Institute of Medicine calls for savvier vaccine strategy

As the vaccine campaign against the H1N1 swine flu ramped up last year, experts across government agencies scrambled to get safety testing and monitoring systems running smoothly. In the US, the jumble of data all funneled through one place: the National Vaccine Program Office (NVPO).

The 13-person office coordinated ten monitoring systems, bringing together a hodgepodge of state and federal agencies, academic institutions, health insurance providers and professional organizations.

But the big part this little office played in the pandemic is an anomaly. The NVPO is underfunded and lacks the clout it needs to coordinate day-to-day vaccine operations, such as helping to prioritize research and assessing the safety of childhood vaccines, according to a report released in mid-December by the US Institute of Medicine called the 'Priorities for the National Vaccine Plan'. The draft report, due to be finalized in early spring, recommends the first updates to the country's vaccine strategy since 1994.

Currently, vaccine safety testing, research and delivery occur through a maze of US agencies, including the Food and Drug Administration, the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH) and dozens of other public and private entities, including vaccine manufacturers. The NVPO has the potential to coordinate all of these players, but it needs more money and authority, according to the report.

The response of the NVPO to the pandemic shows that it can do the job, says Edgar Marcuse, a vaccine researcher at the University of Washington in Seattle and a member of the committee that put together the report. "That kind of coordination needs to be extended to the immunization issues we deal with every day," he says.

In addition to recommending a centralized role for the NVPO, the committee urged more funding for vaccine safety research, pointing out that although the NIH is charged with studying vaccine safety, the committee's analyses showed that the agency has issued relatively few grants in the area. Moreover, the office in charge of safety at the CDC has operated on a flat budget since 2004, while the number of childhood vaccines has increased. "The committee really had no specific concerns about the safety of currently licensed US vaccines but felt that the growth and funding of the safety system has not kept pace with the growth of the vaccine research and production system," says Marcuse.

The committee also called for a transparent and systematic assessment of priorities for vaccine safety research, coordinated by the NVPO, along with an assessment of research priorities for new vaccines. In addition, the committee also called for strengthening the vaccine delivery system, particularly to underserved populations, and—given public concerns about vaccine safety—a strengthened communication strategy.

Such recommendations have gained particular urgency as the H1N1 pandemic revealed weaknesses in coordination among regulatory and research agencies and vaccine manufacturers. For instance, European regulatory agencies, unlike US regulators, were poised to quickly approve adjuvants in their pandemic flu vaccine (*Nat. Med.* **15**, 984–988; 2009).

"Many of the recommendations of the report will resonate positively as being good ideas" to the agencies involved, says Charles Helms, an infectious disease expert at the University of Iowa and a former head of the National Vaccine Advisory Committee, which advises the NVPO on vaccine issues. But he cautions that, to be implemented, the vaccine plan will need strong support from the Secretary of Health and Human Services, Kathleen Sebelius, who oversees many of the agencies that work with vaccines.

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For cost effectiveness, real data trumps trial results

As healthcare systems look to save cash, many are turning to cost-effectiveness analyses that show which drugs make the most economical sense. But current methods for comparing the returns on medications might be trickier than previously thought, according to new research.

In a UK study, randomized clinical trials (RCTs) did not hold up to actual clinical practice in determining cost effectiveness (*PLoS Med.* **6**, e1000194; 2009). In particular, researchers compared nonsteroidal anti-inflammatory drugs (NSAIDs), which carry a risk of gastrointestinal side effects, to more expensive Cox-2 inhibitors that do not have the same side effect.

Though Cox-2 inhibitors include the now-banned Vioxx, which has shown a risk of heart complications, data from the UK's General Practice Research Database (GPRD)—an anonymous repository of general practitioners' medical records, including demographic information, prescriptions and clinical events—showed the drug's true price has been underestimated. Randomized clinical trials found that switching patients from NSAIDS to Cox-2 inhibitors, for the sake of avoiding an adverse gastrointestinal event, cost an average $18,000 per person. When researchers used information from the GPRD, however, the cost of switching to Cox-2 inhibitors skyrocketed to $104,000 per person.

The comparison shows that even when a drug doesn't have years of clinical practice data behind it, there needs to be better evaluation of tested and targeted populations, says Tjeerd-Pieter van Staa, one of the study's authors. "This adds another piece to the evaluation of a drug when it enters the market," he suggests.

Van Staa also notes that guidelines by the UK's National Institute for Health and Clinical Excellence (NICE)—which conducts drug evaluation for the country's National Health Service—do not distinguish the analyses needed for cost effectiveness, instead relying heavily on randomized trials.

According to Carole Longson, director of the Centre for Health Technology Evaluation at NICE, the new study highlights "the need to be cautious in taking randomized control trial data and accepting it at face value, without scrutiny of the applicability of the trial population to the population likely to receive the medicine in routine practice."

Alan Garber, an American health economist, said the US can also derive lessons from the study findings. The US lacks a repository of information similar to the UK's GPRD and may need to invest in one. "It's all a matter of implementation, and this study demonstrates a need for much better monitoring of how we treat and how we administer these kinds of medications," Garber says.

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