Priority Area 06: Developmental Delays, ADHD, and Autism

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Contract No. HHSA290201000006C

Prepared by:
ECRI Institute
5200 Butler Pike
Plymouth Meeting, PA 19462

December 2012
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.

Disclaimer Regarding 508-Compliance
Individuals using assistive technology may not be able to fully access information in this report. For assistance contact info@ahrq.gov.

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.

Public Domain Notice
This document is in the public domain and may be used and reprinted without special permission. Citation of the source is appreciated.

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.

Carolyn M. Clancy, M.D.  
Director  
Agency for Healthcare Research and Quality  

Jean Slutsky, P.A., M.S.P.H.  
Director, Center for Outcomes and Evidence  
Agency for Healthcare Research and Quality  

Elise Berliner, Ph.D.  
Task Order Officer  
Center for Outcomes and Evidence  
Agency for Healthcare Research and Quality
Contents

Background ........................................................................................................................................1

Methods........................................................................................................................................1

Results ..........................................................................................................................................2

Discussion ....................................................................................................................................2
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

Results

No topics were eligible for high impact consideration in this priority area (among the 13 topics
being tracked as of October 26, 2012), for which (1) preliminary phase III data for drugs, phase II or
III data for devices and procedures, or some human data for off-label uses or programs were
available; (2) information was compiled by September 21, 2012, in this priority area; and (3) we
received six to nine sets of comments from experts by October 26, 2012.

Discussion

Although we performed intensive scanning for interventions and innovations in this priority
area, we found a paucity of leads and innovations. The dearth of topics on diagnosis, treatment, and
services for developmental disorders including attention-deficit hyperactivity disorder and autism
spectrum disorders (ASDs) implies a lack of progress in basic understanding of these disorders and
how to diagnose and treat them.

ASDs, also sometimes referred to as pervasive developmental disorders, are a wide continuum
of associated cognitive and neurobehavioral disorders that have three core-defining features:
impairments in socialization, impairments in verbal and nonverbal communication, and restricted
and repetitive patterns of behavior. While all children with ASDs demonstrate similar core features,
the severity of impairment, age of onset, and associations with other disorders (e.g., mental
retardation, specific language delay, epilepsy) vary considerably. ASD diagnoses have been
increasing, and recent estimates place the prevalence at about 1% of children in the United States,
with occurrence in males being more than four times as common as occurrence in females. Experts
think that the earlier a definitive diagnosis can be established and the earlier that intervention can
begin, the better chance an affected child has of improving cognitive development and social
functioning. Early-intervention treatment includes behavior and communication therapies (including
applied behavior analysis), technology aids aimed at improving social interaction, medication, and
dietary and other complementary therapies.

The ASD clinical pathway is complicated, however, by the subjective nature of diagnosis,
which relies on clinician assessment of behavior and parents’ perceptions and responses to clinician
inquiries and questionnaires. The constellation and severity of ASD symptoms vary in each
individual, ranging from verbal and nonverbal communication difficulties to social interactional and
emotional skill deficiencies to repetitive behaviors. Researchers have been unable to pinpoint one or
even a few predispositions or causal factors for autism development. As a result, the path to
developing effective pharmacotherapies and behavior or communication therapies addressing the underlying pathogenesis of disease remains a major hurdle. Compounding these issues are parents’ perceptions about appropriate treatment for their children and frustration about the lack of effective treatment options after a diagnosis has been made.

Nonetheless, early diagnosis of autism is of high interest for early intervention, and researchers have been studying functional magnetic resonance imaging (fMRI) to differentiate ASDs from psychiatric conditions that sometimes present similar symptoms. Through fMRI, researchers have detected consistent abnormalities in cortical gray and white matter volume in subjects with ASDs. One imaging study observed age-related changes in gray matter volume and cortical thickness associated with symptom severity in children with autism. However, additional observational studies are needed before relying on expensive diagnostic tools such as fMRI for ASD diagnosis, and experts commenting on this topic thought use of fMRI could increase health disparities. This technology has been archived from the horizon scanning system after ECRI Institute updated the topic and received additional expert comments expressing skepticism over fMRI’s ability to distinguish ASD from other mental health disorders or psychiatric conditions.

Other technologies for ASDs that were tracked and archived from the horizon scanning system after expert comment processes include hyperbaric oxygen therapy (HBOT), interactive robotic dolls, and weighted blankets. These are examples of interventions intended to mitigate symptoms of the disorders or to aid behavior treatment programs. At this time, none is deemed as having potential for high impact because most experts commenting on these interventions view them as complementary and unlikely to have as significant an impact on autism treatment as interventions that address the underlying causes of ASDs.

One intervention that generated controversy among clinicians is HBOT. The underlying theory of using HBOT to treat ASDs suggests that some children with ASDs have decreased cerebral perfusion, evidence of neuroinflammation, and increased markers of oxidative stress. Some studies showing that HBOT has some anti-inflammatory effects and appears to reduce oxidative stress prompted interest in HBOT for treating symptoms of autism. Significant clinical opposition to its use exists because of its potential risks to children and a paucity of data demonstrating a benefit. Nonetheless, some parents are willing to pay out of pocket, especially if other treatments have yielded little success.

Researchers have also explored some existing pharmacotherapies (e.g., antianxiety medications, antipsychotic medications, nutritional medications [methylated form of vitamin B12], selective serotonin and norepinephrine reuptake inhibitors, stimulants, tricyclic antidepressants) for ASD treatment. However, the efficacy of these treatments is unpredictable and varies widely, and when they do work, they address only certain symptoms in some patients. They also subject patients to risks of adverse events, some of which could be serious. Several drugs in phase I and II development are aimed at targeting social symptoms of ASD and are being tracked in the horizon scanning system. They are ineligible for consideration in the High Impact report at this time because they have not yet produced phase III data. Intranasal oxytocin (Syntocinon®, Novartis International AG, Basel, Switzerland; investigated by Montefiore Medical Center, Bronx, NY) might improve social function, reduce repetitive behavior, and improve social and emotional processing by influencing activity in several regions of the brain, most notably the amygdala. This drug is being investigated for off-label use. STX209 (arbaclofen, Seaside Therapeutics, Cambridge, MA) is a gamma aminobutyric acid (GABA)- B agonist that is intended to improve synaptic functioning by regulating glutamate and increasing GABA, an inhibitory neurotransmitter that, researchers suggest, could be out of balance in children with ASD.

Addressing an underlying theory about the pathogenesis of autism, companies are developing new pharmacotherapies (e.g., enzyme therapies) intended to enhance protein digestion; however,
these drugs are in preclinical or very early stages of clinical development. These drugs will probably face intense scrutiny, considering the challenges of accurately diagnosing autism and the absence of adequate insight about the disorder’s causes and progression.