

HEALTH TECHNOLOGY ASSESSMENT AND VACCINE

Could be Health Technology Assessment a tool for assessing new vaccines? The case of anti-Human Papillomavirus (HPV) vaccines

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Introduction

Health Technology Assessment developed in the last 30 years as a tool to evaluate alternative technologies, both on the clinical and the economic point of view. It is a multidisciplinary approach to evaluate safety, effectiveness, costs and organisational, legal and ethic repercussions of a new technology.

Health Technology denotes non only drugs and instruments but all measures used to promote health, prevent and treat diseases and improve rehabilitation or long-term care.

Since HTA permits a global evaluation of a new technology, it can be a useful tool to support decision makers at national Public Health level, at Companies levels and at daily levels; it may be considered a bridge between the world of research and the world of decision-making, particularly policy-making.

Based on this considerations, could be useful an HTA approach to vaccine? Scientific literature is very poor in evidences about HTA and vaccine and this topic is actually not well developed.

Nevertheless we firmly believe that HTA would be a valid tool in vaccines field. Infectious diseases are still responsible for about 25% of global mortality, especially in children and developing world, and vaccines gave an important contribution in the control infectious diseases incidence and mortality.

Over the past two decades, the scientific progresses have opened the way to the development of new prophylactic vaccines against many acute infectious diseases. Despite of this, since the limited economic health resources, it will not be possible for Governments to finance all vaccines and it will be necessary to decide how to best allocate resources, according to the populations needs.

For this reason, Health Organizations need by now an instrument that let them appraise all the aspects of a new technology.

Currently, decision-making process is based on evidence based medicine and cost-effectiveness evaluation. Anyway, the political choices are influenced by a lot of other aspects which are not commonly faced. Health Technology Assessment could so represent a valid instrument to supply decision-makers with.

HTA well integrates in Evidence Based Vaccinology (EBV), that must be defined as the identification and the use of the best evidences to take decisions through all vaccines development and introduction phases.

The HTA framework applied to vaccine

We developed a possible framework of HTA regarding a generic vaccine composed by these follow steps:

1. Evaluation of the epidemiology of disease/infection;
2. Investigation of the disease burden in different Countries (hospitalisations, excess death, etc.);
3. Study of the current treatment practices of the disease/infection, of the preventive measures to avoid infection and of the adverse effects of immunisation;
4. Elaboration of a mathematical model predicting epidemiological and economical impact of vaccination;
5. Economic evaluation of immunisation by a cost-benefit and a cost-effectiveness analyses;
6. Investigation of biotechnological aspects and of the view of the manufacturers;
7. Evaluation of ethic, legal and social issues of infection and related diseases;
8. Study of organisational aspects and of vaccination impact on Health System.

Epidemiologic impact of vaccines on populations

The Public Health decisions on the introduction of new vaccines have to be based on the evaluation of infection/disease burden and health impact and of the population health needs.

Information on the vaccine safety and effectiveness represent a further important issues for policy makers.

From a Public Health point of view, the epidemiologic impact of a new vaccine can be assessed evaluating incidence rate, mortality rate, permanent sequelae, complications and hospitalisations.

These topics can be addressed by projecting a mathematical model apt to forecast even the long term effects of a new vaccine introduction.

Economic evaluation and vaccines

Vaccines economic significance lies in the burden of disease and in the competition for resources between vaccines and other interventions. Economic evaluation permits to best allocate limited resources, on the basis of both the reachable benefits and the availability of good quality evidence.

From the Public Health point of view, new vaccines warrant a cost-effectiveness approach, in order to determine if they are worthwhile, while just recommended ones might be more usefully assessed by either cost-effectiveness analyses or budget impact.

Economic evaluation of infectious diseases and attendant preventive interventions is complex since the potential for “herd immunity” and the need to consider indirect costs associated with vaccine development and infection/disease.

The main types of economic evaluation are the cost-benefit, the cost-effectiveness and the cost-utility analyses. Cost-effectiveness analysis determines which alternative accomplishes an objective at the lowest cost and cost-utility analysis allows a direct comparison of a wide range of medical interventions and is based on the quality-adjusted life year (QALY) or on the disability-adjusted life year (DALY). Cost-benefit analysis is computed by reducing the costs and benefits to monetary terms.

Manufacturer's view, industry and research in vaccine development

There is evidence of the need of a cooperation among all stakeholders of immunization practices, including Countries, industry, research institutions, foundations and international agencies.

As regards the manufacturers' view, it would be guarantee the intellectual property protection and the partnerships between industries and public sector to promote the development of new therapies and to enhance access to both patented and generic medicines all over the world, especially in developing countries. Moreover, since, in 2002, vaccines spending accounted for only 1.7% of the total pharmaceutical market and UNICEF estimated that 34 million children were not reached by routine immunisation, financial resources would be provided to meet the goal of universal immunisation in developing countries over the 2004-2014 period.

Financial resources are needed to purchase and introduce vaccines in the developing countries, to reduce the time lag from their availability in industrialised countries and to stimulate researchers and manufacturers to study and develop needed vaccines for developing world.

Since the need to change presentation and delivery of current vaccines, an HTA approach and the study of biotechnological and organizational aspects of new vaccines would be useful to investigate the best way to launch them.

Social and legal questions

These items could be very different if one considers the setting where applying the vaccine procedure.

Developed Countries

Vaccinology is one of the medical branches that has contributed most to the relief of human poverty and the increase in life expectancy in the last two centuries.

The success of vaccines in controlling and eliminating diseases has, paradoxically, been the cause of a revival of the anti-vaccination movement and vaccines are becoming a victim of their success.

After the development of a vaccine, some legal questions arise. Since field trials should be performed in those age groups which shall be protected--can children give an "informed consent"? Should the vaccination be compulsory or should it be recommended by public health authorities? Should there be a compensation for injuries related to immunisation? The possibility to develop new vaccines and the readiness of the population to cooperate in vaccination campaigns depends very much on a clear solution of those questions.

Providing basic information to parents regarding vaccines and vaccine-preventable diseases may help to reduce opposition to compulsory vaccination. Continued efforts must be made to educate parents about the utility and safety of vaccines, especially parents requesting non medical exemptions to school immunization requirements.

In developing countries

On the other hand, in developing countries, countries infectious diseases are the main cause of mortality and morbidity. Although childhood immunizations have proved to be one of the most effective means of preventing and controlling the spread of infectious and communicable diseases, thousands of preschool children, particularly children from urban African American poor families, are not being immunized. Immunization of preschool children is a function of the interrelationship among health-seeking behaviour of parents, financial and non financial barriers to health care, and

provider practices that inhibit appropriate immunization. Two problems that confront the delivery of health services, including immunization, are lack of funds and lack of access to susceptible populations. Improving access to existing public programs, facilitating community organization efforts, assisting communities through self-help and mutual-aid initiatives, and supporting national efforts can improve immunization status among poor children.

Bioethical issues and vaccines

Important ethical reflections about vaccinations concern two preliminary questions: is ethically admissible an obligation to vaccinate population? Can this fundamental prevention activity be entrusted to the voluntary adhesion of the population?

It's well known that the fundamental goal of the vaccination policies is to reach the higher number of citizens, in order to improve population health status by prevention of infectious diseases. The ethical approach in vaccination aims to evaluate the social legitimation of an intervention that could produce adverse effects for single individuals but can produce important gains in saving human lives, improve quality of life and obtain economical advantages.

Utilitarian bioethics approach can give interesting answers to these ethics dilemmas. Utilitarian bioethics is a very controversial branch of Utilitarian ethics that encourage the utilisation of medical resources where they will contribute most to the sum of the number of happy people in the community. The utilitarian ethics states that the rightness of an action entirely depends on the value of its consequences, and that the usefulness can be rationally estimated. Utilitarianism bioethical philosophers direct their arguments in a simple direction: to make the number enjoying a good health condition as great as possible. Utilitarian methods met many difficulties in resolving economic macroallocation problems in health care but it seems to be able to give a valid orientation in the ethical evaluation of vaccinations.

For many years, and still in some countries, vaccinations are obliged by law. This approach is not easy but is necessary. Public Health has in fact the moral obligation to organize public systems to obtain a widely extended vaccination of the most part of the population. Italian Law has well considered the ethical utilitarian approach, by interesting sentences, as well as n. 307 / 1990, in which the Supreme Court affirms that if a treatment is finalized not only to improve or defend the health condition of a single citizen but also to defend the health condition of the other citizens is an interest of the community, the vaccinal obligation is not incompatible with the Italian Constitution.

But the best way for the future is strictly linked to the overcoming of the obliged vaccinations. The free informed choice of the citizens needs deepening about another typical topic in bioethics: informed consent based upon correct information about direct and indirect risks of illness towards which the vaccination is recommended; benefits of the vaccination; risks of the vaccinations and possible alternatives to these practice.

The HTA applied to HPV vaccine

After the tetravalent HPV vaccine approval from the Food and Drug Administration in June 2006, the Italian Higher Health Council established to vaccinate twelve years old females and the Italian Ministry of Health announced the start of vaccination campaign.

Free vaccination of twelve year olds will start in 2008, but most aspects and involvements of vaccination campaign, first of all the organisational ones, are still not clear.

The reason of that lies in the fact that, in Italy, an HTA Agency does not still exist and that decision making process is based upon experts' opinions and advices, such those from the Italian Public Health Association (S.It.I.) which was consulted in the HPV vaccine introduction decision. Accelerated discussions are raising in most European countries to integrate HPV vaccine in national recommendation and reimbursement programs.

Assessments of vaccination strategies in Europe are under way; i.e Norway has just published an HTA report of HPV vaccine and Denmark is working on.

These are the reasons why we applied HTA to HPV vaccine.

Conclusion

Our HTA report on HPV vaccine could be a useful tool to give an answer to some questions raised after the decision to introduce HPV vaccine. The same Superior Council of Health pointed out the need to further investigate which cohorts other than the twelve year olds to vaccinate. Moreover, it could be important to decide how providing vaccine, particularly for women willing to be vaccinated even if not involved in vaccination campaign and implementing screening programs.

We hope that our HTA report will address these topics and that HTA approach will be added to each decision making process to best allocate resources and fulfil health need of each patient and entire population.

This represents a priority since, after HPV vaccine approval by the European Commission in September 2006, vaccination was recommended in Austria for girls and boys aged 9 to 15 years as well as for women before the start of sexual activity, in Germany, for all girls between the ages of 12 and 17, and in French, for girls aged 14 years and girls and young women from 15 to 23 years who have not yet had sexual intercourse. All these decisional processes were not based on scientific proved evidences thus the need for a transparent, clear and valid instrument to support decisions.

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