BY MICHAEL E. PICHICHERO, M.D.

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Consider Vaccine Cost-Effectiveness

I believe the time has come to consider cost-effectiveness when deciding which vaccines the government—that's your tax dollars—will pay for.

At its October meeting, the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention made a paradoxical decision: The committee gave a "permissive" recommendation for use of Merck's quadrivalent human papillomavirus (HPV) vaccine (Gardasil) in males aged 9-26 years, but then voted for coverage of the vaccine under the federal Vaccines for Children (VFC) program, which provides free vaccine to children up through 18 years of age who fall into certain need categories. The program covers approximately 48% of all U.S. children.

A permissive recommendation generally indicates that the vaccine is safe and effective but not cost effective. Permissive recommendations usually are not voted into the VFC program. Although the permissive recommendation still awaits approval by the CDC's director, ACIP's vote for VFC coverage is binding, so it is now official. We will have to wait and see what insurance companies do with the dichotomous signal.

A decade ago, ACIP rarely discussed cost when making its vaccine use recommendations. Now, cost-effectiveness analyses are routine. At the October ACIP meeting, Harrell Chesson, Ph.D., of the CDC, presented data from six studies—four published, two unpublished—demonstrating wide variation in cost per quality-adjusted life year (QALY) estimates for use of Gardasil in adolescent and young adult men, depending in large part on the vaccination status of the female population. In general, he showed that as coverage of Gardasil among females increases, the cost per QALY gained by male vaccination decreases.

Use of the vaccine in males is aimed primarily at preventing warts caused by HPV serotypes 6 and 11. The rates of penile and head/neck cancer caused by the cervical cancer HPV serotypes 16 and 18 are miniscule and do not even factor into the cost calculation. Prevention of transmission of HPV-16 and -18 to females through sexual contact is also a goal of the vaccine, but if it's already being routinely offered to females, the data suggest that there's very little additional gain costwise from giving it to males.

Indeed, Dr. Chesson concluded, "In most scenarios, adding male vaccination to female-only vaccination is not the most cost-effective use of public health resources. Improving vaccination coverage of females is likely to be a more effective—and cost-effective—strategy to reduce the overall burden of HPV-associated conditions."

As readers who follow this column and my other writings know, I am a strong proponent of vaccines. In fact, I serve on the advisory boards for both Merck & Co. and GlaxoSmithKline, which manufactures the bivalent HPV vaccine Cervarix. But in an era where we're debating how to provide even basic health insurance for uninsured Americans, I am becoming concerned about whether our country can afford every vaccine for every person.

I'm looking ahead to other vaccines in the very near pipeline. In December we're likely to see approval of the 13-valent pneumococcal conjugate vaccine for the U.S. market. That vaccine is expected to cost more than the current PCV7 (Prevnar), thus raising the overall costs of routine immunization when the switch is made to the new vaccine. Beyond that we will need to provide catch-up vaccination as well for kids who already received PCV7 in order to provide protection against the newly emerging, virulent, and multidrug-resistant serotype 19A, which is included in PCV13 but not PCV7. This new "superbug" causes fatal sepsis, meningitis, and pneumonia. How can ACIP not vote that into VFC as well?

On the heels of PCV13, there are two new meningococcal conjugate vaccines awaiting licensure: GSK's *Haemophilus influenzae* type b (Hib)–*Neisseria meningitidis* serogroups C (MenC) and Y (MenY)–tetanus toxoid combination, and Novartis's MenACWY-CRM (Menveo). The Hib-MenCY-TT conjugate is likely to be licensed for infants at 2, 4, and 6 months of age, with a booster at 15-18 months. Menveo, which will compete with Menactra, is expected to first be licensed for use in adolescents, then toddlers, then infants. These vaccines also prevent a significant amount of serious and potentially fatal disease.

Although competition usually lowers cost in the marketplace, the same phenomenon generally isn't seen when new vaccine competitors enter the market. Rather, the major companies with competing vaccines make combination products with ingredients that differ from others so that staying within their family of products is more convenient than switching between companies.

Moreover, companies also provide price advantages to physicians through national buying groups that provide bigger discounts to those who purchase vaccines within their own family of products. This impacts any price reduction that might occur with brand competition.

So where should we draw the line? At one point or another, ACIP may have to say the government can't afford to pay for vaccines that do not have a strong cost-benefit argument behind them. Yes, the alternative is a two-tiered system where those who can afford the vaccine can get it, and those who can't, don't. ACIP has tried to avoid that scenario in the past, but I fear it won't be able to do so much longer. ■

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Pediatric Oseltamivir Stockpile Drained as H1N1 Deaths Rise

BY BETSY BATES

In the face of a rising number of pediatric deaths from pandemic influenza A(H1N1) virus, the federal government has drained the Strategic National Stockpile of its remaining 234,000 doses of pediatric-strength oseltamivir, Dr. Thomas R. Frieden, director of the Centers for Disease Control and Prevention, said at a press briefing.

He reported that 19 children died of laboratory-confirmed influenza during the 1-week period between Oct. 23 and Oct. 30, bringing the total of pediatric deaths to 114. More than two-thirds of those cases were in children with underlying conditions, but the remainder were in healthy children, Dr. Frieden said.

Serious H1N1-related illness and deaths also are rising in young and middle-aged adults, following the unusual pattern of illness of this influenza strain. Adults over age 65 represent just 10% of deaths from H1N1 influenza, compared with 90% of deaths in an outbreak of seasonal influenza.

Children and young adults have been particularly hard-hit in the early weeks of the autumn H1N1 surge.

"There is a certain rhythm of flu spread in a community where we see first an increase in the number of cases, generally first in children and then in older people, then an increase in hospitalizations … and then, tragically, deaths. We are expecting, sadly, to see an increasing number of deaths [in the coming weeks and months]," Dr. Frieden said.

Several urgent steps are being taken to increase the supply of antiviral medication available to treat children who show serious signs of illness, he said.

The emergency release of stockpiled pediatric oseltamivir (Tamiflu) follows an initial transfer of 300,000 doses on Oct. 1.

Additionally, the government is working closely with commercial pharmacy chains to supplement reserves by compounding adult doses into liquid, pediatric-strength oseltamivir.

"Please don't try this at home. This is something that should be done by a professional pharmacist," Dr. Frieden said at the briefing.

He also called attention to new survey data showing that among people with underlying medical conditions such as asthma, heart or lung disease, and pregnancy, just half with flu symptoms have sought medical care.

He stressed that people with such conditions should see their health care providers right away.

At the other end of the spectrum, a large number of otherwise healthy people with mild flu symptoms may be crowding emergency rooms unnecessarily. In most individuals who do not fall into high-risk categories, H1N1 influenza produces a mild illness that can be treated at home.

People at high risk should also be prioritized to receive the 26.6 million doses of vaccine currently available, said Dr. Frieden, who released a chart explaining which type of vaccine can be received by which group.

He went on to debunk the belief that health care workers should not receive the intranasal form of the H1N1 vaccine, emphasizing that it is an attenuated, cold-adapted vaccine that is safe and will not promote the spread of influenza to patients.

"In contrast, an unvaccinated health care worker does present a risk to patients," he said.

Dr. Frieden briefly commented on the release of a new estimate of the number of probable H1N1 cases in the United States between April and July that was generated by a probability multiplier mathematical model taking into account patients without laboratory-confirmed influenza.

That estimate of 1.8 million to 5.7 million cases was 140 times greater than the number of laboratory-confirmed cases during the period (43,677). The estimate was published online in the CDC's journal Emerging Infectious Diseases.

Federal officials are currently working on a better estimate, he said.

Another unanswered question is whether new findings from the World Health Organization might impact the current U.S. government position that children need two doses of H1N1 vaccine for adequate protection.

On Oct. 30, WHO officials stated that based on evidence reviewed by its Scientific Advisory Group of Experts, one dose of any of the current H1N1 vaccines produces a sufficient immune response to protect populations older than 6 months of age.

The position of the U.S. government has been to "look at the data and follow the data," and for the time being, the two-dose schedule is still recommended, Dr. Frieden said. ■