GAIN Act and the STAAR Act, and for a third bill that would limit the agricultural use of medically important antibiotics. The policy statement also offered recommendations detailing how public and private organizations can work together to combat resistance and promote the development of new drugs.

"We are dealing with rampant antibiotic resistance throughout the United States and the world, but we don't have an effective federal effort," explained Brad Spellberg, MD, assistant professor of medicine at the David Geffen School of Medicine at the University of California, Los Angeles, who helped develop the policy statement. To help fund the coordinated effort described in the statement, the IDSA supports the establishment of an Antibiotic Innovation and Conservation fee that would be added to the wholesale price of antibiotics; 75% of the proceeds would be used to fund new antibiotic development and 25% would be allocated for antibiotic stewardship programs.

"The time for action is now," Spellberg said. □

IOM Sets Out "Gold Standard" Practices for Creating Guidelines, Systematic Reviews

Bridget M. Kuehn

GUIDELINES AND SYSTEMATIC REviews must adhere to tougher standards for transparency and objectivity and adopt consistent formats to make them trustworthy and accessible for both clinicians and patients, according to a pair of reports released by the Institute of Medicine (IOM) in March.

The reports were commissioned by Congress as part of the Medicare Improvement for Patients and Providers Act of 2008 to set standards for clinical practice guidelines (http://www.iom.edu/Reports/2011/Clinical-Practice-Guidelines-We-Can-Trust.aspx) and systematic reviews (http://www.iom.edu/Activities/Quality/SystemReviewCER.aspx). Physicians and other health care decision makers often rely on guidelines and systematic reviews to provide authoritative information on care options and to synthesize data from the literature. However, such efforts vary greatly in how they are conducted and how their results are reported. Each of the 2 reports sets out "gold standard" practices for creation of these tools and aims to establish more consistency in the way different organizations present them.

A key element of both reports is an emphasis on making clinical practice guidelines relevant to and accessible by consumers. Alfred O. Berg, MD, MPH, chair of the IOM Committee on Standards for Systematic Reviews of Comparative Effectiveness Research and professor of family medicine at the University of Washington in Seattle, explained that his committee and the Committee on Standards for Developing Trustworthy Clinical Practice Guidelines are looking to the future of health care, in which reform efforts emphasize greater consumer involvement in both health care research and clinical decision making.

"The whole health care system is moving toward more consumer centeredness and patient involvement," Berg said. "We are trying to bring that into the research process."

GUIDANCE ON GUIDELINES

The number of organizations creating clinical practice guidelines has grown substantially since the early 1990s, and so has the number of guidelines produced, according to the IOM report on clinical guidelines. In fact, there are now about 2700 guidelines in the Agency for Healthcare Research and Quality's National Guideline Clearinghouse and at least 6800 guidelines in the database of the Guidelines International Network.

The impact on care of this growing number of guidelines is not yet clear. Some studies suggest that guidelines can help to reduce inappropriate practice variation, speed the translation of research into practice, and improve care safety and

New reports from the Institute of Medicine call for the development of clinical practice guidelines and systematic reviews that physicians and patients can use together to make clinical decisions.

quality, the report stated. But many stakeholders have questioned the quality and reliability of such guidelines. Concerns have focused, for example, on the quality of the evidence base of many guidelines, a lack of transparency in the creation of guidelines, and the handling of conflicts of interest to prevent bias. Restoring trust was a key goal for the IOM panel that drafted the report on clinical practice guidelines, according to its chair, Sheldon Greenfield, MD, professor of medicine at the University of California–Irvine.

To achieve this, the panel outlined 8 recommendations for creating trustworthy guidelines. The first calls for a detailed and publicly available description of the process for creating the guideline. The second sets out a detailed approach to managing conflicts of interest, suggesting that whenever possible, individuals who create the guideline should be free from conflicts of interest, but when such individuals are necessary, they should make up a minority of the panel. Panel chairs, it recommends, should be free from conflicts. The recommendation also broadens the definition of conflict of interest beyond just those with financial relationships with commercial interests to include subspecialists, who derive a substantial portion of their income from certain types of care. Greenfield acknowledged that this expansion may cause consternation among some organizations.

The report also calls for greater public involvement in the process of clinical guideline development, particularly in the initial and final stages of the process, said Greenfield. He explained that patients should be involved in helping to select the questions to be addressed and that the final deliberations and decisions about what to recommend should be public. He noted that this is particularly important when a lack of evidence on a particular issue requires that a guideline be based on expert consensus.

"Use the best evidence you can, but when evidence is lacking, you must persuade each other in an open forum," Greenfield said.

Additionally, the committee recommended the adoption of a standard format for guidelines to allow them to be easily incorporated into electronic clinical support systems, which could make recommendations immediately available to clinicians during patient encounters.

To help the public and health care decision makers identify trustworthy guidelines, the committee recommended that the US Department of Health and Human Services identify which guidelines are of high quality.

The recommendation to create such a system for vetting guidelines was welcomed by Sandy Zelman Lewis, PhD, who helps coordinate the development of the American College of Chest Physicians (ACCP) guidelines and clinical statements. The ACCP already meets many of the standards set out by the IOM. Lewis noted that many guidelines don't meet the same rigorous standards, but there hasn't been a mechanism to alert the public to differences in quality.

"Physicians were trusting things that sometimes didn't meet minimum standards for rigor," she said.

Ian T. Nathanson, MD, chair of the committee that oversees the creation of guidelines at ACCP, also applauded this recommendation, noting that patients are becoming more sophisticated about finding information and discussing it with their physician. He said having a source where both physicians and patients can access high-quality recommendations "will force clinicians to be as current as they can be, and to be on guard to make sure they are getting information that is vetted."

But many organizations developing guidelines will face challenges in following the recommendations. One challenge may be the expense and resources needed to create guidelines meeting these standards. Nathanson said that some organizations that feel they can't meet the standards may no longer create guidelines, while Lewis suggested that organizations may choose to pool resources.

"It's hard to know how it will impact the number of guidelines developed, but I'm sure it will improve the quality of the guidelines produced," she said.

REVIEWING THE REVIEW PROCESS

The companion report on improving systematic reviews sets a similarly high bar.

The report notes that the quality of systematic reviews varies widely and that some are very poorly done. Yet readers may have a hard time assessing the quality of a systematic review because its methods may not be well explained or documented. Sometimes the methods themselves are questionable. Additionally, varying strategies for assessing and laying out the evidence also can make reviews difficult to use.

To improve the quality and usability of systematic reviews in the United States, the IOM report establishes 21 standards on everything from selecting the questions the review will answer to analyzing and synthesizing the gathered data. The committee acknowledges that it will be a "daunting challenge" for producers of guidelines to meet the standards and notes that few systematic reviews do now.

"The standards will be especially valuable for systematic reviews [SRs] of high-stakes clinical questions with broad population impact, where the use of public funds to get the right answer justifies careful attention to the rigor with which the SR is conducted," the report notes.

Berg explained that even if some systematic reviews are not be able to meet every standard, it's important for groups to consider each standard and to disclose their rationale for choosing not to follow certain ones.

"We can't be reassuring that if you cut any corners you will be safe," he said. "But if a group can be transparent about what they did, users can look under the hood and see where the strengths and weakness are."

The initial reaction to the exacting standards set by the report was positive. "This is a great way to standardize what makes a systematic review rigorous," said Roberta Sherer, PhD, associate director for the US Cochrane Center. She noted that the committee incorporated the best practices of many of the existing groups conducting such reviews, including the Cochrane Center and the Agency for Healthcare Quality and Research.

Similar to its companion report, this report emphasizes patient involvement in the process, especially during the selection of questions. Berg emphasized that this is crucial to providing the answers patients are looking for. For example, he noted that much prostate cancer research has focused on mortality, but patients' top concerns are sexual potency and urinary continence. "You won't come up with those [concerns] as end points unless you include patients," he said.

The report also provides detailed recommendations for dealing with the more technical aspects of review. For example, Berg noted that the panel carefully assessed ways to minimize the impact of a bias toward publishing positive results in the scientific literature. To counteract this, the report suggests including unpublished evidence, such as that submitted to the FDA.

Sherer said that most of the larger groups conducting systematic reviews are likely to have policies similar to those recommended in the report on dealing with conflicts of interest and assembling the team creating the report, and should not have difficulties implementing such recommendations. She noted that the recommendations related to more technical issues may have a greater impact on individuals conducting systematic reviews. For example, in the field of vision research, she noted that some reviews have used only one database to find relevant studies, or don't have independent extraction of the data, or rely on only one individual to extract the data. "We have to be aware of the points where we can introduce bias into the review," she said.

Finally, the report calls for more research on systematic reviews. The committee suggested that the new Patient-Centered Outcomes Research Institute (PCORI), created as part of health care reform, may have an important role in implementing such a research agenda and ensuring that comparative effectiveness research is included in systematic reviews.

Berg, who serves on the methodology committee for PCORI, said both reports may help PCORI set its agenda and make recommendations.

"We hope [release of the reports] is a useful milestone that stimulates more discussion and useful research," said Berg. □

Researchers in Canada Call for Policy to Mandate Single-Embryo Transfer in IVF

Rebecca Voelker

RESEARCHERS IN CANADA HAVE come out in support of mandatory single-embryo transfer during in vitro fertilization (IVF) after their recent study showed that such a restriction would prevent deaths and severe complications associated with multiple gestations from IVF.

Investigators reviewed records from the neonatal intensive care unit (NICU) at the Royal Victoria Hospital in Montreal, Quebec, to determine how many infants admitted from 2005 to 2007 were from IVF-related multiple births and whether that proportion changed over a 10-year period. They also tracked the infants' complications and medical interventions they received.

During the 2-year period, 17% of all NICU admissions—82 infants from 44 multiple gestations—resulted from some form of assisted reproductive technology. Of the 82, 75 were twins or triplets whose mothers used IVF to become pregnant. Among the 75 infants, 6 died and 5 developed severe intraventricular hemorrhages; there were 5 cases of bronchopulmonary dysplasia and 4 infants with severe retinopathy of prematurity that required retinal surgery.

The study also showed that in 1996, about 10% of infants from multiple gestations were born as a result of IVF pregnancies. By 2005, that figure had risen to about 21%.

Studies indicate that in women with a good prognosis, transferring multiple embryos during a cycle increases multiple deliveries without substantially improving live birth rates (http://www.cdc.gov/art/). The investigators noted, however, the idea of having "two babies for the price of one" is appealing to couples who want to pay for the fewest number of costly attempts, and who also are often emotionally drained and willing to accept the higher risks of multiple gestations.

Using data from the Royal Victoria Hospital records and the Canadian Assisted Reproduction Technologies Register's 2005 report, the researchers calculated that a single-embryo transfer policy throughout Canada would prevent 30 to 40 deaths, about 35 severe intracranial hemorrhages, and about 16 retinal surgeries.

The policy restriction also would reduce the use of assisted ventilation in Canadian NICUs by 5424 to 7299 patient-days and overall NICU care by 35 219 to 42 488 patient-days. Cost savings would total about $40 million annually.

"The estimated costs across Canada and other countries in the developed world are of such magnitude that our governments must take a responsible approach to stop the ongoing epidemic of iatrogenic multiple pregnancies," the researchers wrote in their *Journal of Pediatrics* study, which was published online April 14 (http://tinyurl.com/3n5mg94). □