

Regulating Vaccines: Can Health-Economics Tools be used Profitably?

Direct-to-consumer vaccine advertisements are a recent phenomenon. In India a newborn can make up to 27 visits to the doctor for immunizations before his fifth birthday(1) (Table I). The vaccines cost approximately Rs 11,000. There is a built-in incentive for doctors to prescribe the vaccines.

After a market presence is established, in the next stage the equity argument is brought up. Pressure is brought to bear on Government, to bring the vaccine under the Universal Immunization Program (UIP) saying that the well-to-do are protected and it is not equitable that the poor go unprotected(2). The Government of India recently had to take out advertisements in leading newspapers cautioning the public to 'evaluate carefully the commercial claims' of various vaccines beyond the 6 UIP vaccines(3).

Pressure is also put by international organizations like the World Health Organization (WHO) and Global Alliance for Vaccines and Immunization (GAVI). Resolution 45.17 of the World Health Assembly mandates that member countries integrate cost effective 'newer vaccines' into the national immunization programs. Regardless of cost-effectiveness, organizations like GAVI persuade developing countries to use new vaccines by providing donor-grants (effectively driving costs to zero in the initial stages). The full cost implications are only realized once funding is withdrawn, after the vaccine has been included in the UIP.

As more vaccines come on to the market, the government needs a reliable strategy to evaluate vaccines for the UIP. The question is whether Health Economics tools can provide the answer.

Risk-Benefit Analysis

The first step is to assess efficacy and side effects in the context of the disease burden. Sound epidemiological research and good clinical trials are needed to provide the data. Suppose the

lifetime risk of an individual getting a disease is 1 in 1000 and 1 in 10 of those with the disease, develop undesirable consequences. Then 1 in every 10, 000 vaccinated persons, is a potential beneficiary. If the vaccine protects 50% of those vaccinated, the vaccine benefits 1 in 20,000 of those vaccinated. If this vaccine has serious adverse effects in 1 in 10,000 doses, the vaccine has more risks than benefits and should not be used(4).

The lifetime risk is different for different populations and changes with time. The chance of contracting hepatitis A is much lower in Europe than it is in Asia. Hepatitis A vaccine risks may be too high for Europe but it may be acceptable in Asia. Small pox risk is an example of how time alters the risk benefit ratio. As long as small pox was epidemic, the risks of the disease were more than the risks from vaccination. However, after the eradication of small pox, the risk of continuing with vaccination is unacceptably high, compared to the risk from the disease.

Economic evaluation: Cost calculations

If the perspective of the government (as health care provider) is adopted, capital costs (infrastructure and equipment), staffing costs (physician and nursing time), cost of consumables (vaccines syringes, *etc.*), and administration and overhead costs need to be calculated. Cost of treating side-effects of the vaccine is also to be included.

Economic evaluation: Calculation of benefits

The term 'benefit' is used here in a generic sense and implies 'advantages'. Benefits may be estimated in natural units like 'life-years gained' (cost-effectiveness analyses) monetary units (cost-benefit analyses), or in terms of utility units (cost-utility analyses)

The calculation of benefits often generates controversy. It is possible to inflate benefits to justify nearly any intervention. The cost of

TABLE I—*Vaccines on the Indian Market for Children Under Five*

Vaccine	Supplier/Brand* needed	Doses needed	Marked maximum retail price (MRP)	Price to supply	Price from multi-dose vial	Alternative to government supply	MRP for alternate
BCG	Govt Supply	1				Aventis Pasteur	25
OPV	Govt Supply	6				Aventis Pasteur	73
Hep B	Engerix B (SKB)	3	181	152	70		
Hib	Biomed	3	350	235	168		
DPT	Govt Supply	4					
DT	Govt Supply	1					
Measles	Govt Supply	1				M-VAC Sii Serum Institute	33
MMR	Trimovax Merieux Serum Institute	1	71	57			
Hep A	HAVRIX (GSK)	3	712	598			
Meningo coccus	Quadrimeningo (Biomed)	2	650	550	510		
Pneumo-coccal disease	PNU IMMUNE 23 (Wyeth)	1	745	625			
Influenza virus	VAXIGRIP (Aventis Pasture)	6	525	453			
Chicken Pox	VARILIX(GSK)	1	1345	1120			
Typhoid	Typhim Vi (Newgen)	2	290	243			

*In this illustration, where several brands are available, the ones that are profitable for doctors are mentioned.

*UIP vaccines are supplied by government, free-of-charge and this is often used even in private clinics.

interferon treatment and liver transplants may be considered as cost savings from Hepatitis B vaccination, and immunization may be justified although these treatments are not options for the majority of the population. In the same way to justify chicken pox vaccine, wages lost by the parent to stay at home with the sick child, were added as benefit(5).

Cost in terms of deaths averted and cost-utility analyses are more objective. 'Utility gained' may be in terms of quality adjusted life years saved (QALY) or disability adjusted life years saved (DALY). Economists have various methods to adjust for quality of life and disability.

Let us assume polio does not affect life expectancy (60 years) but it produces paralysis of one limb. Quality of life without disability is taken as one. Assume the quality of life with one limb paralyzed is 0.8. The QALYs of a patient who is afflicted with polio around birth, is 60×0.8 , which works out to be 48 years (12 QALYs are lost to polio). The 'time trade-off' and the 'standard gamble' are methods used to arrive at the quality of life associated with disability or illness(6).

Discounting

If benefits accrue more that 2 years after the

Key Messages

1. In the face of pressures from vaccine manufacturers and international organizations, developing countries need a reliable tool with which to decide about what vaccines to include in the EPI. Health-economics tools may be used for this.
2. Cost-utility data helps prioritize the conflicting demands of various interventions on the limited health budget.
3. An independent body like NICE in the UK could weigh the evidence, incorporate opinions of stake-holders and make recommendations

costs were incurred, it is good practice to discount benefits for the opportunity cost of money. Discounting is done at various rates, (3%, 6%, *etc.*) depending on the rate of inflation and interest rate that is anticipated(7).

Comparing costs with benefits: Defining what is cost-effective; Defining what is affordable

After the discounted cost-effectiveness is known, the next step is to decide if it is acceptable and affordable. Cost-effectiveness is compared to that of other interventions already in place. This is not an absolute value and policy makers may desire more clear guidelines.

Defining if the intervention is affordable may help. A general guideline is those interventions that cost less than the per capita gross national product (GNP), per QALY saved are considered cost-effective(8). This can be used as the measure to see if the program is affordable to the country. A corollary to this, is that if benefits of a program are clearly defined in terms of life-years gained, using the GNP we can calculate what is the 'acceptable cost' for a vaccine and utilize this to negotiate prices with producers(9)

However, in the cost-benefit analysis discussed above, intangible benefits for entities like pain and suffering have not been reckoned. These non-monetary benefits may sometimes become crucial in public debate about interventions(10) and a methodology that judges 'willingness-to-pay' can be used to obtain values for intangible costs and benefits. According to the WHO Commission on Macro-economics and Health, any intervention that costs less than three times GDP per capita for

saving a 'healthy life-year equivalent' should be considered worthwhile and good value for money(11).

Allocative efficiency

Evaluations up to this point are mathematical. Interventions that have poor risk-benefit ratio, those that are not cost-effective or affordable are not to be introduced under any circumstance. If it is both cost-effective and affordable, there is also the need to evaluate efficiency of the program – whether it is capable of providing better returns than other uses of this resource. If a cost-utility assessment has been done, the 'optimum decision rule' involves ranking the incremental cost-utility ratios of different interventions and selecting those with the lowest ratio ("best value") until the budget is depleted(12).

A hypothetical example may be used to clarify this. Assume polio control costs Rs. 350 crores and saves 1 QALY per Rs 10,000 spent, rotavirus control costs Rs 200 crores and saves one QALY per Rs. 20,000 spent, and tuberculosis control costs Rs 700 crores and saves one QALY per Rs. 5000 spent. Assume also a budgetary constraint of Rs. 1000 crores. The first program to be accepted would be TB control as it provides the best utility (one QALY / Rs. 5000). Once this is accepted there is only Rs. 300 crores left in the budget. The next program to be accepted must be polio control. Rota virus control costs only Rs. 200 crores which is less than the cost of polio control (Rs. 350 crores) but polio control takes precedence as it provides more utility.

NICE Model

Given contrary pulls and pressures it is not easy

for government to synthesize all the above objectively, to arrive at a truly rational decision on the introduction of vaccines. The authors believe that the solution lies in setting up an independent body similar to the National Institute of Clinical Excellence (NICE) in the UK, to decide these matters(13). The NICE equivalent can be referred to as 'NICE India'. It should be a statutory body made up of health professionals, epidemiologists and health economists.

To start the process the government must publish the vaccine under consideration. Stake holders – (patient groups, health professionals, academic institutions, industry producing the vaccine, trade unions and international organizations like the WHO and GAVI) then register their interest.

In the next stage, 'NICE India' must assess the clinical evidence and the economic data on benefits. Based on the evidence, draft guidelines are drawn up for assessment by the registered stakeholders values that underpin the work of group). 'NICE India' revises the guidelines if more evidence is provided by the stake holders. An 'independent-review-panel' then reviews the guidelines to decide if all stake holder comments are taken into account. The final guidelines are then issued and government has clear and unbiased advice on which to base decisions.

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