

# ***AHRQ Healthcare Horizon Scanning System – Potential High-Impact Interventions Report***

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## **Priority Area 14: Substance Abuse**

**Prepared for:**

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## **Statement of Funding and Purpose**

This report incorporates data collected during implementation of the Agency for Healthcare Research and Quality (AHRQ) Healthcare Horizon Scanning System by ECRI Institute under contract to AHRQ, Rockville, MD (Contract No. HHSA290-2010-00006-C). The findings and conclusions in this document are those of the authors, who are responsible for its content, and do not necessarily represent the views of AHRQ. No statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

This report's content should not be construed as either endorsements or rejections of specific interventions. As topics are entered into the System, individual topic profiles are developed for technologies and programs that appear to be close to diffusion into practice in the United States. Those reports are sent to various experts with clinical, health systems, health administration, and/or research backgrounds for comment and opinions about potential for impact. The comments and opinions received are then considered and synthesized by ECRI Institute to identify interventions that experts deemed, through the comment process, to have potential for high impact. Please see the methods section for more details about this process. This report is produced twice annually and topics included may change depending on expert comments received on interventions issued for comment during the preceding 6 months.

A representative from AHRQ served as a Contracting Officer's Technical Representative and provided input during the implementation of the horizon scanning system. AHRQ did not directly participate in horizon scanning, assessing the leads for topics, or providing opinions regarding potential impact of interventions.

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## Preface

The purpose of the AHRQ Healthcare Horizon Scanning System is to conduct horizon scanning of emerging health care technologies and innovations to better inform patient-centered outcomes research investments at AHRQ through the Effective Health Care Program. The Healthcare Horizon Scanning System provides AHRQ a systematic process to identify and monitor emerging technologies and innovations in health care and to create an inventory of interventions that have the highest potential for impact on clinical care, the health care system, patient outcomes, and costs. It will also be a tool for the public to identify and find information on new health care technologies and interventions. Any investigator or funder of research will be able to use the AHRQ Healthcare Horizon Scanning System to select potential topics for research.

The health care technologies and innovations of interest for horizon scanning are those that have yet to diffuse into or become part of established health care practice. These health care interventions are still in the early stages of development or adoption, except in the case of new applications of already-diffused technologies. Consistent with the definitions of health care interventions provided by the National Academy of Medicine (formerly the Institute of Medicine) and the Federal Coordinating Council for Comparative Effectiveness Research, AHRQ is interested in innovations in drugs and biologics, medical devices, screening and diagnostic tests, procedures, services and programs, and care delivery.

Horizon scanning involves two processes. The first is identifying and monitoring new and evolving health care interventions that are purported to or may hold potential to diagnose, treat, or otherwise manage a particular condition or to improve care delivery for a variety of conditions. The second is analyzing the relevant health care context in which these new and evolving interventions exist to understand their potential impact on clinical care, the health care system, patient outcomes, and costs. It is NOT the goal of the AHRQ Healthcare Horizon Scanning System to make predictions on the future use and costs of any health care technology. Rather, the reports will help to inform and guide the planning and prioritization of research resources.

We welcome comments on this Potential High-Impact Interventions report. Send comments by mail to the Task Order Officer named in this report to: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to: [effectivehealthcare@ahrq.hhs.gov](mailto:effectivehealthcare@ahrq.hhs.gov).

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# Executive Summary

## Background

Horizon scanning is an activity undertaken to identify technological and system innovations that could have important impacts or bring about paradigm shifts. In the health care sector, horizon scanning pertains to identification of new (and new uses of existing) pharmaceuticals, medical devices, diagnostic tests and procedures, therapeutic interventions, rehabilitative interventions, behavioral health interventions, and public health and health promotion activities. In early 2010, the Agency for Healthcare Research and Quality (AHRQ) identified the need to establish a national Healthcare Horizon Scanning System to generate information to inform comparative-effectiveness research investments by AHRQ and other interested entities. AHRQ makes those investments in 14 priority areas. For purposes of horizon scanning, AHRQ's interests are broad and encompass drugs, devices, procedures, treatments, screening and diagnostics, therapeutics, surgery, programs, and care delivery innovations that address unmet needs. Thus, we refer to topics identified and tracked in the AHRQ Healthcare Horizon Scanning System generically as "interventions." The AHRQ Healthcare Horizon Scanning System implementation of a systematic horizon scanning protocol (developed between September 1 and November 30, 2010) began on December 1, 2010. The system is intended to identify interventions that purport to address an unmet need and are up to 3 years out on the horizon and then to follow them up to 2 years after initial entry into the health care system. Since that implementation, review of more than 21,000 leads about potential topics has resulted in identification and tracking of about 2,250 topics across the 14 AHRQ priority areas and 1 cross-cutting area; more than 600 topics are being actively tracked in the system.

## Methods

As part of the Healthcare Horizon Scanning System activity, a report on interventions deemed as having potential for high impact on some aspect of health care or the health care system (e.g., patient outcomes, utilization, infrastructure, costs) is aggregated twice a year. Topics eligible for inclusion are those interventions expected to be within 0–3 years of potential diffusion (e.g., in phase III trials or for which some preliminary efficacy data in the target population are available) in the United States or that have just begun diffusing and that have completed an expert feedback loop.

The determination of impact is made using a systematic process that involves compiling information on topics and issuing topic drafts to a small group of various experts (selected topic by topic) to gather their opinions and impressions about potential impact. Those impressions are used to determine potential impact. Information is compiled for expert comment on topics at a granular level (i.e., similar drugs in the same class are read separately), and then topics in the same class of a device, drug, or biologic are aggregated for discussion and impact assessment at a class level for this report. The process uses a topic-specific structured form with text boxes for comments and a scoring system (1 minimal to 4 high) for potential impact in seven parameters. Participants are required to respond to all parameters.

The scores and opinions are then synthesized to discern those topics deemed by experts to have potential for high impact in one or more of the parameters. Experts are drawn from an expanding database ECRI Institute maintains of approximately 170 experts nationwide who were invited and agreed to participate. The experts comprise a range of generalists and specialists in the health care sector whose experience reflects clinical practice, clinical research, health care delivery, health business, health technology assessment, or health facility administration perspectives. Each expert uses the structured form to also disclose any potential intellectual or financial conflicts of interest

(COIs). Perspectives of an expert with a COI are balanced by perspectives of experts without COIs. No more than two experts with a possible COI are considered out of a total of the five to eight experts who are sought to provide comment for each topic. Experts are identified in the system by the perspective they bring (e.g., clinical, research, health systems, health business, health administration, health policy).

The topics included in this report had scores *and/or* supporting rationales at or above the overall average for all topics in this priority area that received comments by experts. Of key importance is that topic scores alone are not the sole criterion for inclusion—experts’ rationales are the main drivers for the designation of potentially high impact. We then associated topics that emerged as having potentially high impact with a further subcategorization of “lower,” “moderate,” or “higher” within the high-impact-potential range. As the Healthcare Horizon Scanning System grows in number of topics on which expert opinions are received and as the development status of the interventions changes, the list of topics designated as having potentially high impact is expected to change over time. This report is being generated twice a year.

For additional details on methods, please refer to the full AHRQ Healthcare Horizon Scanning System Protocol and Operations Manual published on AHRQ’s Effective Health Care Web site.

## Results

The table below lists the two topics for which (1) preliminary phase III data for drugs or programs were available; (2) information was compiled and sent for expert comment before May 8, 2015, in this priority area; and (3) we received five to seven sets of comments from experts between July 1, 2014, and May 18, 2015. (Fifteen topics in this priority area were being tracked in the system as of May 8, 2015). Both topics were designated as having high-impact potential (indicated below with an asterisk) based on experts’ comments and their assessment of potential impact. The material on interventions in this Executive Summary and report is organized alphabetically. Readers are encouraged to read the detailed information on these interventions that follows the Executive Summary.

### Priority Area 14: Substance Abuse

Topic	High-Impact Potential
1. * Evzio for emergency treatment of opioid overdose by nonclinicians	Lower end of the high-impact-potential range
2. * Interactive text messaging program for prevention of hazardous alcohol use	Lower end of the high-impact-potential range

## Discussion

This priority area encompasses interventions for diagnosis, prevention, and treatment of harmful use of legal and illicit drugs. Standards of care for these indications remain stable; as a result, most new interventions in this area focus on repurposing existing treatments, either through novel delivery systems or off-label administration. Topics tracked since the last Potential High-Impact Interventions Report include an intranasal naloxone spray for treating opioid overdose, which recently received U.S. Food and Drug Administration (FDA) fast-track status, and off-label investigations of zonisamide and intranasal insulin for reducing craving and consumption in patients with alcohol use disorders.

Two topics emerged as having high-impact potential in this report period. The first topic, Evzio, is an approved, injectable, naloxone formulation designed for emergency opioid overdose reversal by lay persons. The second topic involves the use of interactive text messaging systems, primarily

targeting younger adult patients, to prevent hazardous alcohol use and encourage responsible alcohol consumption. The addressed indications are doubly concerning public health issues because of the widespread availability and high safety risk of these substances. The U.S. Centers for Disease Control and Prevention recently estimated that hazardous alcohol use alone was responsible for 10% of deaths among adult Americans aged 20–64 years; combined, opioid overdose and hazardous alcohol use are factors in more than 4% of all deaths nationwide each year.

## **Evzio for Emergency Treatment of Opioid Overdose by Nonclinicians**

- **Key Facts:** Fatal opioid overdoses of both prescription and illicit opioids are a mounting public health concern nationwide. Naloxone is an international standard of care for safely and effectively reversing opioid overdoses. When properly employed within a critical window after an opioid overdose, naloxone can reverse the overdose within 3 minutes of administration; unfortunately, its underutilization contributes to preventable deaths. Clinicians and first responders are equipped with and trained to use naloxone—usually in intravenous formulations—in emergency situations, but they are not the first persons to identify and respond to overdose patients. Instead, inexperienced and underequipped nonclinicians, including relatives and social associates of patients, are often the first on the scene. A significant need exists for interventions that can increase access to and effective use of naloxone by these lay persons.

Evzio is a naloxone auto-injector designed for use by nonclinicians; to facilitate lay use, each auto-injector includes an electronic voice instruction system and written instructions printed on the device. Each auto-injector delivers a single 0.4 mg naloxone dose, equal to a typical dose administered by medical professionals to treat opioid overdoses.

FDA reviewed Evzio under its priority review program, based on bioequivalence studies conducted at the agency’s Center for Drug Evaluation and Research. Pharmacology studies demonstrated that Evzio was generally similar to a reference naloxone product in median peak plasma concentration time and half-life, and Evzio had a 15% higher naloxone peak plasma concentration after administration than observed with the reference product. In April 2014, FDA approved Evzio for the emergency treatment of known or suspected opioid overdose, characterized by decreased breathing or heart rate or loss of consciousness.

Evzio launched commercially in August 2014. As of June 2015, Evzio retailed between \$588 and \$619 per carton; each carton contains two single-use auto-injectors and one trainer device. Additionally, Evzio’s manufacturer distributes auto-injectors to first responders through a charitable donation program and to public health groups and low-income patients via reduced pricing agreements.

To aid diffusion, in 2015, a strategic partnership was announced between Kaléo and the Clinton Foundation Health Matters Initiative. Through this partnership, Kaléo will make Evzio available at a discount, close to Federal Supply Schedule pricing, for colleges, universities, public safety organizations, and community organizations.

- **Key Expert Comments:** Experts thought that Evzio has some potential to reduce fatal opioid overdoses. Although experts anticipated high adoption and acceptance among clinicians and patients, several expressed concern that patient adoption could have unintended consequences, such as promoting continued opioid abuse by increasing the perceived safety of a harmful behavior. Some experts also thought that Evzio’s adoption and overall impact could be hindered by product cost, prescription restrictions, and a lack of data detailing Evzio’s efficacy for treating indicated patients.
- **High-Impact Potential:** Lower end of the high-impact-potential range

## Interactive Text Messaging Program for Prevention of Hazardous Alcohol Use

- **Key Facts:** Hazardous alcohol use is directly or indirectly responsible for more than 100,000 deaths annually nationwide, and it places considerable strain on economic and public health resources across all levels of society. Besides the physical effects of excessive alcohol consumption, hazardous alcohol use has several secondary adverse outcomes, including placing patients at higher risk of contracting sexually transmitted diseases and increasing their likelihood of being a victim of injury or violence. An unmet need exists for effective, well-accepted interventions that reduce hazardous alcohol-use frequency, particularly among younger patients.

Interactive text messaging programs use behavioral therapy techniques delivered through short messaging service (SMS) applications to positively influence hazardous alcohol use among at-risk patients. In clinical trials, interactive text messaging programs are well accepted among patients and have demonstrated efficacy for self-reported reductions in hazardous alcohol use. These programs are also relatively inexpensive, easily replicable, and regarded by younger patients as an effective, unobtrusive intervention.

American, Australian, and European researchers have conducted clinical trials investigating variations of interactive text messaging interventions for this indication; the most developed of these is a phase III clinical trial initiated at the University of Pittsburgh (Pittsburgh, PA) and its affiliated medical school. In 2014, university researchers reported results showing limited reductions in binge drinking and alcohol-related emergency department readmission among at-risk patients completing a 12-week intervention.

The university has licensed a version of this intervention, and a commercial product, branded as CaringTXT, has been marketed since February 2015. Commercial clients pay annual licensing fees for CaringTXT, prorated on projected patient populations; end-user patients incur no cost for this intervention, aside from potential text messaging carrier charges. Through June 2015, CaringTXT was in use at multiple locations, including the University of Pittsburgh and the Central Vermont Medical Center (Barre, VT).

- **Key Expert Comments:** Based on published research and diffusion status in January 2015, experts evaluating this intervention concluded that interactive text messaging has some potential to contribute to reduced hazardous alcohol use. Experts noted that this intervention has significant potential to address adverse behaviors among a patient population (mainly mobile phone–using adolescents and young adults) who might be resistant to present standard of care. However, experts were concerned that the program might be effective only for patients already receptive to modifying their alcohol consumption and related behavior, and some experts thought that intervention adoption could also be limited by patients’ access to mobile phones and associated text messaging services. Although experts were encouraged by some available data, they questioned the efficacy of this intervention in untested populations and wanted to see more data evaluating long-term efficacy and effect size before thoroughly endorsing this intervention’s high-impact potential.
- **High-Impact Potential:** Lower end of the high-impact-potential range



# **Substance Abuse Interventions**

# Evzio for Emergency Treatment of Opioid Overdose by Nonclinicians

**Unmet need:** If not treated within 3 hours, opioid overdoses can be fatal; fortunately, most opioid overdoses can be reversed by administering naloxone during this critical period.<sup>1-3</sup> However, many overdoses occur away from stocked health care facilities and in the presence of lay persons who may not have sufficient training in using or access to naloxone. An unmet need exists for interventions that increase access to naloxone, in formulations that can be effectively used by nonclinicians. Evzio, a naloxone delivery device approved in April 2014, may present an effective option to address this need.

**Intervention:** Evzio is a single-use, pocket-sized naloxone auto-injector, intended for emergency treatment of known or suspected opioid overdose. To support layperson use, the auto-injectors have built-in electronic voice instruction systems and written instructions. Each device has a sealed product indicator window; a removable needle safety guard; and the auto-injector, with a 5/8-inch retractable needle.<sup>4,5</sup> The electronic voice instruction system activates when the outer case is removed.<sup>4,6</sup> Evzio also has a two-color LED status light, to indicate whether auto-injectors are ready for use (green) or have been deployed (red).<sup>4</sup>

The auto-injector delivers one 0.4 mg naloxone dose, equal to the minimum recommended dose for treating opioid overdoses.<sup>6,7</sup> Evzio is intended for intramuscular or subcutaneous administration at a patient's outer thigh; for infants, Evzio should be administered while pinching the middle of the outer thigh.<sup>4</sup> Additional Evzio injectors may be administered at 2- to 3-minute intervals, as needed, until medical personnel intervene.<sup>4,6</sup>

Besides the two single-use auto-injectors, the Evzio carton contains a "trainer" device, which has an identical size, shape, and safety guard as functional auto-injectors but lacks a needle and injectable solution. Trainer devices are distinguishable by their color branding (auto-injectors are yellow and purple, trainer devices are black and white), and are rated for 1,000 simulated uses.<sup>8</sup>

**Clinical trials:** U.S. Food and Drug Administration (FDA) priority review for Evzio was based on evaluation of a series of studies conducted by FDA's Center for Drug Evaluation and Research (CDER).<sup>5</sup> CDER scientists reported results from three bioequivalence studies: a clinical pharmacology study, comparing Evzio's naloxone hydrochloride solution to a reference product; a user-experience study with adult and juvenile volunteers; and a safety study, evaluating the effects of Evzio administered to healthy volunteers.

Pharmacology studies demonstrated that Evzio was generally similar to a reference naloxone product (median peak plasma concentration time [ $T_{max}$ ]: Evzio, 0.25 hours; reference, 0.33 hours; half-life: Evzio, 1.28 hours; reference, 1.36 hours), with a 15% higher naloxone peak plasma concentration ( $C_{max}$ ) after administration than observed with the reference product.<sup>5</sup> User experience and safety study results indicated that most untrained volunteers could successfully use Evzio (90.5% of adult volunteers, 73.7% of adolescent volunteers), although 15% of volunteers administered Evzio to the inner thigh. Noting this user error, the manufacturer stated that Evzio's dosage would still effectively reverse opioid overdose events when injected at this location.<sup>5</sup> Reported Evzio administration-related adverse events were dizziness, nausea, anosmia (loss of olfactory function), dysgeusia (altered taste perception), hyperhidrosis (increased perspiration), and hematoma. In the study's comparator arm, CDER noted that volunteers reported nausea, headache, injection site pain, and presyncope (lightheadedness).<sup>5</sup>

**Manufacturer and regulatory status:** Kaléo, Inc. (Richmond, VA), manufactures Evzio.<sup>9</sup> In April 2014, FDA approved Evzio for emergency treatment of known or suspected opioid overdose, characterized by respiratory system depression, central nervous system depression, or both.<sup>6,10</sup> The

FDA approval announcement notes that Evzio can be used by family members and caregivers to treat known or suspected overdoses.<sup>10</sup>

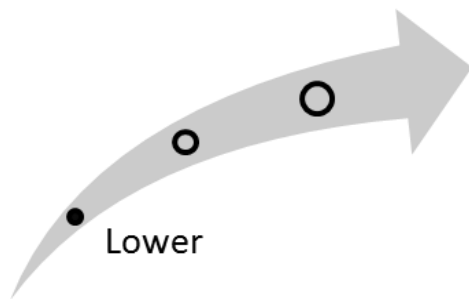
**Diffusion and costs:** Evzio became available by prescription in August 2014. As of June 2015, GoodRx, a U.S.-based, online aggregator of prescription-drug prices, listed retail prices for Evzio ranging from \$588 to \$618 per carton; each carton includes two auto-injectors and one trainer device.<sup>11</sup> To reduce copayment burdens, Kaléo sponsors a patient savings program covering multiple annual Evzio prescriptions.<sup>12</sup>

Kaléo is a private company and, to date, has not released sales data or overall diffusion information for any of its products. In 2014, Kaléo announced Evzio distribution through a charitable donation program, providing eligible law enforcement and first responder applicants with up to 100 Evzio cartons each.<sup>13</sup> Additionally, in 2015, a strategic partnership was announced between Kaléo and the Clinton Foundation Health Matters Initiative. Through this partnership, Kaléo will make Evzio available at a discount, close to Federal Supply Schedule pricing, for colleges, universities, public safety organizations, and community organizations.<sup>14</sup>

## Clinical Pathway at Point of This Intervention

Naloxone—delivered by intravenous or intramuscular injection or intranasally—is the standard of care for reversing opioid overdoses and is recommended by the U.S. Office of the Attorney General and the World Health Organization for this indication.<sup>6,15-17</sup> When naloxone is administered shortly after the onset of an opioid overdose, overdose symptoms can be reversed in as little as 1–3 minutes.<sup>7,18</sup> Evzio is intended as an emergency first-line option for lay persons treating opioid overdoses and could replace or support naloxone administered by first responders.<sup>6</sup>

**Figure 1. Overall high-impact potential: Evzio for emergency treatment of opioid overdose by nonclinicians**



Most experts commenting on this intervention agreed that this intervention addresses a significant unmet need and might be able to reduce opioid overdose–related mortality without dramatically altering health care infrastructure. However, these same experts expressed concerns that Evzio’s cost and prescription-only availability could limit access by patients and caregivers. Experts also critiqued the lack of data indicating the specific number of opioid overdose deaths that Evzio could prevent. Based on this input, our assessment is that this intervention is in the lower end of the high-impact-potential range.

## Results and Discussion of Comments

Six experts, with clinical, health systems administration, health devices, and research backgrounds, provided remarks on this opioid-overdose therapy.<sup>19-24</sup> We have organized the following discussion of expert comments by the parameters on which they commented.

**Unmet need and health outcomes:** Most experts stated that opioid overdose is a significant public health issue and concluded that Evzio has moderate to high potential to address an unmet need by providing an opioid overdose intervention designed for lay use. One health systems expert disagreed with the majority, noting that first responders already use naloxone as a standard of care, limiting Evzio's potential impact.<sup>24</sup> Another dissenting expert, with a research perspective, cited the lack of data demonstrating Evzio's efficacy for treating its intended patient population and suggested that this intervention's true health benefit is somewhat unclear.<sup>20</sup>

**Acceptance and adoption:** The experts generally concluded that Evzio is likely to be accepted and adopted by clinicians, particularly if publicity efforts, such as the Substance Abuse and Mental Health Services Administration's (SAMHSA) prescriber training materials, are successful.<sup>21</sup> However, they offered less positive evaluations of Evzio's adoption potential among patients. Among the reasons cited were the high cost, lack of over-the-counter availability, and hesitance of long-time and high-risk opioid addicts to expose themselves by pursuing treatment. Experts also were concerned that legal restrictions for prescribing medications to caregivers and close associates, rather than directly to patients, could hinder patient acceptance.<sup>21,22,24</sup> One expert also compared Evzio to an investigational intranasal naloxone spray, suggesting that patients might view the pending intervention more favorably than they would Evzio.<sup>21</sup>

**Health care delivery infrastructure and patient management:** Experts' consensus held that Evzio, a portable emergency intervention that does not replace standard treatment, presented minimal disruption to health care delivery infrastructure or patient management. A few experts observed that successful Evzio treatment may cause downstream increases in patient management costs and resource expenditures because patients who survive an overdose will likely require additional health care services as they recover.<sup>22,24</sup>

**Health disparities:** Expert comments on Evzio's impact on health disparities were divided, covering many aspects and potential outcomes without a majority perspective emerging. For example, some experts stated that Evzio's high cost and lack of over-the-counter access would increase disparities.<sup>19,21</sup> Other experts thought that Evzio could reduce health disparities by providing an intervention for patients who normally might not receive adequate treatment for opioid overdoses or opioid dependence.<sup>22,23</sup>

## Interactive Text Messaging Program for Prevention of Hazardous Alcohol Use

**Unmet need:** Hazardous alcohol use is a composite substance abuse indication that includes alcohol consumption during pregnancy, episodic binge drinking, excessive weekly alcohol consumption, and underage drinking.<sup>25-27</sup> This behavior is particularly concentrated among adolescent and young adult Americans and is a strong risk factor for severe outcomes including increased rates of alcohol dependence, morbidity, and mortality.<sup>28-31</sup>

Hazardous alcohol use is a public health issue that has both high patient and per-patient prevalences: Up to 20% of adult Americans have hazardous alcohol use behavior, and most of these patients report several hazardous alcohol use events annually.<sup>32,33</sup> Overall, more than 1.2 billion binge-drinking incidents occur nationwide each year.<sup>34</sup> These incidents also place an excessive burden on the national economy, accounting for about \$223.5 billion in combined annual criminal justice costs, lost productivity, and direct and indirect health care expenses.<sup>35</sup> An unmet need exists for effective, well-tolerated interventions that reduce hazardous alcohol use frequency, particularly for younger patients. Interactive text messaging programs are a group of interventions that present an unobtrusive alternative to standard of care and may cost-effectively contribute to reduced hazardous alcohol use rates among adolescents, young adults, and other patient populations.

**Intervention:** Generally, interactive text messaging programs deliver proven behavioral therapy and motivational interventions via mobile phones. Clinicians or professional staff can identify at-risk patients based on disciplinary proceedings, hospital admission indications, or standardized screening tests. Patients then opt to receive text messages, delivered at regular intervals, to their personal phones. Text messages may provide reminders of healthy alcohol consumption or consequences of hazardous alcohol use, suggest risk-reduction strategies, or assess drinking behavior, allowing patients to engage in self-evaluation.<sup>36-38</sup> Patients interact by reporting recent or long-term hazardous alcohol use and related behaviors via text or secure Web site interface and may also provide feedback regarding intervention tolerability and efficacy. They may also be prompted to provide feedback before or after periods of potential hazardous alcohol use; limited data have shown that this added step may encourage corrective behavior in some patients.<sup>39</sup>

Depending on their design, interactive text messaging programs allow clinicians to provide regular or real-time information and reminders and obtain feedback from patients; patient feedback can hypothetically be used to dictate emergency responses or other professional interventions. Overall, patients are accepting of text messages for this intervention and in some cases find it a better, less intrusive form of communication than traditional mail or phone calls.<sup>40,41</sup>

**Clinical trials:** Completed and ongoing trials have examined forms of this iteration in Australia, Europe, and the United States, with varying success. The majority of completed studies have been unphased or early-phase clinical trials with limited patient interaction components; published data from these trials show varied intervention efficacy, although patients frequently reported high intervention tolerance and acceptability.<sup>36,37</sup>

In July 2014, a group of researchers at the University of Pittsburgh (PA) reported results from a phase III trial of this intervention.<sup>39</sup> Young adult patients (n=765) at risk for hazardous alcohol use were identified based on admission to one of four Pittsburgh-area emergency departments. Across a 12-week study, patients randomly received no text messaging intervention (control group), weekly text messaging assessments (SA group), or twice-weekly text messaging assessments with feedback (SA+F group). Patients in the SA+F group were probed for their planned or recently finished weekend drinking behavior and received real-time positive feedback based on their responses;

patients were encouraged to set goals to reduce overall alcohol consumption and binge drinking events.<sup>39</sup>

Analyses demonstrated that overall, patients in the SA+F group reported fewer binge drinking days, while patients in control and SA groups reported increased numbers of drinking days. Additionally, after 3 months, patients in the SA+F group had significantly greater reductions in total number of patients with any reported binge drinking days (baseline: 79.3%; 3 months: 64.8%; change: -14.5 percentage points) than either SA (baseline: 78.1%; 3 months: 75.0%; change: -3.1 percentage points) or control (baseline: 79.7%; 3 months: 77.7%; change: -2.0 percentage points) groups.<sup>39</sup> Unpublished data from the university also suggest that text messaging intervention efficacy can persist for 6 months or longer after patients conclude using these programs. This finding, if robust, would support this intervention's long-term utility.<sup>42</sup>

**Manufacturer and regulatory status:** Multiple groups in the United States and internationally have developed interactive text-messaging programs for preventing hazardous alcohol use. To date, researchers have published intervention efficacy data based on adult patients in Scotland, Switzerland, and the United States, and we identified related ongoing registered clinical trials in Australia, the United Kingdom, and the United States.<sup>38,43,44</sup> The most mature program, with aforementioned results from a phase III clinical trial, was developed and implemented at the University of Pittsburgh and its affiliated hospital, the University of Pittsburgh Medical Center. This program was subsequently licensed to HealthStratica, LLC (Pittsburgh, PA), and a commercial version, branded as CaringTXT, has been available since February 2015. CaringTXT is marketed to clients at colleges and universities, medical centers, and emergency departments.<sup>42</sup>

FDA does not regulate interactive text-messaging programs such as this because it is not considered to be a medical device app.<sup>45</sup> However, we note that FDA guidelines for these interventions are nonbinding and subject to change.<sup>45</sup>

**Diffusion and costs:** The prevalence of mobile phones and mobile phone usage suggests that text-messaging programs for preventing hazardous alcohol use can easily diffuse, developed by health care facilities or distributed as commercial products. According to a 2011 Pew Research Center study, 83% of adult Americans own a mobile phone, and 73% of these mobile phone owners regularly use text messaging features.<sup>46</sup> Among Americans aged 18–29 years, 95% own a mobile phone and 97% of mobile phone owners regularly send and receive text messages, averaging 109 texts daily.<sup>46</sup>

In addition to ease of diffusion, text-messaging interventions project low end-user costs and relatively inexpensive per-patient costs for intervention providers. According to HealthStratica's CEO, CaringTXT annual licenses cost about \$12,000 to \$18,000 for an average-sized university or college client; we were unable to obtain estimated costs for medical facility users before publishing this report. Across all client types, patients pay for text messages only if the service is not included in their standard mobile phone plans. As of June 2015, CaringTXT was in use by clients including the University of Pittsburgh and the Central Vermont Medical Center (Barre, VT).<sup>46</sup>

Aside from HealthStratica's CaringTXT, our searches found no current commercial text messaging interventions for preventing hazardous alcohol use.

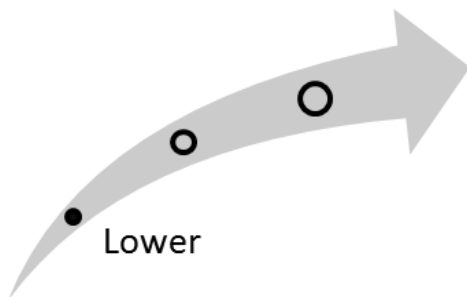
## Clinical Pathway at Point of This Intervention

Alcohol brief interventions (ABIs) are the standard of care for patients in whom hazardous alcohol use has been diagnosed.<sup>47,48</sup> ABI models are primarily designed to modify overall drinking behavior and reduce or eliminate hazardous alcohol use. In these models, clinicians or other care providers first use various diagnostic tests to screen for potential hazardous alcohol use; patients who screen positive are then engaged in several short, one-on-one counseling sessions. During these

sessions, care providers use personalized motivational interviewing techniques to inform patients of potential negative outcomes of hazardous alcohol use and to encourage patients to make healthy future drinking decisions.<sup>48</sup>

ABIs could be used in conjunction with interactive text-messaging programs or potentially could be replaced by this new preventive option. The latter intervention may offer a more amenable treatment route for patients unwilling to participate in face-to-face therapy or for whom geographic, socioeconomic, or other factors make in-person counseling untenable. A text-messaging intervention that effectively reduces binge drinking could present an attractive, scalable option for hospitals and clinics to incorporate into routine screening, brief intervention, and referral to treatment protocols for hazardous-drinking young adults.<sup>48</sup>

**Figure 2. Overall high-impact potential: interactive text-messaging program for prevention of hazardous alcohol use**



Experts commented on this intervention based on published research and diffusion status as of January 2015. At that point, experts concluded that interactive text-messaging programs have limited potential to contribute to reduced hazardous alcohol use. Although they acknowledged that this intervention could particularly address hazardous alcohol use among adolescents and young adults, they thought that it may be effective only among patients already interested in improving their alcohol-use behavior, restricting overall impact. Experts thought that available clinical trial data indicated interactive text-messaging's efficacy but failed to demonstrate broad value for multiple patient populations or long-term efficacy for preventing hazardous alcohol use. Based on this input, our assessment is that this intervention is in the lower end of the high-impact-potential range.

## Results and Discussion of Comments

Six experts, with clinical, health devices, and research backgrounds, provided remarks on this hazardous alcohol use prevention therapy.<sup>49-54</sup> We have organized the following discussion of expert comments by the parameters on which they commented.

**Unmet need and health outcomes:** Experts universally agreed that hazardous alcohol use is a significant public health issue, with an unmet need for well-accepted, effective interventions that can reduce national hazardous alcohol use rates. These experts concluded that interactive text messaging interventions could provide moderate improvements, primarily among adolescents and young adult mobile phone users. However, experts also acknowledged that this patient population does not include all hazardous alcohol use patients, and without additional data indicating broader, sustained efficacy, this intervention's effectiveness is potentially limited.

**Acceptance and adoption:** Five of six experts stated that this intervention could be widely accepted and adopted by clinicians and patients. Several likeminded experts also favorably compared interactive text messaging to standard of care, suggesting that, for receptive patients, interactive text messaging would offer an intervention with less potential embarrassment and

discomfort than traditional ABIs.<sup>49,50,53,54</sup> One dissenting health systems expert argued that acceptance would be low because of an anticipated lack of third-party payer reimbursement and coverage.<sup>52</sup>

**Health care delivery infrastructure and patient management:** Experts' consensus held that as a mobile phone application that will likely be heavily automated, interactive text messaging would not significantly disrupt health care delivery infrastructure or patient management. One research expert and one clinical expert noted that this intervention, if not sufficiently automated, would create additional burden on clinicians and staff because it requires another post-screening treatment step.<sup>51,53</sup>

**Health disparities:** Overall, experts projected that interactive text messaging could positively affect health disparities; these experts primarily noted that many underserved patients could use this intervention because of the broad availability of mobile phones and minimal costs to end-users. Two experts, however, noted that some socioeconomically disadvantaged patients would still be unable to afford mobile phones and texting plans necessary for this intervention or may not sufficiently interact with the health care system to be identified as candidates for this preventative option.<sup>49,52</sup>



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