

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

Priority Area 14: Substance Abuse

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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. 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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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 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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Contents

Executive Summary	ES-1
Background.....	ES-1
Methods	ES-1
Results.....	ES-2
Discussion.....	ES-2
Nicotine and Opioid Dependence Interventions	1
Interactive Text Messaging Program (Text2Quit) for Smoking Cessation	2
Long-Acting Pharmacotherapy for Opioid Dependence	5
References	8
Figures	
Figure 1. Overall high-impact potential: interactive text messaging program (Text2Quit) for smoking cessation	3
Figure 2. Overall high-impact potential: long-acting pharmacotherapy for opioid dependence	6

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 identifying 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 7 years out on the horizon and then to follow them for up to 2 years after initial entry into the health care system. Since that implementation, review of more than 15,000 leads about potential topics has resulted in identification and tracking of about 1,600 topics across the 14 AHRQ priority areas and 1 cross-cutting area; about 950 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 annually. Topics eligible for inclusion are those interventions expected to be within 0–4 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 potential high-impact 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 potential 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 (1) preliminary phase III data were available for drugs, or a pilot was under way for a program; (2) information was compiled by September 21, 2012, in this priority area; *and* (3) we received six to eight sets of comments from experts between October 13, 2011, and October 26, 2012. (Fifteen topics in this priority area were being tracked in the system as of October 26, 2012.) We present two summaries on two topics (indicated below by an asterisk) that emerged as having potential high impact on the basis of experts’ comments and their assessment of potential impact. The material on interventions in this Executive Summary and report is organized alphabetically by disease state. Readers are encouraged to read the detailed information on each intervention that follows the Executive Summary.

Priority Area 14: Substance Abuse

Topic	High-Impact Potential
1. * Buprenorphine implant (Probuphine) for treatment of opioid dependence	Moderately high
2. * Interactive text message program (Text2Quit) for smoking cessation	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. Of those that we entered into the system and tracked, we have dropped out several because their development did not progress over 2 years of tracking or because expert comment processes deemed them to have low or no potential for high impact. For this report, topics that emerged as higher impact focused on treatments for opioid and nicotine dependence. No topics on alcohol, cannabis, or cocaine dependence emerged as having potential for high impact.

Interactive Text Messaging Program (Text2Quit) for Smoking Cessation

- **Key Facts:** Although many smokers have attempted to quit, successful cessation rates remain extremely low. To address the need for more effective cessation tools, Voxiva, Inc., and The George Washington University School of Public Health and Health Services (both

of Washington, DC) created the Text2Quit program. It is a novel, interactive, text-messaging platform that is intended to improve the success of smokers' quit attempts. The theory underlying the use of a texting platform is based on studies that have shown that (unidirectional, noninteractive) text-based smoking-cessation programs have resulted in an approximate doubling of abstinence rates. The program is intended to be user-interactive and delivers customized education content based on the user's own quit date, which he or she enters into the system. Once a user has signed up for the program, he or she receives personalized education text messages over the course of 4 months and can play games to fight off cravings, set weekly pledges to remain smoke-free, receive information on prescription or over-the-counter cessation aids (e.g., nicotine-replacement therapy), and supply data that the system uses to monitor progress and track goals. If users need additional motivation when they are having a craving or a relapse, they are able to text in for support. After a user signs up for the free program, he or she fills out a personal profile that covers information such as number of cigarettes smoked per day, personal triggers for smoking, preferred pharmacological support, and anticipated quit date. After the profile has been created, the user has access to the text platform, emails, and a Web portal, although the program can be accessed and used through the text interface alone. Combined, the portals allow participants to update their profiles and monitor their progress before and after their quit dates. The program has been launched in the United States, and a small pilot trial has been completed. A larger trial is planned.

- **Key Expert Comments:** Because of the high prevalence of smoking and its associated morbidity and mortality, experts strongly agreed that the unmet need for effective smoking-cessation interventions is important, but they were divided in their opinions of whether this particular program would meet that need, citing the need for additional data from larger trials. Experts agreed that this text messaging platform could be easily incorporated into the health care system and has the potential (if adopted and proven effective) to reduce health care costs and improve access to smoking-cessation tools for marginalized populations.
- **Potential for High Impact:** Moderately high

Long-Acting Pharmacotherapy for Opioid Dependency

- **Key Facts:** Opioid abuse is one of the most common forms of prescription drug abuse. Opioid dependency management includes medically supervised detoxification and 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 within the patient population, including low adherence to treatment recommendations and medication diversion, which can lead to cravings, withdrawal symptoms, and drug-use relapse. Long-acting formulations of these pharmacotherapies might address these issues. One long-acting version of currently used pharmacotherapy (buprenorphine) has been developed for treating opioid dependence. Implanted buprenorphine (ProbuphineTM, Titan Pharmaceuticals, Inc., South San Francisco, CA) is under study to address the unmet need of low adherence to opioid-addiction therapy. Titan Pharmaceuticals has developed a new delivery system for the drug, made up of 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. The buprenorphine implant is in two phase III trials, one of which is funded by the National Institute on Drug Abuse. The

company filed a new drug application with the U.S. Food and Drug Administration in late October 2012 requesting priority review status.

- **Key Expert Comments:** Overall, experts commenting on this topic viewed the unmet need for opioid-addiction treatment as moderately important, noting that some medications are available for this purpose, although adherence is an important issue. They viewed this intervention as having some ability to meet the need for improved patient adherence to treatment. However, they believe that questions remain about how much additional benefit this intervention would offer over currently approved therapies, especially because the newer intervention requires a shift from at-home oral medication to the clinical treatment setting and might have higher upfront costs.
- **Potential for High Impact:** Moderately high

Nicotine and Opioid Dependence Interventions

Interactive Text Messaging Program (Text2Quit) for Smoking Cessation

Although about 70% of all smokers have attempted to quit at least once and up to 44% try to quit annually, only 5% of those who attempt to quit without assistance achieve abstinence for an extended period of time.¹ An unmet need exists for interventions that can improve smokers' chances of success when they try to quit.

The Text2Quit program (Voxiva, Inc., in conjunction with The George Washington University School of Public Health and Health Services, both of Washington, DC) is a novel, interactive, text-messaging platform that is intended to improve the success of smokers' quit attempts.² The program was created by the developers who created Text4Baby, a text-based platform for maternal and infant health information that has become a widely used mobile health service in the United States since its launch in 2010.^{2,3} The theory underlying the use of a texting platform is based on studies that have shown that (unidirectional, noninteractive) text-based smoking-cessation programs have resulted in an approximate doubling of abstinence rates.²

According to its developers, Text2Quit is intended to be user-interactive and delivers customized educational content based on the user's own quit date, which he or she enters into the system.² Once a user has signed up for the program, he or she receives personalized education text messages over the course of 4 months and can play games to fight off cravings, set weekly pledges to remain smoke-free, receive information on prescription or over-the-counter cessation aids (e.g., nicotine replacement therapy), and supply data that the system uses to monitor progress and track goals.^{2,3} If users are having cravings or have relapsed and need additional motivation, they are able to text in for support.⁴

The program is free to users, who can sign up for the program through the Text2Quit Web site. Additionally, the program's developers are positioning it to be offered through employers, health plans, and public health departments.^{2,3}

As a user signs up for the program, he or she fills out a personal profile that covers information such as number of cigarettes smoked per day, personal triggers for smoking, preferred pharmacological support, and anticipated quit date.³ After the profile has been created, the user has access to the text platform, emails, and a Web portal, although the program can be accessed and used through the text interface alone.³ Combined, the portals allow participants to update their profiles and monitor their progress before and after their quit dates.³

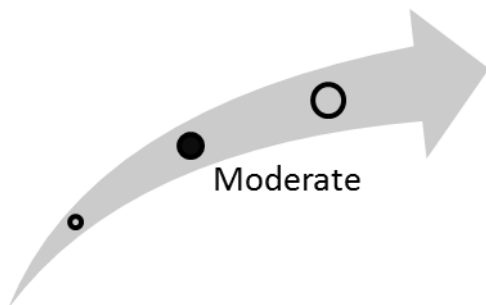
The Text2Quit program was launched in the United States in June 2011.² In results of a 4-week pilot test of the intervention with 23 participants who were smokers, the study authors reported that 14.3% of the participants quit smoking at 4 weeks and that the "majority of users reported liking the program, reading most/all of the texts, and replying to the texts."⁴ Although no clinical trials investigating the program's efficacy are registered at the National Clinical Trials database, the program's developers state that they are conducting a randomized, controlled trial that will investigate the Text2Quit program combined with the Smokefree.gov program in the experimental arm and the Smokefree.gov program alone in the control arm.⁵ The trial is expected to enroll 500 participants and to gather followup cessation data at 6 weeks and 3, 7, and 12 months.⁵

Clinical Pathway at Point of This Intervention

According to the U.S. Public Health Service, guidelines for smoking cessation recommend drug therapy (e.g., bupropion, varenicline) and all forms of nicotine replacement therapy (e.g., chewing gum, inhaler, nasal spray, lozenges, patch) as first-line treatments for tobacco dependence.⁶ Current standard of care also recommends using nonpharmacologic interventions (e.g., behavior therapy,

exercise) in conjunction with drug and nicotine replacement therapy.⁷ The Text2Quit program is being positioned as an adjunctive intervention to these therapies to improve a patient's chances of successfully quitting.

Figure 1. Overall high-impact potential: interactive text messaging program (Text2Quit) for smoking cessation



Experts commenting on Text2Quit strongly agreed that the unmet need for effective smoking-cessation interventions is important, but were divided in their opinions of whether this particular program would meet that need, citing a need for additional data from larger trials. Experts agreed that this text messaging platform could be easily incorporated into the health care system and has the potential (if proven effective) to reduce health care costs and improve access to smoking-cessation tools for marginalized populations. Based on this input, our overall assessment is that this intervention is in the moderate potential high-impact range.

Results and Discussion of Comments

Seven experts, with research, clinical, or health systems backgrounds, offered their perspectives on the Text2Quit program.⁸⁻¹⁴ In general, experts strongly agreed that the unmet need for interventions that will improve smoking-cessation rates is very important, citing the large population of smokers in the United States, the morbidity and mortality associated with smoking, gaps in access to care, and the inadequacy of current treatments. However, experts were less certain about whether this intervention will be efficacious. On one hand, some experts commented that data collected on the intervention to date are not particularly strong, stating that the 14.3% quit rate is not particularly impressive and that long-term efficacy and outcomes data are not yet available. On the other hand, some experts suggested that the quit rate seen in trials suggests the program's potential to improve smoking-cessation rates, and one expert, speaking from a clinical perspective, stated that "any reduction in smoking should be a welcome addition, considering the vast unmet need."¹⁴

Some experts suggested that this intervention may have particular implications for health disparities, in that it may offer a free intervention to patients who are underinsured or may not otherwise have access to smoking-cessation interventions and that smoking rates tend to be higher in populations of lower income. Other experts disagreed, suggesting that this intervention—which requires access to a cell phone and a text messaging data plan, along with a certain literacy level—may worsen disparities.

Experts generally agreed that this intervention would be widely accepted by both physicians and patients and could be easily incorporated into the current health care system as an adjunct to available pharmacotherapies and other programs for smoking cessation. However, a couple of experts raised questions about the role of the patient's physician and how he or she would fit into this program, which exists outside the realm of the physician-patient relationship.

In terms of cost, most experts thought that if the program were successful in improving smoking-cessation rates, some of the long-term costs associated with treating smoking-related medical programs would be avoided. Most experts agreed that for the patient, this intervention is extremely affordable, especially when compared with other smoking-cessation tools (e.g., pharmacotherapy).

Long-Acting Pharmacotherapy for Opioid Dependence

Short-acting treatments for opioid dependence (e.g., naltrexone, methadone, buprenorphine) are associated with limitations including low patient adherence to treatment recommendations and medication diversion, either of which can lead to cravings, withdrawal symptoms, and drug-use relapse.¹⁵ Long-acting formulations of these pharmacotherapies might address the unmet need and problems of low adherence and medication diversion because the drugs' effects may last for several weeks. A novel, long-acting version of currently used pharmacotherapy (buprenorphine [ProbuphineTM]) has been developed for treating opioid dependence. Titan Pharmaceuticals has developed a new delivery system for the drug, made up of a sublingual buprenorphine-naloxone tablet induction, followed by implantation of Probuphine.

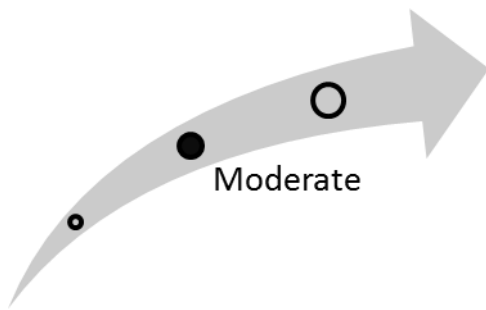
Buprenorphine is a partial opioid agonist that is known to reduce opioid cravings and is U.S. Food and Drug Administration (FDA)-approved in other formulations (i.e., sublingual tablet, film formulations) for treating opioid dependence.^{15,16} Buprenorphine falls into the Schedule III drug class under the Controlled Substances Act of 1970.¹⁷ Titan Pharmaceuticals, Inc. (South San Francisco, CA), recently developed a new subcutaneous implant delivery system for buprenorphine.¹⁶ According to the manufacturer, the system consists of a polymer rod that releases a sustained level of buprenorphine for up to 6 months.¹⁸ The rod is implanted under the patient's skin, typically in the upper arm, during an office-based procedure. It is removed at the end of the 6-month period.^{16,19}

A phase III trial of the implant was recently completed. In a July 2011 press release, the manufacturer stated that data from the phase III, placebo- and active-drug-controlled confirmatory trial of 287 patients with opioid addiction demonstrated superiority of the implant over placebo in opioid-negative urine screens over the 24-week treatment period.²⁰ In an August 2011 press release, the company stated that additional results from the phase III confirmatory study suggested that treatment with the implant significantly improved the global severity of opioid dependence ($p=0.0003$) and overall patient improvement ($p=0.0002$) versus placebo, as assessed by clinicians. The company further asserted that additional data analyses confirmed the implant's noninferiority to the approved combination drug buprenorphine and naloxone (Suboxone[®]).²¹ A February 2012 press release announced additional positive data from a re-treatment trial of patients who had previously completed a full 6 months of treatment in the phase III trial program and announced the manufacturer's plan to submit a new drug application (NDA) to FDA.²² The manufacturer announced filing the NDA October 29, 2012, and requested a priority review designation from FDA.²³

Clinical Pathway at Point of This Intervention

According to American Psychiatric Association (APA) guidelines, patients with opioid dependence should adhere to one of the following treatment regimens: (1) substituting the opioid with methadone or buprenorphine, followed by a gradual taper; (2) abruptly discontinuing the opioid and using clonidine to suppress withdrawal symptoms; or (3) detoxifying and using clonidine-naltrexone.²⁴ The long-acting pharmacotherapy formulations described in this report would compete with shorter-acting oral, sublingual, injectable, or patch-delivered therapies. Nonpharmacologic interventions for opioid dependence, such as behavior therapy and counseling, are expected to remain as complementary interventions.

Figure 2. Overall high-impact potential: long-acting pharmacotherapy for opioid dependence



Overall, experts commenting on this topic viewed the unmet need for opioid-addiction treatment as moderate because some medications are available, although patient adherence to treatment is an important issue. They viewed these interventions as having a moderately high ability to improve adherence. However, they believe that questions remain about how much additional benefit this intervention offers over other approved therapies, especially because the newer intervention requires a shift from at-home oral medication to the clinical treatment setting and might have higher upfront costs. Based on this input, our overall assessment is that this intervention is in the moderate potential high-impact range.

Results and Discussion of Comments

Seven experts, with clinical, research, or health systems backgrounds, offered their perspectives on the buprenorphine implant.²⁵⁻³¹

Experts generally agreed that opioid-dependence therapies that offer improved patient adherence to treatment recommendations represent an answer to a moderately important unmet need, especially in light of low treatment adherence in this population and the devastating effects that opioid dependence has on patients, their families, and employers. However, this view was tempered by the understanding that other treatments for opioid addiction are already available.

Most of these experts agreed that the theories underlying the proposed intervention are sound, based on the historical success of other buprenorphine formulations in treating opioid addiction. Most also expressed confidence in this intervention's potential to improve health outcomes in terms of opioid and methadone addiction, adherence, and medication diversion. However, experts shared the belief that the benefits would prove to be only incremental over available treatments, especially considering that newer interventions are likely to be more expensive than current treatments.

Experts were divided about how this intervention would affect patient management and treatment models. For the experts who compared the buprenorphine implant delivery system to other buprenorphine formulations, consensus was that this would not dramatically change current treatment models. For those who compared this formulation to inpatient methadone treatment, a large shift in care from rehabilitation clinics to physicians' offices, a reduction in the number of followup visits, and reduced use of complementary behavioral interventions were expected.

Experts offered different perspectives about potential patient and clinical acceptance. Regarding the buprenorphine implant, experts thought that clinicians would be more accepting than patients, with only a small amount of provider reluctance because of the intervention's "invasive" nature and possible implant side effects. In terms of patient acceptance, some experts thought that patients would appreciate the convenience of an implant, but most experts expected that patients would resist an implant because it is technically a "surgical" intervention. Alternatively, some experts opined that patients would appreciate the discretion of use and the elimination of methadone clinic visits. Experts believe that this intervention would have higher upfront costs compared with

currently available therapies' initial costs, but some stated that if adherence is improved and the need for daily medication is obviated, some of these costs might be offset over the long term.

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