

<b>MANAGEMENT OF HEALTH CARE PRACTICE</b> A Handbook for Teachers, Researchers and Health Professionals	
<b>Title</b>	<b>ECONOMIC EVALUATION AS A TOOL FOR PLANNING AND EVALUATING PUBLIC HEALTH INTERVENTIONS: THE CASE OF FOLIC ACID FOOD FORTIFICATION</b>
<b>Module 2.6</b>	<b>ECTS (suggested): 0.2</b>
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<b>Keywords</b>	Economic evaluation, public health, decision-making, folic acid, folic acid food fortification
<b>Learning objectives</b>	After completing this module students and public health professionals should be able to: <ul style="list-style-type: none"> <li>• understand the role of economic evaluation in public health decision-making;</li> <li>• be aware that types of economic evaluation are more applicable in some areas of public health than in others;</li> <li>• understand different possibilities of neural tube defects' prevention;</li> <li>• recognize public health benefits and potential adverse effects of folic acid food fortification;</li> <li>• understand that the decision for folic acid food fortification, its implementation, and evaluation is a complex process, where different professionals need to be fully involved and where economic evaluation needs to be introduced.</li> </ul>
<b>Abstract</b>	<p>The central problem addressed by the discipline of economics is that of resource scarcity, and so the purpose of economic evaluation is, in a very broad sense, to help decision-makers when addressing problems arising due to the scarcity issue. Therefore, such evidence is generated with the direct intention of influencing policy. Over recent years, there have been repeated expressions of concern about the usefulness of health economic analyses, and responses have tended to centre on questions of how research by health economists can be made more useful and accessible to policy makers.</p> <p>How an economic evaluation can be used in practice, is presented in the case of folic acid food fortification. After the introduction of folate deficiency problem and discussion of strengths and weaknesses of folic acid food fortification, it is demonstrated how an economic evaluation can add value to decision-making process.</p> <p>However, it is important to understand that, even if the best possible economic evaluations were available, they would be only one element in a complex process of decision-making that is also shaped by scientific evidence and political feasibility.</p>

<b>Teaching methods</b>	<p>After introductory lecture students should critically discuss role of economic evaluation and its use in public health decision-making process.</p> <p>Afterwards, students should think about data they need in order to support folic acid food fortification in their own country.</p>
<b>Specific recommendations for teachers</b>	<ul style="list-style-type: none"> <li>• work under teacher supervision/individual students' work proportion: 30%/70%;</li> <li>• facilities: a computer room;</li> <li>• equipment: computers (1 computer on 2-3 students), LCD projection equipment, internet connection, access to the bibliographic data-bases;</li> <li>• training materials: recommended readings or other related readings;</li> <li>• target audience: master degree students according to Bologna scheme.</li> </ul>
<b>Assessment of students</b>	<p>Assessment is based on seminar paper and oral exam.</p>

# **ECONOMIC EVALUATION AS A TOOL FOR PLANNING AND EVALUATING PUBLIC HEALTH INTERVENTIONS: THE CASE OF FOLIC ACID FOOD FORTIFICATION**

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## **THEORETICAL BACKGROUND**

### **Introduction**

Decision-making is a crucial element in the field of medicine. The physician has to determine what is wrong with the patient and recommend treatment, while the patient has to decide whether or not to seek medical care, and go along with the treatment recommended by the physician.

Decision-making is vital component of public health as well. Health policy makers and health insurers have to decide what to promote, what to discourage, and what to pay for. Together, these decisions determine the quality of health care that is provided. Therefore, public health and health care policy-makers need a trustworthy source of evidence on which to build health policy.

World Health Organization (WHO), Regional Office for Europe, brought out at the Fourth Futures Forum of High-Level Decision-Makers, entitled Tools for decision-making in public health, which was held in Brussels in 2003 (1), several important conclusions, among which two could be pointed out as most important ones:

1. the need for evidence-based decisions and, as a consequence, evidence-based recommendations, has never been greater, and that
2. the use of evidence enables decision-makers to be transparent and explicit about the basis for decisions.

At the same time we should be aware that (1):

1. evidence changes with time and the utility of evidence-based recommendations is therefore time limited;
2. the speed of decision-making does not always allow time for the generation and use of evidence;
3. evidence-based decisions may not always be acceptable to the public and this will inevitably be a consideration in taking public-health decisions and in determining policy;
4. a lack of evidence about the effectiveness of an intervention does not mean that the intervention is necessarily ineffective; it may be that the research has yet to be undertaken;
5. interventions known to be successful in improving population health can fail if the necessary organizational capacity is not made available to ensure their success. Implementation factors, such as finance, skills and organizational capacity, are therefore an essential part of the evidence review process.

In the frame of WHO, Regional Office for Europe, a body entitled Health Evidence Network (HEN) was established, aiming at giving rapid access to independent and reliable health information and evidence (2).

Nowadays, medical, as well as public health decision-making is a rapidly expanding field that includes different quantitative theoretical tools for modelling decisions,

psychological research on how decisions are actually made, and applied research on how decision-making can be improved. Economic evaluation is one of these tools.

### **Economic evaluation as a tool for public health decision-making**

Health care resources are limited, and where, how and when to allocate them are the main questions if we want the health care system to be efficient. We all agree that this issue is extremely complicated. The situation is even more complicated when in this story public health, especially disease prevention and health promotion, is placed. Health economic through economic evaluation can give some answers to this set of questions.

The central problem addressed by the discipline of economics is that of resource scarcity, and so the purpose of economic evaluation is, in a very broad sense, to help decision-makers when addressing problems arising due to the scarcity issue. Therefore, such evidence is generated with the direct intention of influencing policy. Over recent years, there have been repeated expressions of concern about the usefulness of health economic analyses, and responses have tended to centre on questions of how research by health economists can be made more useful and accessible to policy makers (3,4). The increasing need for economic evidence to inform policy decisions, but the inevitable limits on the rate at which such studies can be undertaken and published, has raised questions about the extent to which the conclusions of a given study undertaken for one specific context hold true for others. This has also stimulated interest in new methods to assess quantitatively the extent of variability in results and to make adjustments across contexts.

#### *Recent developments in economic evaluation concerning public health*

In recent years, there have been some important developments in economic evaluation concerning public health.

1. The first important development has been its increasing prominence in public health decision-making. Although there is continued uncertainty about the role of economic evaluation studies in decision-making at the level of individual hospitals and health authorities (3), a number of health care systems are now using economic evaluation to make system-level decisions about which interventions to fund from collective resources (4).

Economic evidence has been used for some years in Australia and Canada to establish whether new pharmaceuticals represent a cost-effective use of the resources available to the public health care system (5,6). More recently, a number of European countries have developed an economic dimension to the regulation of health care technologies, including Portugal, Sweden and Finland (7). Even in the USA, the need to ensure efficient use of collective health care resources has led some health maintenance organisations to use formal economic criteria in decision-making about which interventions will cover (8).

2. The second development is the emergence of new economic evaluation methods in particular areas. These include alternative approaches to handling uncertainty in the context of studies based on patient-level data (e.g. randomised trials), and in decision models; and preference-based measures of health status which link data on patients' health states, as collected in trials and similar studies, with the public's health state preferences to facilitate estimates of QALYs (7). There remain, however, a number of important sources of controversy in the field, for example, the role and methods of productivity cost estimation and how to reflect equity considerations in economic

evaluation (9). One area of methodology on which much has been written but in which few new methods have emerged relates to the generalisability of economic evaluation (9).

The proposal put forward is that the objective of health care services should be to maximise population health benefits (3). For many this appears not to be a highly controversial suggestion and, in broad terms, receives support from policy makers and the public more generally (10). The difficulties and disputes arise primarily around attempts to measure health.

### *How to make valuation of health in economic analyses?*

Over the course of the last 20 years or so, the subdiscipline of health economics has had a methodological focus on the measurement and valuation of health. The result is a measure of health that can be operationalised for use in policy making, i.e. the quality-adjusted life-year (QALY) or quality-adjusted life expectancy (QALE) (10). The decision rule, therefore, for normative health economic analyses, is to advocate investment in those technologies that produce the largest QALY gains for a given level of cost. In order to inform such decisions, normative analyses tend to provide results in the form of the incremental cost-effectiveness ratios (ICER), net-benefit statistics and cost-effectiveness acceptability curves (CEAC):

1. the ICER reports the ratio of additional costs to additional health effects associated with a new intervention (e.g. cost per QALY gained);
2. the net-benefit statistic expresses the additional health effects in monetary units by using an estimate of the “maximum willingness to pay” per unit of health gain, where available;
3. the CEAC plots the probability that the intervention in question is cost-effective against threshold values to define cost-effectiveness (11).

### *The role of economic analyses in public health decisions*

Yet while economic evaluation is often of little help in deciding whether to undertake an intervention in the first place, it has rather more potential in helping to decide which of a series of options should be chosen to achieve a specified goal, by means of cost-effectiveness analysis. While recognizing the potential benefits of cost-effectiveness analysis, it should also be noted that it is more applicable in some areas of public health than in others (11). For instance, secondary prevention initiatives like screening, for example, have been subject to numerous cost-effectiveness analyses, to help choose between different methods of screening or target groups. However primary prevention has been subject to rather less economic evaluation to date, in part due to the difficulties of measuring costs and effects and determining causation.

Recent review by Allin and colleagues describes the models of public health decision-making in eight countries: Denmark, Finland, France, Germany, Netherlands, Sweden, Australia, and Canada. It has been written to inform the debate on future policy options and it represents an initial attempt to map priority-setting in public health (12). This investigation revealed that none of the eight countries has explicit, systematic procedures for making decisions affecting public health or setting priorities among different public health interventions. The methodology used for making decisions and setting priorities in public health across the eight countries is consistently related to population health status, epidemiological data, burden of disease and, often, scope for prevention. Also important in this process are political negotiations, pressure from

interest groups and informal processes. In addition to the other methods, Sweden bases decisions on an “ethical framework” encompassing human dignity, need and solidarity. Likewise, France highlights the importance of ensuring that decisions fit with societal values. Australia and the Netherlands increasingly are utilizing economic evaluation and evidence of interventions’ effectiveness to guide decision-making. In this way, they are progressing more rapidly towards creating an evidence-based policy environment (12).

However, it is important to understand that, even if the best possible economic evaluations were available, they would be only one element in a complex process of decision-making that is also shaped by scientific evidence and political feasibility. Like every analytical tool, also economic analysis has its limitations. And not at the end, also the public health decisions should (to the reasonable extent) keep in touch with society’s health values (13,14). Comprehensive example would be a case of folic acid food fortification.

## **CASE STUDY: CASE OF FOLIC ACID FOOD FORTIFICATION AS AN EXAMPLE OF PUBLIC HEALTH DECISION-MAKING**

### **Prevention of neural tube defects**

Neural tube defects (NTD) are a group of heterogenous and complex congenital anomalies of the central nervous system resulting from failure of normal neural tube closure between the third and fourth week of embryonic development (15). Each year approximately 4500 pregnancies in the European Union result in a livebirth, stillbirth or termination of pregnancy of an infant affected by NTD, mainly spina bifida and anencephaly (16). All infants with anencephaly are stillborn or die shortly after birth, whereas many infants with spina bifida have substantially enhanced survival rate thanks to recent improvements in medical and surgical management. However, these individuals continue to be at increased risk for morbidity and mortality throughout their life as they face severe, life-long disabilities and are at risk for psychosocial maladjustment. Their medical problems may result from the neurologic defect itself or from its repair (e.g., paralysis, hydrocephalus, endocrine abnormalities, deformations of the limbs and spine, bladder, bowel or sexual dysfunction, and learning disabilities) (17).

In addition to the emotional cost of spina bifida, the estimated monetary cost is staggering. In the United States alone, the total cost of spina bifida over a lifetime (the direct costs of medical, developmental, and educational services and the indirect costs associated with morbidity and mortality, in 1992 dollars) for affected infants born in 1988 was almost \$500 million, or \$294,000 for each infant (18). Recently, Centers for Disease Control and Prevention published data about average cost of caring for a child born with spina bifida for life, which is about \$636,000 (19).

NTD develop within the first few weeks of embryogenesis, at a time before many women know that they are pregnant. Studies of Smithells and colleagues (20), confirmed by many other studies and randomized clinical trials by the early 1990’s (21,22), showed that supplements containing folic acid, when consumed around the time of conception and early in pregnancy, can reduce NTD by an estimated 70% or more. It is generally accepted that prevention can be obtained at a dose corresponding to 400 µg of folic acid per day. Three different strategies are available to reach the daily dose; women may consume a diet rich in folate, they may take supplements with folic acid, or consume foods fortified with folic acid.

Because folic acid is inexpensive, safe, and easy to use, many professional organizations and some governmental agencies promote the use of folic acid

supplements to prevent NTD (23). The format of such recommendations varies, but they typically include statements that women should eat a healthy diet and take folic acid supplements when planning a pregnancy or throughout childbearing age. In a few countries, including the United States, Canada, Chile, and South Africa, recommendations to consume folic acid are integrated with a policy of widespread fortification of flour to ensure that the entire population receives at least a small additional amount of folic acid regardless of access to supplements (23).

A crucial question is how effective are recommendations alone, in the absence of fortification. A study was conducted by the EUROCAT Working Group to review progress in the last decade in European countries in terms of developing and implementing public health policies to raise periconceptional folate status, and analyze data on the prevalence of NTD to determine the extent to which NTD have been prevented up to the year 2002 (16). Representatives from 17 countries participating in EUROCAT provided information about policy, health education campaigns and surveys of folic acid supplement uptake in their country. Surveys showed that in all countries, a minority of women were taking supplements during the entire advised periconceptional period, with supplementation rates varying from 5% to 46% between countries. The situation regarding lack or low uptake of supplementation advice is reflected in the lack of a clear decline in the prevalence of NTD across Europe. Authors concluded that the potential for preventing NTD by periconceptional folic acid supplementation is still far from being fulfilled in Europe (16). The most likely possibility is that recommendations were not implemented to the point of inducing a sustained change in behavior in a sufficiently large proportion of women to cause measurable effects (23). Whereas any improvement in primary prevention is desirable and should be promoted, a detectable change in the population requires a major shift in the proportion of women consuming adequate amounts of folic acid. It is unclear how successful recommendations alone will be in achieving this goal, given the influence of cultural, social, and economic factors such as the acceptability, availability, and cost of daily supplements. In general, use of supplements tends to follow economic and educational lines, so targeting the entire population through recommendations on supplementation alone may not be practical (23). Only a public health policy including folic acid fortification of staple foods is likely to avoid widening socio-economic inequalities in NTD prevalence and result in large scale prevention of NTD (23,24).

In view of the findings that there has been a lack of substantial decline in NTD prevalence in Europe since 1991, and even countries which have pursued supplementation policies relatively actively have found a limited preventive impact, EUROCAT has issued the following recommendations:

1. Countries should review their policies regarding folic acid fortification and supplementation, taking account of WHO Europe recommendations.
2. European countries could prevent most neural tube defects in planned pregnancies by putting in place an official policy recommending periconceptional folic acid supplementation and taking steps to ensure that the population are aware of the benefits of supplementation and the importance of starting supplementation before conception.
3. As many pregnancies are unplanned, European countries could achieve more effective prevention of neural tube defects by additionally introducing fortification of a staple food with folic acid. The particular objectives of this policy would be preventing neural tube defects among women who do not plan their pregnancy, and reducing socio-economic inequalities in neural tube defect prevalence.

4. Health effects of supplementation and fortification should be monitored, and policies should be reviewed periodically in light of the findings.
5. The European population should be covered by high quality congenital malformation registers which collect information about affected pregnancies (live births, stillbirths and terminations for fetal abnormality). One important use for the information would be to assess the effect of folic acid supplementation and fortification on NTD rates as well as rates of other congenital malformations (16).

### **Folic acid food fortification – pro et contra**

In this context, fortification of flour represents an additional opportunity to deliver some folic acid to nearly the entire population, across social and economic barriers. Where dietary and food processing conditions are favorable, fortification can be effective quickly and at low cost (24). In countries that have fortified flour, blood folate concentrations have risen quickly, and although the reductions in incidence were not as large as that achievable through supplementation, such reduction occurred soon after fortification was implemented (25,26).

In 1992, the United States Public Health Service issued a recommendation that all women of childbearing age should consume 400 µg of folic acid per day to reduce the risk of having an infant with an NTD (27). The Institute of Medicine made a similar recommendation in 1998 suggesting that women of childbearing age should consume 400 µg of folic acid per day from fortified foods, supplements, or both, in addition to consuming food folate from a varied diet (28). In 1993, the United States Food and Drug Administration (FDA) Folic Acid Subcommittee recommended that folic acid fortification be implemented to ensure that 90% of women of childbearing age consume 400 µg folate daily or folic acid from all sources, but the FDA did not implement fortification at the level required to achieve this because of safety considerations (29). The FDA began requiring folic acid fortification of enriched cereal-grain products in 1998 at a level (140 µg /100 g) that was estimated to provide an average person approximately 100 µg additional folic acid daily (30). On November 11, 1998, fortification with folic acid of all types of white flour, enriched pasta, and cornmeal became mandatory in Canada with the goal to increase by approximately 30 to 70% the average intake of folic acid among women of childbearing age without posing a risk to the general public (25). In any case, average serum folate concentrations increased significantly after the implementation of folic acid fortification, and the prevalence of NTD in the United States in 2000 was 26% lower than that before folic acid fortification (26). In Canada, a 46–48% decrease in NTD was seen to coincide with folic acid food fortification (25).

Although the primary goal of folic acid fortification is to reduce the occurrence of NTD in women of reproductive age, the potential benefit to the general population in reducing the risk of chronic disease via homocysteine lowering is also highly relevant (31). Recently published population-based study suggests that the temporal decline in stroke-related mortality in the United States and Canada coincided with the introduction of folic acid fortification (32). More importantly, a meta-analysis of clinical trials just published shows that supplementation with folic acid reduced the risk of stroke by 18% overall, by 29% in trials with a treatment duration of less than 36 months, and by 25% in those trials in subjects with no history of stroke which strongly suggests that either folic acid or homocysteine lowering plays a role in the primary prevention of stroke (33).

Population-based exposure to folic acid through fortification, however, is controversial because of concerns about potential adverse effects on health. The most widely documented concern is the possibility that high-dose folic acid may mask the diagnosis and thereby delay the treatment of vitamin B-12 deficiency in older adults (34). In addition, there is some concern that high-dose folic acid may promote the development of colorectal cancer if precancerous lesions or neoplasms are already established in the mucosa (35). Thus, mandatory fortification with folic acid remains virtually nonexistent in Europe. Furthermore, although many European countries allow the addition of nutrients to foods on a voluntary basis (ie, at the manufacturer's discretion), others prohibit fortification of any kind. Thus, national fortification policy varies considerably throughout the European Union (23). The European Commission, however, is aiming in the near future to regulate in its member states the minimum and maximum amounts of vitamins and minerals allowed to be added to foodstuffs (36).

### **Economic evaluation of folic acid food fortification**

Economic evaluation plays an important role in translating research findings into practice and policy. Economic evaluations can be ex-ante, conducted before the adoption of a policy on the basis of results from pilot studies and theoretical assumptions, or ex-post, carried out after implementation using information on observed outcomes.

Before the adoption of fortification in United States, 3 independent economic evaluations concluded that folic acid fortification at 140  $\mu\text{g}$  of folic acid per 100 g of cereal grain product would yield net economic benefits or cost savings (37-39). This conclusion was confirmed and strengthened by postfortification analysis where Grosse and colleagues calculated the economic impact of fortification using both cost-benefit and cost-effectiveness analytic techniques on the basis of prefortification and postfortification epidemiological data (40). They believe that folic acid fortification has proven to be a public health success in the United States and Canada, although an economic evaluation of fortification in Canada has yet to be conducted. The net benefit and cost savings surpass estimates prepared before fortification. By any measure, folic acid fortification provides a remarkable return on investment. Other industrialized countries could benefit by following the lead of the United States and Canada in adopting folic acid fortification of cereal-grain products (40). Furthermore, the benefits of fortification are not restricted to higher-income countries; wheat flour folic acid fortification program in Chile showed an increase in blood folate levels and a 40% decrease in the risk of NTD (41). Llanos and colleagues conducted ex-post economic evaluation, findings of which strongly support the continuation of fortification of wheat flour with folic acid in Chile. Furthermore, these findings serve as important evidence for policy makers from other countries to consider the implementation of folic acid fortification of cereal grain products (42).

Due to uncertain risks, the Dutch Health Council advised the government against fortifying food with folic acid, in 2000 (43). Their conclusions were based on uncertain risk suggested above. In particular, the elderly population would be at risk for excess intake of folic acid, which was considered to be highly undesirable. Jentink and colleagues produced estimations of the costs, savings, health gains, cost-effectiveness and cost-utility for bulk food fortification with 140  $\mu\text{g}$  folic acid per 100 g flour (43). Estimations were conducted in a base case analysis (presenting the most likely situation) and in sensitivity analysis around the base case assumptions. They applied the societal perspective for economic analysis, which included the whole spectrum of direct, indirect, medical and non-medical costs. Their model suggested that folic acid

fortification of bulk food to prevent cases of NTD might be a cost-saving intervention in the Netherlands as well (43).

## **EXERCISES**

### **Task 1**

Individually, carefully read the theoretical part of this module and recommended readings.

### **Task 2**

Make two groups for discussion using method “pro et contra”. The group No.1 prepares arguments for “pros”, and the group No.2 for “contras”. Perform the “pro et contra” discussion in a limited time.

### **Task 3**

Fortification of food with folic acid has the potential to reach a large proportion of the population and increase the level of folate consumed. Some governments in Europe are now seriously considering folic acid food fortification. What information would you need to support this public health policy in your own country? Make a short written report, and present it to your colleagues.

### **Task 4**

Discuss the fortification of food with folic acid issue in a plenary session.

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