Vaccine Economics: What Price Human Life?

IN THE AGE OF GOOGLE “IMAGES,” A FEW KEYSTROKES REVEAL THE FORGOTTEN HUMAN experience in the prevaccination era of public health. With only a few search terms—such as polio iron lungs, tetanus spasms, smallpox scars, or meningitis amputations—we receive vivid reminders of the horrendous price of ignorance, paid before we knew how to prevent infectious diseases through vaccination campaigns and childhood immunization. Therefore, it is more than a little ironic when we are told that we cannot “afford” a needed vaccine despite the fact that it will save lives.

Such a telling tale has surfaced in the UK. The UK Joint Committee on Vaccination and Immunisation (JCVI)—which recommends vaccines for inclusion in the country’s childhood immunization program—failed to recommend a recently approved vaccine against bacterial meningitis primarily on the basis of a fallacious argument of low cost-effectiveness (1). The committee’s action undermines an unheralded guideline that has served science and society for nearly a century: We must develop and deploy vaccines to prevent death and alleviate human suffering, rather than have the anticipated cost benefits drive the process.

The new trend, epitomized by the recent JCVI opinion, prioritizes health care outcomes in economic rather than humanistic terms. This represents a type of health care rationing that threatens not only our immediate well-being but also the long-term viability of an essential business sector—vaccine development and manufacturing. Would anyone be surprised if vaccine developers began to seek more fruitful areas of investment?

COURAGE AND CONSEQUENCES

On 24 July 2013, JCVI chose not to recommend for routine use in the UK a vaccine called 4CMenB (licensed in Europe as Bexsero by Novartis) (1), which very likely protects against a highly infectious form of invasive meningococcal disease (IMD) called MenB. Some 10,000 cases of this bacterial infection occurred in the UK over the past decade, resulting in ~500 deaths and 5000 victims who suffer long-term disabilities ranging from brain damage to limb amputations (2).

The world burden of MenB is high, particularly in developing countries. Vaccines developed for other forms of IMD are highly effective and have virtually eliminated the disease where they have been introduced and thus have saved countless lives and limbs. The approach used to make earlier non-MenB vaccines (that is, polysaccharide protein conjugation) cannot be applied to MenB because of immunological cross-reactivity of the MenB polysaccharide antigen with human polysaccharides. 4CMenB is the first of a new generation of nonconjugate vaccines that are predicted to be protective by inducing bactericidal antibodies to nonpolysaccharide protein surface determinants of the meningococcus—a property that led in part to its licensure in Europe.

The 4CMenB vaccine is safe, but JCVI chose to focus its analysis largely on (i) the vaccine’s cost-effectiveness and (ii) the design of the human clinical studies performed to determine the vaccine’s ability to protect specifically against MenB. JCVI stated that the 4CMenB vaccine is not cost-effective at any price—meaning that even if a company provided the vaccine for free, the cost of vaccine implementation alone would exceed the value of the vaccine to society. The ability of vaccines to prevent disease has traditionally been determined in clinical trials. But because the occurrence of MenB in the developed world is low and epidemics are hard to predict, classical placebo-controlled clinical trials to determine the ability of 4CMenB to protect against MenB are virtually impossible to conduct. Much larger, population-based studies would be needed to define the vaccine’s efficacy, duration of protection, and ability to induce herd immunity (the concept that even unvaccinated individuals benefit because their vaccinated neighbors slow or prevent spread of the microbe in their community). However, such postdeployment studies presuppose that advisory agencies have the courage to recommend a needed and safe vaccine for implementation in a public health setting without prioritizing economic arguments to support the decision.
COSTLY DECISIONS
Most importantly, why is cost-benefit analysis driving the 4CMenB decision at all? Some might argue that we can accurately determine the value of young human lives and assess the impact of death and disability using purely economic concepts and algorithms. However, the criteria and mechanisms we use to estimate the value of preventive medical care in general, and vaccine implementation in particular, need more careful scrutiny and debate (3, 4). Such economic criteria are not routinely applied to the implementation of therapies that extend life marginally for patients with terminal illnesses frequently associated with aging. For example, we have no qualms about administering expensive treatments such as surgery and chemotherapy to some very sick cancer patients who will likely see only a minor extension of their life span at best. Sick adults have strong and loud political advocates that make insurers pick up the bill; healthy (but at-risk) children have far fewer. Clearly a disproportionate amount of our health care dollars goes to end-of-life care. If health care is a zero-sum game, then the societal benefit of such expenditures should be scrutinized no less rigorously than that of an efficacious new vaccine.

In the end, how should society value a young life? Although the absolute numbers of deaths and disabilities prevented by a MenB vaccine might be modest in comparison with other infectious diseases, the humanistic impact is immeasurable. Parents who have lost a young child to MenB or who must care for a meningococcal victim suffering from brain damage or multiple amputations are perhaps the best source of information when it comes to determining a reasonable price tag for prevention of such a devastating disease.

Decades ago, the aggressive use of antibiotics led some leading lights to pronounce the imminent elimination of infectious diseases. These opinions drove industry out of the antibacterial-discovery business and further drove many universities to disband their microbiology departments. Tens of millions of annual infectious-disease deaths later, we now know better: Week after week, news articles chronicle examples of the imminent threat of drug-resistant and emerging pathogens. There is no reason to assume that we will be spared from future new threats that require intervention in the form of vaccines, arguably the most effective public health measure ever put into practice.

The 4CMenB vaccine story is a watershed event in the field of vaccinology in that a badly needed vaccine is being effectively blocked by a policy driven by hypothetical financial concerns of cost-effectiveness. This vaccine took 17 years to develop, and its approval in Europe by regulatory agencies analogous to the U.S. Food and Drug Administration underscores the validity of the science that predicts the vaccine’s utility in saving lives. JCVI should consider carefully the effect that its recommendations have on enterprises that protect human health. Such decisions send shock waves through the very industries we must sustain for the public good, as no government agency or academic institution is currently equipped to step into the breach. Vaccinology is not like photography, in which new digital formats simply displaced old Kodachrome film in a matter of a few years. Technological replacements for traditional vaccines such as genetic immunization are nowhere on the horizon. Vaccines have prevented the loss of countless lives and have alleviated human suffering well beyond the capabilities of economists to measure in numerical terms. Policies that block access to vaccines or prioritize vaccine-development efforts purely on the basis of economic considerations are both ethically and strategically flawed.

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