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

Priority Area 14: Substance Abuse

Prepared for:
Agency for Healthcare Research and Quality
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Contract No. HHSA290201000006C

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December 2013

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. HHSA290201000006C). 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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Financial Disclosure Statement

None of the individuals compiling this information has any affiliations or financial involvement that conflicts with the material presented in this report.

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Suggested citation: ECRI Institute. AHRQ Healthcare Horizon Scanning System Potential High-Impact Interventions: Priority Area 14: Substance Abuse. (Prepared by ECRI Institute under Contract No. HHSA290201000006C.) Rockville, MD: Agency for Healthcare Research and Quality. December 2013. http://effectivehealthcare.ahrq.gov/index.cfm/who-is-involved-in-the-effective-health-care-program1/ahrq-horizon-scanning-system/

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 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.

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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 16,200 leads about potential topics has resulted in identification and tracking of about 1,900 topics across the 14 AHRQ priority areas and 1 cross-cutting area; about 500 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 350 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 seven or 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 two topics for which preliminary phase III data were available for a drug or a pilot was under way for a program; information was compiled and sent for expert comment by October 27, 2013, in this priority area; *and* we received six to eight sets of comments from experts between April 9, 2012, and October 29, 2013. Nine topics in this priority area were being tracked in the system as of October 29, 2013, and two of them were eligible for high-impact consideration at this time. One topic was designated as having high-impact potential (marked with an asterisk in the table below); the other topic, which previously had high-impact potential, was deemed to have no high-impact potential at this time because of recent regulatory setbacks. See the discussion below.

Priority Area 14: Substance Abuse

Topic	High-Impact Potential
1. Buprenorphine implant (Probuphine) for treatment of opioid dependence	No high-impact potential at this time
2. *Community-based opioid overdose prevention program (Project Lazarus)	Moderately high

Discussion

In this priority area, relatively few topics have met criteria for tracking in the horizon scanning system, relative to other, broader priority areas. We are tracking substance-abuse topics that span the areas of alcohol, cocaine, and opioid dependence, as well as novel technologies for detecting substance abuse. No topics on alcohol, cannabis, or cocaine dependence emerged as having high-impact potential. A topic considered this time that had previously been designated as having high impact potential, experienced recent, unexpected delays in regulatory approval that now call into question further development of the drug. The topic, buprenorphine implant (Probuphine™, Titan Pharmaceuticals, Inc., South San Francisco, CA), is a potential long-term treatment for opioid dependence. The implant uses a new delivery system that includes a sublingual buprenorphine-naloxone tablet induction followed by a buprenorphine implant placed under the skin in a physician's office and removed after 6 months. Opioid abuse is one of the most common forms of prescription drug abuse. Opioid dependency management includes medically supervised detoxification and/or opiate replacement therapy. For this condition, pharmacotherapy (e.g.,

buprenorphine, naltrexone) is already available in oral, injectable, and skin-patch forms. Available short-acting treatments for opioid dependence (e.g., naltrexone, methadone, buprenorphine) have limitations, including low adherence to treatment recommendations and medication diversion, which can lead to cravings, withdrawal symptoms, and drug-use relapse. A long-acting formulation might address these issues. The 6-month buprenorphine implant completed phase III trials, one of which was funded by the National Institute on Drug Abuse. The company submitted a new drug application to the U.S. Food and Drug Administration (FDA) in October 2012. In March 2013, an FDA advisory panel voted to recommend approval; however, on April 30, 2013, the company announced that FDA did not approve the drug and issued a complete response letter for Probuphine calling for more data.

According the company's press release, "FDA cannot approve the application in its present form." FDA has requested additional data supporting efficacy, including:

- The ability of Probuphine to provide opioid blockade of relevant doses of agonists
- The effect of higher doses of Probuphine, ideally doses more closely approximating the blood plasma levels associated with sublingual doses of buprenorphine of 12–16 mg/day
- Human-factors testing of the training associated with Probuphine's insertion and removal.

The company has stated that it believes it has met the evidence requirements for approval and is formulating its response and next steps. The company was scheduled to meet with FDA on November 19, 2013, to discuss issues regarding the Probuphine submission. If new trials are needed, resubmission of a new drug application could be delayed for a considerable time. Because of these late-breaking regulatory setbacks, we determined that this topic has no potential for high impact at this time. We are continuing to track the topic in the horizon scanning system to see whether its development continues.

Community-Based Opioid Overdose Prevention Program (Project Lazarus)

- **Key Facts:** Increasing prevalence of prescription opioid use for treating chronic pain has contributed to the rise in opioid dependence, abuse, and overdose. Unfortunately, opioid abuse and overdose remain persistent public health concerns despite implementation of various types of prevention and treatment programs. The limited success of these efforts may be due to the isolated and separate nature of individual efforts within the community. In response to above-average rates of overdose fatalities in Wilkes County, North Carolina, community leaders partnered with the Community Care of North Carolina (CCNC, the State's nonprofit Medicaid management entity) to design and implement a community-based, integrative opioid-overdose prevention program and care model. This program, Project Lazarus, is a secular, nonprofit public health organization with the following central tenets: activating the community and building coalitions, monitoring and conducting epidemiologic surveillance of health data, preventing overdose through medical education and other means, providing community members with rescue medication they can use to reverse overdoses, and evaluating and adjusting project components. Project Lazarus works towards its goals through collaboration with CNCC, the North Carolina Hospital Association, local hospitals and emergency departments, local health departments, primary care providers, law enforcement, and faith-based programs. Preliminary data from the pilot program demonstrated decreased opioid-overdose death rates between 2009 and 2011, as well as fewer overdose fatalities among patients who received the opioid prescription implicated in their overdose from a Wilkes County prescriber. Project Lazarus has been implemented in numerous counties across North Carolina. Statewide expansion efforts are

ongoing with grant support from the Kate B. Reynolds Charitable Trust and the North Carolina Office of Rural Health and Community Care. Statewide and local health data analysis and program evaluation efforts are also ongoing.

- **Key Expert Comments:** Experts commenting on this intervention saw significant potential of the program to improve health outcomes for individuals at risk for opioid overdose. They anticipated widespread adoption and acceptance among both clinicians and patients but noted the substantial collaboration and resources required to establish a fully integrated, community-based program. The experts provided an overall positive assessment of this program, but they expressed a need for additional outcomes data to determine the full magnitude of its potential impact on patient health.
- **Potential for High Impact**: Moderately high

Substance Abuse

Community-Based Opioid Overdose Prevention Program (Project Lazarus)

Unmet need: Increased prescribing of opioids has led to a corresponding increase in abuse, misuse, overdose, and deaths associated with these pharmacologic agents.[1] Illegal use of prescription pain relievers (i.e., opioids) is the second most common form of drug abuse.[2] Current approaches to address this growing epidemic, such as treatment programs and law enforcement, often operate in isolation, independent of one another. Consequently, many of these efforts fall short. Project Lazarus aims to address these issues by offering a multifaceted, community-based approach to preventing opioid overdose. The approach enhances collaboration among many existing programs and resources to purportedly boost efficacy.

Intervention: Project Lazarus was developed in response to a high drug-overdose death rate in Wilkes County, North Carolina.[3] At the onset of the program, the unintentional poisoning rate in the county was four times that of the State as a whole, and the high mortality rate was almost exclusively due to prescription opioid overdose.[3] The primary roles of Project Lazarus are to coordinate overdose-prevention efforts, build community coalitions, develop and implement strategic action plans, train community organizers, and raise awareness of the overdose problem.[3]

Project Lazarus is built around a public health model of community activation for health promotion; it is based on the idea that the collaborative efforts of multiple organizations (e.g., health departments, schools, government agencies, hospitals, primary care practices) are key to a successful public health campaign. The project coordinates and integrates existing community efforts by the medical community, local government, law enforcement, schools, and other organizations to boost efficacy.[3] Based on this model and the premise that overdose deaths are preventable, Project Lazarus encompasses the following five components:[4]

- Activating the community and building coalitions. A central community organizer is responsible for coordinating prevention efforts, minimizing duplication of efforts, and disseminating information to collaborating organizations. All major community-wide decisions are brought to advisory boards. Central to the model, community boards are continuously involved in prevention, program reevaluation, and program adjustments as needed.[3]
- Preventing overdose. A primary program component, in conjunction with the Community Care of North Carolina (CCNC) Chronic Pain Initiative, is teaching primary care providers about outpatient chronic pain management and safe opioid prescribing. Physician education is achieved primarily through a physician toolkit for chronic pain management and in-person meetings. The toolkit contains pain management guidelines, opioid risk-assessment tools, precautions for opioid prescribing, an example of a patient-prescriber agreement, defensive prescription-writing information, patient education materials, and modules for screening, brief intervention, and referral to treatment. Additional overdose prevention efforts include making hospital emergency department policy changes, placing a case manager in the ED to coordinate chronic pain care (including followup care and subspecialty care) for patients with Medicaid or no health insurance, placing specially trained law enforcement officers dedicated to cases involving the criminal diversion of prescription drugs, and using patient-prescriber agreements. Patient-prescriber agreements lock the patient into using a single pharmacy and single prescriber for all opioid treatment.[3] To facilitate this agreement, additional links are put in place to simplify communication between physicians.
- Using rescue medication to reduce overdoses in the community. Project Lazarus makes a naloxone kit available for free to patients and encourages them to tell family and friends

about it.[3] Naloxone is an antidote for opioid overdose.[5] This program component begins when a patient sees a Project Lazarus–trained physician for routine medical care and is identified by the physician as a naloxone priority patient (according to the opioid risk-assessment tools provided in the physician tool kit). Once the patient consents to participating in the program, he or she watches a 20-minute DVD in the physician's office. It covers patient responsibilities in pain management, storage and disposal of opioid medications, recognizing and responding to an opioid overdose, and different options for opioid abuse treatment. The participant then picks up a free naloxone kit at a predetermined Project Lazarus pharmacy.[3]

- Monitoring and conducting epidemiologic surveillance. Sources for monitoring in this program are drawn from four State-run entities: data on emergency department visits for substance abuse and accidental poisonings via North Carolina Disease Event Tracking and Epidemiologic Collection Tool; reporting on outpatient-dispensed controlled substances via the Controlled-Substances Reporting System; data on fatal accidental poisonings from the North Carolina Office of the Chief Medical Examiner; and vital statistics from the North Carolina State Center for Health Statistics.[3]
- Evaluating these components. Because of the multifaceted approach of Project Lazarus, determining the impact of each individual program component is not possible. The program reports that a rigorous evaluation is currently under way, emphasizing the assessment and measurement of potential confounders.[3]

Within this framework, the latter four components operate in a cyclical manner, built around community advisory boards that serve in a central capacity to develop and guide aspects of the intervention as a whole.[4] Recent efforts of the program include installing unwanted-drug drop boxes to allow for free and anonymous disposal of opiate or other medications and ongoing grant-funded expansion efforts across the State [6-8]

Clinical trials: Evaluation and subsequent improvement of Project Lazarus is an ongoing process that involves continually monitoring local health data from various State agencies. In 2011, Project Lazarus' founders published preliminary efficacy data from 2009 and 2010. These pilot data showed a significant reduction in the rate of overdose deaths from 46.6 per 100,000 individuals to 29.0 per 100,000 between 2009 and 2010.[3] Based on unpublished Wilkes County Health Department data, the rate of overdose deaths further decreased to 14.4 deaths per 100,000 individuals by 2011.[9,10] Hospital emergency department visits related to substance abuse and overdose also decreased 15% between 2009 and 2011, despite the State average rising by almost 7%. The program contributed to these declines despite steady opioid prescribing rates in the county.[10] Program data evaluation is ongoing.

Program developers and funding: Project Lazarus is a secular, nonprofit public health organization founded in 2008 by community leaders in Wilkes County, in collaboration with the CCNC Chronic Pain Initiative. The organization collaborates closely with CCNC, the North Carolina Hospital Association, local hospitals and emergency departments, local health departments, primary care doctors, law enforcement, and faith-based programs.

Project Lazarus is funded and supported by the CCNC, Northwest Community Care Network, the Drug Policy Alliance, Qualla Boundary Eastern Band of the Cherokee Indians, Smoky Mountain LME (local management entity), Wilkes Healthy Carolinians Council, and The Governor's Institute.[3] These programs and organizations may have also received material or in-kind support for overdose prevention efforts.[3] Funds for the statewide expansion of Project Lazarus across North Carolina were recently provided by the Kate B. Reynolds Charitable Trust and the

North Carolina Office of Rural Health and Community Care. A $2.6 million grant was provided to fund a 2-year, statewide expansion effort.[11]

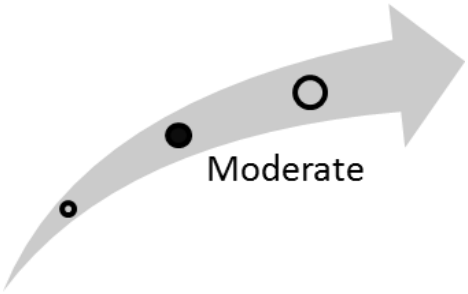
Project Lazarus costs include naloxone purchase, data evaluation, educational initiatives, travel, overhead, and salaries for its employees.[3] However, multiple organizations contribute resources such as staff time and in-kind donations on an ongoing basis, the exact monetary value of which is unknown.

Diffusion: Project Lazarus was created in 2008 in Wilkes County, NC.[12] The program reports that by 2010, 70% of Wilkes County prescribers were registered with the State's prescription-drug monitoring program as compared with the 26% statewide average.[12] During its first several years, Project Lazarus expanded to 30 counties in North Carolina, and received backing from the State Medical Board.[13] Diffusion across the State has continued in recent years. In April 2013, Project Lazarus received a $2.6 million grant to support statewide expansion to all 100 counties. The program's founders also report diffusion is occurring in New Mexico, Ohio, Virginia, and Maine.[9]

Current Approach to Care

Many existing programs seek to prevent opioid abuse and overdose through educational programs designed to teach preventative measures to medical providers, community organizations, or patients and community members. For patients requiring chronic opioids for pain management or help with opioid dependence, treatment interventions may include opioid detoxification, opioid replacement therapies (i.e., methadone or buprenorphine maintenance therapy), or other substance abuse treatment programs.

Figure 1. Overall high-impact potential: community-based opioid overdose prevention program (Project Lazarus)



Most experts commenting on this intervention agreed on the significant unmet need associated with the challenging public health issues of prescription opioid abuse and overdose. The majority of experts indicated that this program has moderate to significant potential to improve patient health outcomes and noted the potential demands on infrastructure to implement an integrated, community-based care model. Although experts overall commented positively on this program, some noted that their enthusiasm for the model was tempered by the preliminary nature of the efficacy data. Based on this input, our assessment is that this intervention has moderate high-impact potential.

Results and Discussion of Comments

Six experts, with clinical, research, health devices, and health systems backgrounds, offered perspectives on this community-based opioid overdose prevention program.[14-19] We have organized the following discussion of expert comments by the parameters on which they commented.

Unmet need and health outcomes: Overall, opioid dependence, abuse, and overdose represents a moderate to significant unmet need, the experts thought. Several experts with research or health

systems background acknowledged the preliminary nature of the overdose prevention efficacy data, but the majority indicated that the program has a moderate to significant potential to improve patient outcomes. A clinical expert indicated that the data were impressive for a community-based intervention intended to address a major public health problem.

Acceptance and adoption: Most experts anticipated widespread adoption of this program by clinicians and patients. One expert wondered whether added training for physicians might be an initial barrier or whether patients would hesitate to acknowledge substance abuse. Overall, experts felt that the positive data and program performance indicated strong acceptance and adoption potential.

Health care delivery infrastructure and patient management: Development and implementation of a community-wide program could moderately disrupt health care delivery infrastructure and patient management, several experts indicated, but they differed in their reasoning. One clinical expert thought this program could ease demand by significantly reducing ED visits and hospitalizations for overdose. But two other experts cited increased strain on infrastructure from the challenges and resource requirements of a collaborative and comprehensive community-based effort. Conversely, minimal disruptive potential was seen by a few experts, who noted that much of the overall treatment structure would remain in place and that the intervention could largely proceed within the context of the existing care environment and structure.

Health disparities: The majority of experts believe that this intervention is likely to have moderate potential to lessen health disparities by delivering care and support to a typically underserved patient population. However, an expert with a research background suggested that certain patients (i.e., poor or illiterate) may be unaware of the program or unwilling to participate, thereby widening health disparities for these individuals.

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