

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

Priority Area 04: Dementia (Including Alzheimer's Disease)

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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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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 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 report. Send comments by mail to the Task Order Officer named in this report to: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to: 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 24,500 leads about potential topics has resulted in identification and tracking of about 2,400 topics across the 14 AHRQ priority areas and 1 cross-cutting area; about 750 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 195 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).

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 associate 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

Since the time of the last Potential High-Impact Interventions report in June 2015, no topics in this priority area met the Horizon Scanning System Protocol’s requirements for preparing detailed profiles and obtaining experts’ comments. Thus, no topics were eligible for consideration or inclusion in this Potential High-Impact Interventions report. Twenty-one topics in this priority area were being tracked in the system as of November 30, 2015. We discuss below our general observations of five years of horizon scanning for innovative treatments in this priority area.

Discussion

Dementia is a general term encompassing several disorders marked by mental function and cognitive skills. Alzheimer’s disease (AD) accounts for up to 70% of all dementia cases worldwide. Experts estimate that more than 5 million Americans aged 65 years or older have AD; without significant therapeutic developments, this population may approach 14 million by 2050. No approved disease-modifying agents are available for treating AD, and standard therapy is limited to managing symptoms. Investigators in basic science and clinical research domains continue to probe model systems and patient pools in an effort to elucidate the mechanisms underlying AD and other dementias. Recent results suggest that certain AD medications may be more effective if administered at prodromal stages often unexamined in clinical trials. This finding implies that both “how” and “when” patients are treated are key to any successful therapies for AD and other potentially reversible dementias. By extension, researchers may incorporate this perspective to generate new treatments and revive previously discarded investigational therapies.

Although evidence confirming the efficacy of anti-amyloidogenic (amyloid-beta aggregation-targeting) pharmacotherapies has dominated headlines, several recent developments in identifying other AD-associated biological factors and advancing and standardizing diagnostic timelines are also notable. For example, in November 2015, Gothenburg University researchers announced a new reference method for measuring spinal amyloid-beta levels, enabling diagnosis of probable AD decades before standard symptoms appear. Later that month, a research team from California’s Gladstone Institutes also reported the first link between AD and decreased levels of the DNA-repairing protein breast cancer 1 (BRCA1); this result confirmed that BRCA1 is required for normal learning and memory and implicates a new putative therapeutic target.

We identified four new topics under this priority area since the June 2015 Potential High-Impact Interventions report. Two new topics, aducanumab and ALZT-OP1, are investigational medications

targeting amyloid beta aggregation in an effort to prevent or halt AD-associated cognitive decline. Aducanumab is an intravenously infused human monoclonal antibody that preferentially binds parenchymal amyloid peptide, targeting specific aggregated amyloid beta deposits. These deposits are associated with AD progression, and researchers have observed them posthumously and in patients who have advanced probable AD. Biogen (Cambridge, MA) has advanced this candidate drug to phase III testing, despite initial analysis of intermediate doses used in phase I testing showing no clinical efficacy. ALZT-OP1 is a combination of inhaled cromolyn, an FDA-approved asthma medication recently shown to have antiamyloidogenic properties, and oral ibuprofen, a common nonsteroidal anti-inflammatory drug. ALZT-OP1's developers hypothesize that administering these drugs in concert will relieve symptoms of early probable AD and may also delay disease progression; the developers have initiated a pivotal phase III trial in collaboration with clinicians at Massachusetts General Hospital (Boston). The AHRQ Healthcare Horizon Scanning System is monitoring the progress of both of these topics and will update their status accordingly.

AVP-786 is one of two investigational therapies—AVP-923, originally identified by the system in 2012 and marketed for other indications as Nuedexta, is the second drug—combining the widely-used cough suppressant dextromethorphan with quinidine, a class Ia antiarrhythmic drug, for treating AD-related agitation. AVP-786's mechanism of action is unknown, but developers designed the drug using deuterium-modified dextromethorphan in an attempt to produce a long-lasting, well-tolerated medication capable of effectively reducing physical or verbal outbursts often observed among patients who have probable AD. The developer is conducting phase III trials with AVP-786 and AVP-923 for this indication, and we continue to track associated developments and clinical data releases.

The fourth new topic is Cognivue®, a noninvasive computer-based system intended for early detection of age-related cognitive decline and dementia; we identified this topic and generated a detailed profile, but did not receive sufficient expert comments in time for inclusion during this reporting cycle. This system, developed by Cerebral Assessment Systems, Inc. (Pittsford, NY), presents laboratory-validated psychophysics tests for use in a clinician's office. Testing takes about 10 minutes, and the system generates rapid, easily interpreted assessments of patients' cognitive performance. In June 2015, FDA designated Cognivue as a Class II medical device and granted de novo clearance as a first-in-class computerized cognitive assessment aid, indicated for use as an adjunctive tool for evaluating perceptual and memory function in patients between age 55 and 95 years old. Cerebral Assessment Systems has begun developing commercial Cognivue units, with plans to distribute up to 10,000 devices by the end of 2016.

Overall, the complexity and unresolved questions within this priority area have correlated with fewer tracked interventions relative to several other AHRQ priority areas. However, we continue to monitor multiple information sources to update developments in this clinical area as they arise.