidly enough. There is a shortage of healthcare professionals trained to provide substance abuse treatment services.<sup>4</sup> Notably, in Rhode Island, there were only eight medical professionals per every 100,000 people approved to treat opioid-addicted patients with buprenorphine.<sup>4</sup> While Rhode Island fares better than two-thirds of all states (who have fewer than six prescribers per every 100,000 people), the high prevalence of opioid misuse and the alarming increase in overdose events necessitate a broader treatment response, accessible throughout the state.

## ADDRESSING OPIOID OVERDOSE IN RHODE ISLAND

In response to the growing overdose epidemic, Rhode Island has instated several laws, programs, and policies designed to prevent the misuse of opioids and reduce the number of overdose events. Below we focus on interventions that directly have an impact on healthcare professionals including: the Prescription Monitoring Program, access to naloxone, an opioid overdose antidote, “Good Samaritan” laws, and the Collaborative Practice Agreement for Naloxone.

### The Prescription Monitoring Program

In 2012, Rhode Island launched an electronic Prescription Monitoring Program (PMP),<sup>5</sup> a database used to track the dispensing of controlled prescription drugs to patients.<sup>4</sup> Information obtained from PMPs can be used to identify high-risk patients, problem prescribers and identify trends in opioid use and misuse<sup>4</sup>; their utility in helping to reduce overdose deaths is yet unproven. Research examining the effectiveness of PMPs remains a relatively new area of inquiry; however, preliminary evidence suggests that PMPs are effective at changing prescribing practices and reducing “doctor shopping” (i.e., seeking out multiple providers to acquire controlled substances), and prescription drug abuse.<sup>11</sup> PMPs may also be most effective for overdose prevention by facilitating a discussion about prescribing naloxone, medication-assisted therapies, and other drug treatment options.<sup>12</sup>

There are limitations to Rhode Island’s PMP program. As of January 2014, only 18% of all prescribers were registered to use the PMP.<sup>5</sup> Furthermore, the database has been consulted for less than 10% of all controlled-substance prescriptions written statewide.<sup>13</sup> Legislation signed in May 2014 requires healthcare providers to register for the PMP when they obtain or renew their controlled substance license. Though this legislation targets increasing prescriber registration, it does not require that prescribers consult the PMP prior to prescribing a controlled substance.<sup>13</sup> The CDC and other organizations have identified PMPs as a key strategy for improving patient safety and reducing prescription drug misuse and diversion when they are universal (i.e., used by all healthcare providers for all controlled substances) and are actively managed.<sup>10</sup>

To improve our response to the increasing number of opioid overdose events, licensed prescribers in Rhode Island should register with the PMP and routinely consult it prior to prescribing controlled substances. **Figure 1** (next page) presents screenshots of Rhode Island’s PMP registration page (which can be found at [ripmp.com](http://ripmp.com)) and a sample patient prescription history report. Detailed instructions of how to register and use Rhode Island’s PMP can be found on the Department of Health’s website ([www.health.ri.gov/programs/prescriptionmonitoring/](http://www.health.ri.gov/programs/prescriptionmonitoring/)). Another novel Rhode Island resource specifically designed for prescribers is the *Physician Consult* program, which provides primary care physicians with immediate assistance to assess (within 1 hour of call) and facilitate

drug treatment entry for patients who are using illicit drugs or misusing prescription drugs and seek help (see links on [health.ri.gov](http://health.ri.gov) or call 401-781-2700/TTY 401-354-7640).

### Naloxone Access and Good Samaritan Laws

Naloxone is an opioid antagonist used to counter the effects of opioid-induced respiratory depression.<sup>14</sup> Once administered intramuscularly, intranasally, intravenously, or subcutaneously, its effects occur within minutes and can last anywhere between 20 to 90 minutes.<sup>14</sup> Though naloxone is a prescription drug, it is not a controlled substance and has no abuse potential.<sup>14</sup> Naloxone has been routinely used in healthcare settings to reverse opiate overdose,<sup>15</sup> however, naloxone prescriptions can also be provided to at-risk patients or their caregivers (a practice known as “third-party prescribing”).<sup>15</sup>

Although opioid antagonists are legal, there are barriers that may prevent healthcare professionals from prescribing naloxone to at-risk patients or their caregivers (i.e., fear of criminal liability).<sup>16</sup> State laws, known as “Good Samaritan” laws, have been implemented to encourage increased prescribing of naloxone and to protect those who call 911 or administer the drug to an individual who is overdosing.<sup>15</sup> Rhode Island’s Good Samaritan law provides partial immunity for individuals who summon medical help during an overdose event.<sup>4</sup>

Given that most overdose victims typically are unable to self-administer naloxone, providing overdose education and a prescription for naloxone to caregivers is an essential component of overdose prevention efforts.<sup>17</sup> Community-based overdose education and naloxone distribution (OEND) programs for lay individuals have proven successful at reducing community-level overdose mortality. Since 1996, US OEND programs have distributed naloxone to 53,032 persons nationwide, resulting in the reversal of 10,171 opioid overdoses.<sup>2</sup> Good candidates for naloxone prescriptions include individuals who are taking opioids for long-term pain management or who have a suspected or confirmed history of substance abuse, or their caregivers.<sup>15</sup>

The Substance Abuse and Mental Health Services Administration’s “Opioid Overdose Toolkit,” provides additional guidance on who may be best suited to receive overdose education and naloxone prescriptions (<http://store.samhsa.gov/product/Opioid-Overdose-Prevention-Toolkit/SMA13-4742>).<sup>15</sup> An additional resource is the website [prescribeprevent.org](http://prescribeprevent.org) which demystifies the prescribing and dispensing of naloxone for healthcare professionals. Prescribers are encouraged to work with community-based OEND programs to improve naloxone access in their state.<sup>2</sup> A more detailed description of Rhode Island’s community-based OEND programs can be found elsewhere in this issue.

### Pharmacists and Collaborative Practice Agreement

Pharmacists are the most accessible healthcare provider in the community, working in highly visible and convenient

Figure 1.

**State of Rhode Island**  
**Department of Health**

### New Registration

**Registration Instructions**  
Welcome to the PMP registration process.  
To begin the registration process, please select your job type that best describes your profession.

- Enter the form of identification requested:
  - DEA Number, if you're a Pharmacist or Practitioner
- Click the Next button. The system will display your information if found. Please make necessary corrections and fill in any missing information. If no information is returned, please fill out the information requested.
- Click the Register button and follow the on screen instructions. If you have any questions please contact the PMP help desk at (866)-683-2476.

• Please enter DEA Number for practitioner

Job:

DEA Number:

**RI Dept of Health: Prescription Monitoring Program**  
3 Capitol Hill, Room 205, Providence, RI 02908  
Phone: 866-683-2476 Fax: (614) 547-0063 Email: rixreport@otech.com

### Patient RX History Report

**Mary Smith** Date: 04-01-2014  
Page: 1 of 1

This report may contain another person's controlled substance information. Please review the "Patients that Match Search Criteria" section located below to ensure all prescriptions belong to the requested individual.

**Search Criteria:** (( Last Name Begins 'smith' AND First Name Contains 'mary') AND ( D.O.B = 'XX/XX/XXXX' AND State = 'RI')) AND Request Period = '01/01/2009' To '04/01/2014'

**Patients that match search criteria**

Pt ID	Name	DOB	Address
4297	Smith, Mary	xx/xx/xxxx	anywhere

**Prescriptions**

Fill Date	Product, Str, Form	Qty	Days	Pt ID	Prescriber	Written	Rx #	N/R	Pharm	Pay
04/28/2011	AP AP HYDROCODONE BITARTRATE, 750 MG-7.5 MG, TAB	10	5	4297	DOC ID	04/28/2011	1443926	N	AP9086869	

**N/R:** N=New R=Refill  
**Pay:** 01=Private Pay 02=Medicaid 03=Medicare 04=Commercial Ins. 05=Military Inst. and VA 06=Workers Comp 07=Indian Nations 99=Other **Total Prescriptions:** 1

**Prescribers for prescriptions listed**

DocID # Doctor name

**Pharmacies that dispensed prescriptions listed**

AP9086869 P DRUG INC, NULL PO BOX 20250 1300 OAKLAWN AVE CRANSTON RI 02920

Disclaimer: Department of Health does not warrant the above information to be accurate or complete. The Report is based on the search criteria entered and the data entered by the dispensing pharmacy. For more information about any prescription, please contact the dispensing pharmacy or the prescriber.

Source: McDonald, J.V. (2014) "How to Use the Rhode Island Prescription Drug Reporting Program (PMP): The Very Basics." Retrieved August 10, 2014, from <http://www.health.ri.gov/publications/guides/HowToUseThePMP.pdf>

locations. Nationally, pharmacists already participate in harm-reduction activities for people at risk of opioid overdose, including over-the-counter needle sales, prescription monitoring program review, and counseling patients on buprenorphine.<sup>18</sup> Evidence shows that pharmacists who participate in these activities are more likely to accept the notion of providing naloxone to caregivers of potential overdose victims.<sup>19</sup> Since pharmacists dispense the prescription opioids that result in 60% of all reported opioid overdose deaths,<sup>20</sup> they are key stakeholders in harm-reduction activities, including stocking naloxone, promoting naloxone co-prescription by prescriber, and initiation of naloxone through collaborative practice agreements. Collaborative practice agreements (CPA) are formal agreements in which a licensed provider makes a diagnosis, supervises patient care, and refers patients to a pharmacist under a protocol that allows the pharmacist to perform specific patient-care functions.<sup>21</sup>

Rhode Island has implemented a CPA, where pharmacists can furnish naloxone without an individual prescription, alongside overdose prevention, identification, and response training;<sup>5</sup> a practice supported by the American Pharmacists Association.<sup>22</sup> As of August 2014, approximately 300 people accessed naloxone using the CPA, nearly doubling community-based naloxone efforts for the year.<sup>23</sup> Healthcare professionals should educate and refer their at-risk patients to Walgreens, CVS, or other CPA-participating pharmacies, to realize maximum public health impact.

## FUTURE DIRECTIONS

The strategies outlined above represent an important step forward, but, as noted, the current approaches can be better utilized and interconnected. Below we suggest two promising strategies that can be adopted to enable a more comprehensive healthcare response to opioid overdose prevention efforts in Rhode Island: improving prescriber education and adequately treating opioid addiction.

### Prescriber Education

Prescriber education is critical to reduce the incidence of prescription drug abuse and misuse,<sup>4</sup> however, most health professional schools do not provide comprehensive training on substance abuse or provide limited training on treating pain.<sup>4</sup> On average, medical students receive only 11 hours of training in pain management.<sup>24</sup> Rhode Island does not currently require or recommend education for pain medication prescribers.<sup>4</sup>

To address this gap in prescriber education, the Food and Drug Administration approved the Risk Evaluation and Mitigation Strategy, requiring drug manufacturers to offer free or low-cost training programs to licensed prescribers in the US.<sup>4</sup> Recommended training components include: knowledge and awareness of holistic approaches to pain treatment, appropriate opioid prescribing practices, use of PMPs,

addiction identification, and referral to treatment.<sup>5</sup> To these national recommendations, we urge the explicit addition of overdose prevention and prescribing of naloxone as critical topics in prescriber education.

### Addiction Treatment

Treatment for opioid addiction typically combines counseling and behavioral therapies with the provision of medications (e.g., methadone, buprenorphine, and naltrexone) designed to ease/eliminate withdrawal symptoms or block the effect of opioid drugs; an approach known as Medication-Assisted Treatment.<sup>25</sup>

Special authorization is needed for healthcare professionals seeking to treat addiction using controlled substances (i.e., methadone and buprenorphine).<sup>4</sup> Therefore, in addition to ensuring that individuals in need of treatment are identified and referred to treatment, an adequate number of healthcare providers trained and licensed to provide addiction treatment is also needed.<sup>4</sup> Given local trends in opioid addiction and overdose events, more medical professionals approved to treat patients for addiction are needed.

## CONCLUSION

Opioid overdose casualties in Rhode Island continue to increase at an alarming rate. Healthcare providers are in a unique position to significantly reduce the number of opioid overdose events. In order to affect long-lasting change in this epidemic, the response from Rhode Island's healthcare professionals needs to be collaborative, comprehensive, and consistent, with a focus on preventing, identifying and treating opioid addiction, providing overdose education, and ensuring timely access to rescue medications.

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# The Rhode Island Community Responds to Opioid Overdose Deaths

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## ABSTRACT

The challenge of addressing the epidemic of opioid overdose in Rhode Island, and nationwide, is only possible through collaborative efforts among a wide breadth of stakeholders. This article describes the range of efforts by numerous partners that have come together to facilitate community, and treatment-related approaches to address opioid-involved overdose and substance use disorder. Strategies to address this crisis have largely focused on increasing access both to the opioid overdose antidote naloxone and to high quality and timely treatment and recovery services.

**KEYWORDS:** Opiate addiction, overdose, opioid, naloxone

## INTRODUCTION

Rhode Island experienced a dramatic increase in opioid-involved overdose deaths in the first half of 2014. Prior to the first broad acknowledgment of opioid overdose as a public health crisis, statewide collaborations were underway to reduce opioid overdose deaths and address the crisis of opioid addiction.

The Drug Overdose Prevention and Rescue Coalition, convened in 2012 by The Rhode Island Department of Health (HEALTH), has grown from a handful of advocates to more than 100 members. Active members represent the state public health and behavioral health agencies, Department of Corrections, law enforcement, treatment providers, recovery organizations, healthcare providers, researchers, prevention councils, and other affected community members. The charge for the Coalition was to establish, and now implement, a state-wide strategic plan (see **Table 1**).<sup>1</sup> Strategic priorities were informed by national and local research and published best practices.<sup>2-6</sup>

This article outlines the context, and efforts to date, to implement six community and treatment-related aspects of the strategic plan (other elements of the plan are addressed elsewhere in this issue).

### 1) Establish statewide overdose surveillance mechanisms

Data is essential in guiding intervention efforts. Understanding the scope and breadth of the epidemic

includes examining non-fatal, as well as fatal, overdoses. Until recently, EMS data could not be accessed from a centralized source and ED, hospital, and death data had a two-year lag time.

- Beginning in January 2014, the RI emergency medical system started collecting real-time, electronic data on drug overdose incidents and naloxone administration in the pre-hospital setting. The report form includes pre-hospital naloxone administration data (if administered and by whom).
- In April 2014, HEALTH passed emergency health regulations requiring all hospitals and emergency departments to report any opioid overdose-related events to the health department within 48 hours. The reporting form includes naloxone administration data (if administered and by whom) and whether the patient was referred to treatment or recovery services.<sup>7</sup>
- The Medical Examiner reports all confirmed accidental drug overdose deaths on the 15th of the month for the prior month. The data is posted on the HEALTH website: <http://www.health.ri.gov/data/drugoverdoses/>. The Medical Examiner also provides more detailed updates on accidental drug overdose death data at quarterly Coalition meetings.

**Table 1.** 2011–2016 Injury Prevention Strategic Plan Drug Overdose Prevention and Rescue Recommendations

1. Establish statewide overdose surveillance mechanisms
2. Increase usage and effectiveness of the Prescription Monitoring Program (PMP).
3. Increase access to naloxone training and distribution programs.
4. Increase licensed healthcare worker and institutional responsibility
5. Implement and expand disposal units throughout the state.
6. Support prevention policies that work.
7. Increase general public awareness of drug overdose as a preventable public health problem.
8. Support and affirm people at risk for drug overdose.
9. Increase access to substance abuse treatment.
10. Build state capacity to implement drug overdose prevention and rescue programs.

## 2) Increase access to naloxone training and distribution programs

Naloxone, an opioid antagonist, reverses opioid overdose by blocking the opioid receptors. Bystander use of naloxone began over a decade ago, through the pioneering efforts of physicians in the harm-reduction field. Expanded prescription and distribution of naloxone for bystander use is recognized as a best practice in response to the epidemic of opioid overdose fatalities.<sup>8-10</sup>

As a prescription medication, each state’s prescribing and dispensing guidelines govern naloxone access. HEALTH issued emergency regulations, in March 2014, expanding naloxone access, by authorizing the following: Any licensed prescriber can issue a non-patient-specific order to certain organizations, such as police departments and treatment facilities; naloxone can be prescribed to a family member or friend of an individual at risk of experiencing an opioid-related overdose; and any licensed prescriber may dispense naloxone to family members or others on site, during an office or emergency department visit.<sup>11</sup> These regulations expand providers ability to reach individuals at highest risk of opioid overdose.

- The Miriam Hospital PONI Program (Preventing Overdose and Naloxone Intervention) began in 2006 as a pilot program in collaboration with HEALTH.<sup>12</sup> Since 2012, PONI has trained almost 700 individuals in overdose prevention, recognition and intervention and distributed a corresponding number of naloxone kits at no cost to the client. The program relies on clients to contact the program to report naloxone use and request a refill. To date, 60 clients have reported using naloxone to reverse an opioid overdose.
- Since 2007 PONI has collaborated with the Rhode Island Department of Corrections (RIDOC) to provide overdose prevention training (without naloxone distribution) to inmates prior to release from incarceration. Distribution of naloxone at release has been piloted (see below), but lack of resources to purchase naloxone has been a barrier to implementation.
- In 2011, researchers at Rhode Island and Miriam hospitals launched a pilot program to train inmates approaching release from RIDOC and to dispense naloxone kits upon release. This research effort included creation of “**Staying Alive on the Outside,**” a video geared toward overdose prevention and response immediately following release from incarceration. Results of the study concluded implementation of a naloxone training and distribution program is a feasible component of pre-release training and skills building.<sup>13-14</sup> Participants were able to effectively able to recognize an overdose and administer naloxone, based on pre-post intervention evaluation, including simulating response to an overdose one month post-release from incarceration.
- In 2012, with the leadership of the Rhode Island Medical Society, the Good Samaritan Overdose Prevention law was passed to promote naloxone use by lay responders and

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calling 911 in case of an overdose. The law protects anyone who administers naloxone in good faith from civil or criminal liability. It also protects the victim of overdose, and bystanders who call 911, from prosecution for minor drug charges. Similar legislation has passed in 20 states. Efforts are underway to reauthorize the law (due to sunset in 2015).

- In 2012, Walgreens Pharmacy entered into a **Collaborative Practice Agreement** with Dr. Josiah Rich to distribute naloxone, on a walk-in basis. A Collaborative Practice Agreement allows pharmacists to furnish naloxone without an individual prescription. Along with the medication, pharmacists provide overdose prevention, recognition, and response training. (Also, see elsewhere in this issue).
- Butler Hospital initiated a naloxone program in 2013 for patients treated for opioid dependence. At-risk patients watch an instructional video and receive individual education from physicians, nursing staff, and pharmacists on the safe administration of naloxone. From October 2013 through June 2014, naloxone was distributed in the Partial Hospital Alcohol and Drug Treatment Program to 119 (69% of eligible patients) patients with opioid dependence. The program was expanded to inpatients in April of 2014. Naloxone was

distributed to 45 inpatients (12% of eligible inpatients).

- The RI Disaster Medical Assistance Team and Medical Reserve Corps developed the Naloxone and Overdose Prevention Education Program of Rhode Island (NOPE-RI) in 2013 to address the opioid overdose epidemic. This program recruits, trains, and deploys volunteer medical professionals to educate community members about addiction, overdose prevention, and the use of naloxone. NOPE-RI trainings target the medical community and public safety professionals. NOPE-RI also serves as a clearinghouse for naloxone and overdose prevention educational resources in the state, and supports efforts to expand access to naloxone. [www.nopeRI.org](http://www.nopeRI.org).
- Early 2014 the Department of Behavioral Health, Developmental Disabilities and Hospitals (BHDDH) issued emergency regulations requiring all staff in state-licensed behavioral health organizations to be trained in overdose prevention, recognition and intervention. At least one staff person from each organization is certified as a Trainer, who is responsible for training other staff, who train at-risk patients. Residential and detox facilities are responsible for distributing naloxone to at-risk patients before discharge. BHDDH purchased 500 naloxone kits for provision to uninsured, indigent patients.<sup>15</sup>
- Law enforcement and other non-medical public safety professionals are often first on the scene when 911 is called. NOPE-RI, with Coalition support, created and delivered a training curriculum and toolkit to facilitate engagement with law enforcement agencies. Over 500 law enforcement officers in RI have been trained and many more trainings are planned. The State Police and some municipality police have begun carrying naloxone. [www.nopeRI.org/law.html](http://www.nopeRI.org/law.html).<sup>16</sup>
- Emergency Department distribution of naloxone began in August 2014 (see elsewhere in this issue).

### 3) Implement and expand disposal units throughout the state

In the last 15 years, availability of prescription opioids for pain relief has exponentially expanded. One outcome has been the proliferation of prescription opioids in medicine cabinets, which has contributed to increased non-prescription use. In an effort to curb this access, law enforcement agencies, prevention councils, and municipalities have collaborated to provide safe disposal sites for unused opioids. Many police stations in the state have 24/7 disposal sites. For a complete list, see <http://nopeRI.org/drugdisposal.html>. Another strategy for safe disposal is "Prescription Drug Take Back Days." On April 26, 2014, 45 sites in Rhode Island collected prescription drugs in 36 cities and towns.

### 4-5) Increase general public awareness of drug overdose as a preventable public health problem and support and affirm people who are risk of overdose

The purpose of public awareness campaigns is to: inform the

community regarding the extent and impact of opioid overdose and addiction; educate the public regarding its role in preventing addiction and overdose; and informing affected individuals, family members and loved ones of resources available to them. Reducing stigma associated with the disease of addiction is interwoven in all these efforts. Anchor Recovery Community Centers (<http://www.anchorrecovery.org/>) and Rhode Island Addiction Recovery Efforts (<http://ricares.org/>) are leaders in this effort and have been key in ensuring that addiction treatment and recovery support are integral messaging in all public awareness efforts. Additionally, local media have been present and conscientious in informing the public regarding opioid addiction and overdose.

- Rhode Island Hospital researchers, in collaboration with BHDDH and HEALTH, created and distributed "If you let her sleep it off she might not ever wake up" poster. Walgreens utilized this poster in its efforts to promote naloxone distribution through the Collaborative Practice Agreement.<sup>17</sup>
- Community forums have occurred across the state in 2014 to educate the public about the extent of the opioid overdose and addiction, steps taken by authorities to address the problem and steps that the public can take to protect themselves and their loved ones. These forums have also been an opportunity for the public to give feedback and guidance.<sup>18</sup>
- In collaboration with HEALTH, CVS pharmacy donated three prominent, highway billboards in early 2014. The billboards featured the tagline: "Addiction is a Disease, Treatment is Available, Recovery is Possible."
- HEALTH is developing a communications campaign targeting healthcare providers, first responders and drug users, and their families and friends. HEALTH will host grand rounds (CMEs) for prescribers in fall 2014 on the disease of addiction and safe prescribing practices. Focus groups were held with drug users and their families/friends to develop messaging and placement of a public education campaign on drug overdose awareness and prevention.<sup>19</sup>
- BHDDH, HEALTH and other state leaders recently participated in SAMSHA's 2014 Prescription Abuse Policy Academy. BHDDH and HEALTH have partnered to devise and implement innovative responses to the prescription abuse epidemic, including building on existing public awareness campaigns and ways to improve utilization of the Prescription Drug Monitoring program.

### 6) Increase access to substance abuse treatment

Coalition members recognize that opioid overdose deaths are happening in the context of dramatic increases in prescription opioid addiction. Current efforts to increase access to substance use treatment include:

- BHDDH and The Providence Center are administering a pilot program providing hospital emergency rooms with peer recovery coaches to meet with drug overdose survivors. Recovery coaches train patients on overdose and naloxone

and engage patients in discussions about treatment and recovery services. Recovery coaches are on call all weekend. The program is underway at Kent Hospital, and will expand it to emergency departments statewide.

- BHDDH, HEALTH, and Bridgemark partnered to offer The Physician Consult Program, a program to provide physicians immediate assistance with patients who may be at high risk for misuse of opioid medication. Interested physicians may call 401-781-2700. Also see <http://www.health.state.ri.us/healthrisks/addiction/for/providers/>.
- United Way's 211 is well known throughout the state by people looking for assistance with social service needs. BHDDH, HEALTH and United Way partnered to have 211 as a resource for substance use treatment referrals.
- With the passage of the Affordable Care Act, access to affordable health coverage and Medicaid expansion to low-income adults, access to addiction treatment services has increased considerably. Addiction treatment services can serve as primary prevention in reducing future incidence of overdose events and fatalities.

## CONCLUSION

This crisis has prompted collaboration among state agencies and integration of a broad range of community members. These efforts are ongoing and building. Nonetheless, opioid-overdose fatalities remain a public health crisis. While we are poised to make a considerable impact on the epidemic, adequate resources are a barrier to realizing that potential. A next important step is to work with our state leaders and law makers to recognize the pandemic of addiction as a funding priority.

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# Emergency Department Naloxone Distribution: A Rhode Island Department of Health, Recovery Community, and Emergency Department Partnership to Reduce Opioid Overdose Deaths

ELIZABETH SAMUELS, MD, MPH

## ABSTRACT

In response to increasing rates of opioid overdose deaths in Rhode Island (RI), the RI Department of Health, RI emergency physicians, and Anchor Community Recovery Center designed an emergency department (ED) naloxone distribution and peer-recovery coach program for people at risk of opioid overdose. ED patients at risk for overdose are offered a take home naloxone kit, patient education video, and, when available, an Anchor peer recovery coach to provide recovery support and referral to treatment. In August 2014, the program launched at Kent, Miriam, and Rhode Island Hospital Emergency Departments.

**KEYWORDS:** opioid overdose prevention, naloxone, peer coaching, emergency medicine

Each NRK contains two doses of intranasal naloxone (1mg/ml 2ml luer-lock needleless prefilled syringes), one nasal atomizer, and instructions in English and Spanish on what to do in the event of an opioid overdose and how to use naloxone. Individuals who receive an NRK are shown an educational video<sup>10</sup> and, when available, an Anchor Recovery Community Center recovery coach is consulted to provide patients with support, naloxone education, and referral to addiction treatment. The recovery coaches also follow up with patients 24-48 hours after their ED visit. Coaches are trained, certified, and hired through Anchor Recovery Community Center, a peer-to-peer recovery support organization in RI. They are paid through state funding from the RI Department of Behavioral Healthcare, Developmental Disabilities and Hospitals, another partner in the OPRC. In August, Rhode Island, Miriam, and Kent County Hospitals started ED naloxone distribution and consulting Anchor recovery

## INTRODUCTION

The Rhode Island (RI) Department of Health (HEALTH)'s naloxone emergency regulations released in March 2014 provided new opportunities for naloxone access through direct provider distribution and third party prescribing to family members or friends of an individual at risk for opioid overdose. Community opioid education and naloxone distribution programs have been shown to decrease opioid overdose deaths in Massachusetts<sup>1</sup> as well as Chicago.<sup>2</sup> Nationally, naloxone distribution programs have shown that lay people, including intravenous drug users, can reliably administer naloxone,<sup>3-8</sup> and research evidence has also suggested that these programs are cost effective.<sup>9</sup>

HEALTH's Overdose Prevention and Rescue Coalition (OPRC) identified the ED as an underutilized arena to prevent opioid overdose deaths as RI emergency department (ED) visits for non-fatal opioid overdoses were growing alongside increasing opioid overdose mortalities. Currently, only a few EDs distribute naloxone to patients at risk for opioid overdose. Rhode Island Hospital (RIH) emergency medicine physician members of OPRC collaborated with Lifespan Pharmacy and Anchor Recovery Community Center to finalize a protocol for direct distribution of a naloxone rescue kit (NRK) to patients at risk for opioid overdose (see **Table 1**) paired with overdose prevention education, addiction counseling and referral to treatment.

**Table 1: Patients at Risk for Opioid Overdose**

1. Have suspected substance abuse or non-medical opioid use.
2. Are currently being prescribed methadone or buprenorphine through a prescriber or program.
3. Are receiving an opioid prescription for pain and:
  - a) Given higher-dose (>50 mg morphine equivalent/day).
  - b) Rotated from one opioid to another because of possible incomplete cross tolerance.
  - c) Have poorly controlled COPD, emphysema, asthma, sleep apnea, or respiratory infection where the provider is concerned concurrent opiate use will compromise their respiratory status.
  - d) Have pre-existing renal dysfunction, hepatic disease, cardiac illness.
  - e) Have known or suspected concurrent excessive alcohol use or dependency.
  - f) Concurrent usage of a benzodiazepine or other sedative prescription.
  - g) Suspected poorly controlled depression.
4. Patients who fall into categories listed above and may have difficulty accessing emergency medical services (distance, remoteness).
5. Recent abstinence from use and/or incarceration/release from prison.

coaches to provide needed services to patients presenting with an opioid overdose.

Key steps to program establishment were finding funding for NRK purchase, engagement of community and institutional stakeholders, provider and staff engagement and education, and protocol review and approval by institutional risk management, legal, and pharmacy departments. Moving forward, funding will be the primary obstacle. While prescribed naloxone is billable to insurance, an NRK given in the ED is not reimbursable since the first dose of the medication is not administered in the ED. At RIH, whose ED treats approximately 11 overdoses a week (40-50 a month), the Lifespan leadership chose to cover the cost of the NRKs as a community service. The OPRC is pursuing other avenues of funding, from state or private grants, to allow other hospitals to provide direct naloxone distribution without incurring additional cost.

Provider and staff reception of the program has been generally positive, which is a departure from prior surveys of provider attitudes.<sup>11</sup> This may be due to general attitude change over time, or may reflect a more recent shift related to the recent dramatic rise in opioid overdose mortality in combination with high profile deaths.<sup>12</sup>

**CONCLUSION**

In addition to decreasing deaths to overdose, our program’s ultimate is goal to help make recovery an option for anyone in RI who may need or want it. By bringing together representatives from different state departments, community organizations, and local hospitals, the OPRC designed and implemented a forward-thinking initiative to decrease opioid overdose deaths, create jobs for individuals in the recovery community, and prioritize the health and future wellbeing of people struggling with addiction or at risk for opioid overdose.

**Acknowledgements**

The author would like to acknowledge and thank Dr. David Portelli, Dr. Brian Zink, Kristen Bunnell, PharmD, Dr. Michael Mello, Dr. Jason Hack, Dr. Laura Ruhland, Sarah Bowman, MPH, Michelle McKenzie, Traci Green, PhD, Dr. Gary Bubly, Dr. Ilse Jenouri, Dr. Latha Sivaprasad, Dr. John Murphy, and Kristi Mangiocca for their collaboration and dedication to this project.

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**Disclosures**

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# Response of Colleges to Risky Drinking College Students

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## ABSTRACT

Heavy drinking and related consequences continue to affect college campuses due to fatalities, assaults, serious injuries, and arrests that occur among students. Several approaches aimed at reducing the harm incurred by students and the college communities as a result of heavy drinking are being used with varying success. A review of interventions including educational, individual, and environmental approaches are described, as well as new, promising, strategies. Despite some success, elevated and risky drinking patterns continue. As such, concerns over implementation of evidence-based treatments and areas in need of further study are discussed.

**KEYWORDS:** College, alcohol, heavy drinking, interventions

## INTRODUCTION

Alcohol is the most pervasively misused substance on college campuses.<sup>1</sup> National studies of college students<sup>2</sup> continue to document significant prevalence rates of alcohol consumption (68% consumed alcohol in the past 30 days) and alcohol misuse (40% report having “been drunk” in the past month). Even more concerning are the rates of extremely heavy drinking within the past two weeks: 37% of college students had five or more drinks in a row, 13% had 10 or more, and 5% had 15 or more.<sup>2</sup> The association between heavy drinking in college and alcohol use disorders later in life is well established,<sup>3,4</sup> yet the primary goal for colleges is the need to reduce immediate alcohol-related harm. Alcohol use is linked to sexual aggression and assault, impaired academic performance, vandalism, physical assaults and injuries, motor vehicle crashes and fatalities, and transmission of sexual diseases.<sup>5,6</sup> A large number of students are brought to the attention of their institution following arrests, medical transports, or campus citations after violating alcohol policies.<sup>7,8</sup> As the majority of students consume alcohol,<sup>9</sup> research efforts have continued to evaluate prevention and intervention approaches to reduce consumption and related harms in the college environment. While effective strategies have been identified,<sup>10-12</sup> challenges exist in implementing and maintaining such approaches. This article will present and discuss the research evidence behind various levels of

campus responses, including general prevention efforts, personalized interventions, and environmental strategies.

## General Prevention

At the most primary level, colleges are charged with educating students about campus rules and regulations and the effects of alcohol. The most common approach to educating students is through the implementation of basic awareness and education programs. This type of prevention work on most college campuses is typically delivered at orientation sessions for new students, alcohol awareness weeks and other special events, and, in some instances, instructors infusing alcohol-related facts and issues into regular academic courses.<sup>13</sup> Although this approach has the potential to reach a large number of students at a relatively low per-student cost, this category of prevention has been found ineffective when conducted in isolation<sup>1</sup>; however, further research is needed to investigate the way in which these programs can be used in conjunction with and contribute to the impact of a more comprehensive prevention program.

## Personalized Interventions

As noted, the majority of college students have consumed alcohol within the past semester,<sup>9</sup> therefore colleges typically focus on ways in which to affect current drinkers, using harm reduction models of intervention. The National Institute for Alcohol Abuse and Alcoholism (NIAAA) has identified Tier 1 interventions as those with favorable outcomes among college students in independent evaluations (NIAAA, 2002). Two of the example programs, Brief Alcohol Screening and Intervention for College Students BASICS<sup>14</sup>, and Alcohol Skills Training Program ASTP,<sup>15</sup> are commonly used on college campuses. Both the group ASTP and one-on-one BASICS programs incorporate educating students on basic alcohol information relevant to their experience; building motivation to change drinking; challenging expectancies about alcohol’s effects; correcting misperceptions through normative feedback; providing cognitive-behavioral skills training, including how to monitor daily alcohol consumption and stress management; and developing a tailored plan for reducing alcohol use or harm. Most often, these approaches are used to intervene with college students sanctioned for violating campus alcohol policies. These motivational interventions have shown the ability to reduce alcohol use among heavy drinking college students<sup>16,17,18</sup>,

however, the implementation of such programs can be costly and therefore limits the number of college students who may receive such intervention approaches. Additionally, the support for delivering the interventions with fidelity has become a concern as universities use published evidence-based interventions.<sup>19</sup> The training and supervision needed to implement intervention approaches as they were designed for research is challenging, which has the potential to reduce effective execution of evidence-based treatments.

Given the importance of reaching a large number of students while minimizing financial and clinical burdens within overextended departments, universities have implemented computer and web-based intervention approaches aimed at reducing drinking among heavy drinking students.<sup>12</sup> Students receive personalized normative feedback (PNF) about their own drinking behaviors, which then compares their drinking to normative drinking rates of students on campus. Suggestions also include ways to reduce consumption and minimize harm if the student chooses to make changes. Results have identified students receiving the PNF report have significantly fewer drinking days and significantly less heavy drinking compared to those who do not.<sup>10,12</sup> These findings suggest web-based alcohol interventions with personalized feedback is an effective way to reach large populations of college and university students with minimal cost and personnel effort needed for implementation. Challenges to this approach are decisions about implementation methods and the potential for mandatory participation by various student sub-groups (e.g., first-year students, athletes, Greek Life). More recently, PNF interventions have been extended for Event Specific Prevention (ESP) high-risk and predictable situations, including 21<sup>st</sup> Birthday celebrations and Spring Break.<sup>20,21</sup> Preliminary evidence suggests support for this approach but more research is needed to clarify the potential reach and limitations of this strategy.

### Environmental Strategies

Finally, various strategies seek to reduce consumption and related harms through altering the environment or changing expectations of acceptable behaviors. These strategies include increasing enforcement of the minimum, legal drinking-age laws, implementation and enforcement of other laws to reduce alcohol-impaired driving, restrictions on alcohol outlet density, increased prices and excise taxes on alcoholic beverages, and responsible beverage service policies have also been evaluated as ways in which to curb high risk college student drinking.<sup>22,23,24</sup> These approaches have the potential to be highly effective; however, the challenges of instituting and then evaluating these methods has reduced support for wide-scale implementation. In Rhode Island (RI), the potential implementation of these approaches has the ability to reduce drinking rates at a limited number of colleges, given the relatively small size of the state. As such, making a statewide policy change may be more feasible than in other states. However, the proximity to neighboring states

could undermine those efforts if students have options to circumvent RI laws by obtaining or consuming alcohol in bordering states. Regardless, RI faces the same challenges as other states and communities regarding policy change and implementation of new or adjusted local laws. As a result, at the national level, there have been fewer attempts to reduce drinking and associated harm using these approaches.

In RI, in one study (Common Ground) conducted at the University of Rhode Island, officials reached out to specific constituencies in Narragansett and South Kingstown to implement environmental prevention strategies. This included a public media campaign identifying the addition of greater police enforcement and a cooperating tavern program. There were two phases to the implementation. In Phase 1 of the media campaign, investigators targeted potential student resistance to environmentally focused prevention. This was done through reporting majority student support for the alcohol policy and enforcement initiatives. During Phase 2, students were informed about state laws, university policies, and Common Ground's environmental initiatives. Annual student telephone surveys showed increases in awareness of formal efforts to address student alcohol use, perceived likelihood of apprehension for underage drinking, and perceived consequences for alcohol-impaired driving. When examining the potential impact on reduced drinking and alcohol related incidents, police reports of student incidents in the target community decreased by 27% over the course of the project; however, there were no significant reductions in reported alcohol use or alcohol-impaired driving.<sup>25</sup>

### SUMMARY

Despite decades of research and targeted intervention approaches, high-risk drinking and related consequences continue to be problems on the majority of college campuses. There is good evidence of promising approaches toward reducing alcohol-related harm and the efficacy of interventions, yet the implementation of these approaches on college campuses remains a challenge due to limited resources (e.g., staffing) and execution within individual colleges. Although individual level interventions have been strongly supported in the literature, environmental approaches and the integration of multiple approaches are more challenging. Traditional education programs have consistently had limited success as stand-alone interventions, yet they are often used by colleges to affect large numbers of students. As new intervention approaches are being developed (e.g., texting interventions (short message service (SMS) and web applications) to adapt to the ever changing college student populations, college students remain at high-risk for alcohol-related harm and college campuses must continue the charge to understand drinking behaviors and derive new, effective interventions to reduce adverse consequences and the impact of alcohol on campus.

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Disclosures

The authors have no financial disclosures to report.

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