



ВСЕМИРНАЯ ОРГАНИЗАЦИЯ ЗДРАВООХРАНЕНИЯ
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Meeting on Economic Aspects
of Viral Hepatitis

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REPORT

1. Introduction

Health resources in all countries are limited in relation to the need for the prevention and control of diseases and the growing demand for care. At the same time, the burden of many diseases on the economy is becoming increasingly heavy. An evaluation of the economic burden of various diseases, together with an economic evaluation (in terms of cost effectiveness, cost benefit, etc.) of procedures for their prevention and control, should stimulate and facilitate the selection of more effective and economical measures.

The natural history and the prevention and control of many communicable diseases have been intensively studied and constitute therefore a suitable subject for economic appraisal. Due account has, of course, to be taken of difficulties in applying economic concepts to health. While a number of individual economic studies have already been made in European countries, there is a need for a more systematic and more widely applicable approach. In particular, there is a great need to review and standardize economic evaluation and methodology in this field.

The purpose of the European Programme on Economic Aspects of Communicable Diseases is to contribute to the development and proper testing of such a standard methodology. As a result of a planning meeting held in March 1975 and of subsequent discussions, it was decided to implement the programme in three phases: first to invite interested national institutes to design "study protocols" on a limited number of diseases and to carry out such multinational studies on a pilot basis; secondly, to inform governments in the Region of the results of the pilot studies, inviting them to apply and adapt the methodology developed; and thirdly, to convene a working group to analyse the results achieved and subsequently, a larger conference to review the methodologies and results.

The first activity of the pilot phase, which is an integral part of the health economics programme of the Regional Office, consisted of obtaining the advice of experts and institutes in the fields of communicable diseases and health economics in a number of countries. They stated that they would like to study the economic aspects of communicable diseases in the following order of priority: viral hepatitis, sexually transmitted diseases, enteric infections, rabies, and a few other diseases. In accordance with the expressed preference of the interested experts and institutes, the Regional Office convened a first Meeting on Economic Aspects of Viral Hepatitis in Copenhagen from 9 to 11 November 1976. The list of participants is given in Annex II.

The purpose of the meeting was to outline a common approach to (a) estimating the cost of viral hepatitis, and (b) study collaboration and coordination. In all the discussions, it was recognized that the report of the Working Group on Viral Hepatitis, Bucharest, 25 to 29 August 1975, (document no. ICP/VIR 001), provided an essential background. Attention is drawn, in particular, to Annex IV of that report, on the Economic Aspects of Hepatitis A and B.

2. The problem of viral hepatitis

Soon after its establishment, the World Health Organization recognized viral hepatitis as a major public health problem, and deplored the fact that knowledge of its etiology and epidemiology was limited. Since that time much progress has been achieved in this field with the development of specific laboratory methods for detecting infection. Viral hepatitis is defined as acute inflammation of the liver caused by one of two different viruses, which are referred to as hepatitis A and hepatitis B, or by other hepatitis viruses.

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Hepatitis A

This infection has a worldwide distribution, but the exact incidence is difficult to estimate because of the high proportion of subclinical infections and infections without jaundice, differing patterns of disease, and differences in surveillance and reporting. The degree of under-reporting is believed to be very high.

In most European countries infections occur at all ages, probably about 50% of the clinical cases being in children under the age of 15 years. Some evidence suggests that the incidence of hepatitis A is at present declining and that a greater proportion of cases is occurring among adults.

Hepatitis A virus is spread by the intestinal-oral route, most commonly by close contact, and infection occurs readily in conditions of poor sanitation and overcrowding. Food-borne or water-borne transmission is not a major factor in the maintenance of this infection in Europe, but the ingestion of shellfish cultivated in polluted water is associated with a high risk of acquiring hepatitis A. This infection is not infrequently acquired by travellers to areas of high endemicity. Outbreaks of hepatitis A in handlers of newly-captured nonhuman primates have also been described. Hepatitis A is rarely transmitted by blood transfusion.

The spread of infection is reduced by simple general hygienic measures and the sanitary disposal of excreta. Routine or compulsory admission to hospital is practised in some countries, but recent data suggest that this practice is unnecessary and epidemiologically ineffective. Normal human immunoglobulin may prevent or attenuate a clinical illness, while not always preventing the infection. The use of normal immunoglobulin is of value in the control of outbreaks of infection in given circumstances, such as in institutions and nursery schools. The view has been expressed that the use of immunoglobulin on a very large scale is undesirable because unrecognized subclinical cases and anicteric cases may disseminate the virus, because the practice is wasteful, and because the repeated injection of immunoglobulin, for example in children, may be harmful.

A vaccine against hepatitis A is not available.

Hepatitis B

Infection with hepatitis B virus is associated with the appearance in the serum of a specific surface antigen and its homologous antibody. A second antigen, present in the core of the virus, appears to be intimately related to the infection. A third antigen, named hepatitis B e antigen, appears to correlate with the number of virus particles and the degree of infectivity of surface antigen-positive sera. The presence of this antigen is thought to be associated with an unfavourable prognosis and the development of chronic liver disease. There is some evidence that antibody to the e antigen indicates relatively low infectivity.

The surface antigen thus serves as a useful marker of infection with hepatitis B virus. The availability of a bewildering array of serological methods for detecting antigens and antibodies associated with this infection makes it necessary to consider which methods are best suited for practice and research applications. These techniques vary considerably in their sensitivity, specificity, objectivity, the cost of capital equipment, the maintenance of the equipment and the cost of the reagents. The major uses of these laboratory techniques are: (i) to establish precise diagnosis; (ii) to identify blood donors who are carriers; (iii) to define the epidemiology of the infection, and (iv) to evaluate passive and, in future, active immunization.

The importance of hepatitis B can be considered under a variety of headings which include its effects in every field of medical practice, the impact that it has on blood transfusion services and its association with progression to chronic liver disease, including chronic active hepatitis, cirrhosis, and, in some areas of the world, primary liver cancer. In addition, infection with hepatitis B virus may be followed by the persistent carrier state. Such a carrier state may be associated with liver damage. The survival of hepatitis B virus is ensured by the reservoir of carriers, estimated to number about 120 million. It appears that the prevalence of carriers, particularly among blood donors, in Northern Europe is 0.1% or less, in Central and Eastern Europe up to 5%, while there is a higher frequency in Southern Europe and countries bordering the Mediterranean. The highest prevalence is observed in the 20-40 year age-group. The importance of the parenteral and inapparent parenteral routes of transmission of hepatitis B virus is now well recognized. Although various body fluids such as saliva, menstrual and vaginal discharges, seminal fluid, and breast milk have been implicated in the spread of infection, infectivity appears to be especially related to blood.

The impact of screening of blood for surface antigen on the incidence of post-transfusion hepatitis is difficult to measure, but it appears in some countries to have caused a reduction of about 30%. Many cases of post-transfusion hepatitis remain unrecognized because of their mild or subclinical nature. Certain plasma derivatives prepared from large pools of plasma carry a high risk of contamination with hepatitis B virus. Immunoglobulin prepared by the cold ethanol fractionation method of Cohn has a well-established reputation of freedom from contamination with hepatitis B virus. This may not be true for immunoglobulin prepared by other methods.

High-risk groups include persons requiring multiple transfusions of blood or plasma or injection of blood products, prolonged inpatient treatment, patients in whom frequent tissue penetration or repeated access to the circulatory system is needed, patients with natural or acquired immune deficiency and patients with malignant diseases. Viral hepatitis is an occupational hazard among health care personnel and the staff of institutions for the mentally retarded and other closed institutions. High rates of infection have been reported in drug abusers, prostitutes and homosexuals. Individuals working in areas with high endemicity are also subject to an increased risk of infection.

It appears that specific hepatitis B immunoglobulin is useful for postexposure prophylaxis of single acute exposure such as occurs after accidental inoculation. Considerable progress is being made in the development of vaccines against hepatitis B, but these are likely to be very expensive. Encouraging preliminary findings have recently been reported concerning the use of interferon for modifying the course of chronic hepatitis B virus infection. However, it is essential to establish its safety and therapeutic efficacy. Interferon is not readily available at present and is exceedingly expensive. There are no other methods of specific treatment for viral hepatitis.

Other hepatitis viruses

Progress in the specific diagnosis of viral hepatitis has revealed a new type of hepatitis that is unrelated to hepatitis A or B virus. It appears to be now the most common form of hepatitis occurring after blood transfusion in some areas. There are no laboratory tests available as yet for identifying this agent or agents.

2. Costing

2.1 Introduction

Over the past few years there has been an increasing awareness of the financial consequences of health service development as medical technology steadily improves. The proportion of the national product devoted to health services has risen steadily and this has brought the financial constraint on health services more and more into the limelight. As far as economic research is concerned, this has been reflected in two developments. Firstly, there have been attempts to estimate the size of certain disease problems in cost terms. Secondly, there have been attempts at cost/benefit and cost/effectiveness studies of particular measures for disease prevention and control.

Cost/benefit and cost/effectiveness studies are means of helping decision-makers to choose among a number of alternative ways of using limited resources, in this case to improve health services. Although it is the intention to progress to such studies in relation to viral hepatitis eventually, in the first place it was considered more useful to develop the necessary methodology step by step, to establish the size of the problem as a whole and of its component parts, as measured in monetary terms.

For this reason interest is being confined initially to a costing study of viral hepatitis. An account of the cost of viral hepatitis is useful for assessing the relative economic importance of this disease and its sequelae, for justifying the need for particular items of biomedical and health service research, and for developing arguments for negotiations with other sectors of the economy.

The term "disease costing" here means an attempt to estimate all the financial consequences of disease. It has been customary to divide costs into direct and indirect. The direct cost of a disease means its cost to the health services in terms of health manpower, materials, equipment and facilities; the indirect cost means the consequences of the existence of the disease in question for the output of goods and services in the economy as a whole.

An alternative view is that disease costing attempts to estimate, from the point of view of the overall economy, both the excess consumption and the deficit production which a particular disease causes through the behaviour and care of those who have the disease and those who are at high risk of exposure to it. Excess consumption, which roughly corresponds to direct costs and deficit production, which roughly corresponds to indirect cost, are seen in relation to the typical consumption and production of healthy persons with characteristics similar to those of persons with the disease, especially as regards age, sex, residence, education and occupation. This marginal costing approach is valid only if the disease in question does not change the key relationships and key parameters of the macroeconomic system. Fortunately, this assumption can safely be made in the case of viral hepatitis. A measure of direct and indirect costs which is consistent with the usual forms of national accounting will necessarily exclude such items as housewives' time, non-working time and voluntary efforts. Cost/benefit and cost/effectiveness analyses are not themselves, of course, necessarily consistent with national accounts.

It is hardly necessary to add that monetary costs are not meant to represent the total "cost" of a disease in the sense of the adverse effects that the disease has. In general it is not possible to represent all these ill effects (pain, suffering, disability, premature death, etc.) convincingly in monetary terms, although some of these effects, such as premature death, will have financial aspects. Although not all of these effects are explicitly represented here, they do, of course, form the background to the topics discussed here.

2.2 Direct disease costs (health care costs)

For many diseases, especially infectious diseases, direct health care costs can be seen to follow a predictable cycle over a longer or shorter period. Initially, the disease is either nonexistent or unrecognized. Thus, no preventive or therapeutic measures are applied and the reported cost of the disease is consequently negligible or zero, although therapy may be provided under different diagnoses. When it is first recognized, its incidence is usually underestimated; its treatment is still inadequate, often consisting mainly of custodial hospital care, and its cost therefore remains relatively low. At the third stage, there is an increased awareness of the existence of the disease; its reported incidence increases and there are enhanced public expectations of prevention and treatment. These lead to steeply rising costs. At the same time, major research programmes are usually initiated and these add to the already increasing expenditure.

At the fourth stage, methods of specific treatment are developed so that expensive custodial care starts to be replaced by effective therapy. Methods of prevention are introduced and there should be a recognition that the cost/effectiveness of these new forms of medical intervention (as well as their efficacy) must be taken into account. If this happens, the direct costs of the disease can start to decline. Then, in the final stage, the disease will be brought under effective control, usually by programmes of prevention. Hence, no more than minimal "maintenance" health care will be needed at this stage to keep the disease under control. In some instances, the disease may even be eradicated.

At present, hepatitis B appears to be in the third stage of this cycle. It is, therefore, essential that the cost/effectiveness of measures for its prevention and treatment should be taken into account as soon as possible in order to prevent a further increase in costs and to gain the benefits of declining costs which should be enjoyed at the next stage.

It may be concluded from this that technical progress can raise or lower direct costs, and experience also serves to disprove the myth that prevention is necessarily less costly than cure, the main point here being that the combination of technical progress and the "search" for cases, as in screening, may well increase the reported prevalence of the disease.

To summarize, the main categories under which direct costs occur are:

(1) Preventive activity

- (a) Promotion of environmental health. Many infectious diseases are particularly susceptible to the traditional public health investments in sanitation and hygiene.
- (b) Health education: campaigns to make the public aware of health dangers and to alter its behaviour.

- (c) Early diagnosis and screening. For many diseases it may be hypothesized that detection of the disease at an earlier stage in its natural history will lead to a better prognosis for treatment and control of its spread. It may therefore be wise to devote resources to detecting presymptomatic cases.
 - (d) Immunization. Many communicable diseases are susceptible to immunization and it may be worth devoting resources to this activity as well as to devising procedures to reduce the risk of infection.
 - (e) Prophylaxis: for example, the protection of hospital and laboratory staff from the risk of infection can involve considerable costs.
- (2) Curative and follow-up activity
- (a) Outpatient care. This covers both primary care (by the general practitioner) and diagnosis and treatment in polyclinics and hospital outpatient departments.
 - (b) Hospital care. This tends to be the most expensive sector of health and naturally attracts the most attention.
 - (c) Rehabilitation. This activity, which may also include occupational retraining, can play an important role in reducing the long-term consequences of disease.
- (3) Supportive activity
- (a) Research. In general, certain programmes of clinical and health services research in relation to specific diseases will be in progress or can be commissioned.
 - (b) Identification of high-risk groups. In order to channel resources in the most effective way it will often pay to devote some part of the resources to seeking out those most likely to benefit from health measures, and to focusing preventive care on those groups.
 - (c) Development of a health information system. Epidemiological studies and notification, etc., play an important part in the control of all communicable diseases.
 - (d) Training of health personnel. The control of diseases often needs specific training, e.g. in laboratory techniques.

The example of viral hepatitis

In respect of viral hepatitis in particular, the following four examples illustrate which types of direct cost might need to be taken into account.

<u>Blood donor screening</u>	<u>Research</u>	<u>Primary care/ outpatient</u>	<u>Inpatient</u>
Capital*	Capital*	Capital*	Capital*
Manpower	Scientific manpower	Staff	Staff
Test materials	Ancillary manpower	- medical	- medical
- haemagglutination	Materials (and animals)	- nursing	- nursing
- radioimmunoassay	Equipment	- laboratory	- laboratory
		Materials	- domestic
		- therapy	- other
		- laboratory	Materials
			- therapy
			- laboratory
			- food and other items of patient maintenance ("hotel" cost)

* Capital costs include buildings and equipment. This should not be their total value, but should be converted into an annual sum, e.g. taking into account the expected life of the equipment. Where the equipment or building is used to combat more than one disease, annual capital costs

may be apportioned to viral hepatitis according to the share of hepatitis staff, workload, working space, etc.

Similar lists could be compiled for all the headings mentioned above, such as prophylaxis and follow-up care.

2.3 Indirect disease costs (costs of disease impact)

The question of the indirect costs of disease may be considered under four conceptual headings. These are:

- (1) short-term absence from work,
- (2) change of work situation due to disability,
- (3) loss of work due to premature mortality,
- (4) other personal and social costs of ill health and premature death.

To take the last heading first, it has already been noted that despite the undoubted importance of this factor there is no way in which such costs can be included that is in any form consistent with national income accounting. In addition, although there are many suggested methods for placing monetary values on such effects (e.g. health indices, legal judgements, implicit valuations, etc.) it is unfortunately necessary for the purposes of this multinational collaborative study, which involves countries with differing social and economic systems, to avoid such thorny problems and concentrate on those items which can in practice be quantified fairly easily.

There are many difficulties in measuring "short-term absence from work". Short-term absence is often not recorded or identifiable as being attributable to a particular disease. In the United Kingdom, for example, absences of three days or less are not notifiable for sickness benefit purposes. In addition, there is often misrecording of diagnoses or, as in Denmark, no diagnosis may be given.

When it comes to placing a monetary value on absence from work one can measure the loss of earnings. One can also attempt to measure the loss of productivity by adding to earnings, where applicable, the extra costs which are incurred when an employee is hired, such as the employer's contribution to social insurance schemes, fringe benefits and so on. In some countries sickness payments are a better indicator of loss of productivity than net or gross earnings. Whichever measure it is decided to use, the important thing is to be explicit about one's assumptions.

It is important to avoid committing the potential error of double-counting by adding to foregone earnings the cost of sickness payments. Although the latter may be an additional cost to the Ministry of Finance, the insurance funds or the employer, they are not necessarily an additional cost to the community as a whole. If it is desired to show both lost earnings and sickness payment costs, they should be set out under separate headings.

Because of the difficulties of estimating work absence and because those affected by a particular disease may not be "typical" workers, it may be necessary to carry out special studies rather than rely on routine statistics.

As noted above, national accounting systems do not allow for the time away from work of those who are not in wage-earning employment, e.g. housewives. If it is felt that such factors should be measured and valued to give a total picture of the effect of the disease on social functioning, then these measurements should also be set out separately, rather than added to the measure of lost earnings or lost productivity.

Under the heading "Change of work situation due to disability", account is to be taken of events which may lead a person to change to a less well-paid job or to part-time work or may cause him to withdraw from the work-force altogether. It is often difficult to acquire data on changes in work as a result of impairment and on premature retirement. There may be a need for special studies in this area.

Another item which might be considered under this heading is the effect of the sickness of a spouse or child on a person's ability to work. Here too, special studies may be necessary.

Under the heading "Loss of work due to premature mortality" the financial aspects of premature mortality as measured by the loss of working life are considered. Such measurements bring in their train a host of conceptual and practical problems. How should future earnings be valued compared with present earnings (the discounting problem)? Should consumption expenditures be subtracted or not? What about the deaths of children and the elderly?

If the alternative view on disease costing were adopted (see 2.1), the conceptual answer to the last two questions would be straightforward, namely, one would impute an economic loss corresponding to the expected (future) productive contribution by the average healthy person with characteristics similar to the diseased or deceased, especially as regards age, sex, residence, education and occupation. The practical problems would then seem to be the availability of information on reference groups - special studies may be necessary - and the selection of a socially relevant time or discount rate.

Given these difficulties, the most practical solution is to specify the extent of the premature mortality and allow those who wish to estimate its value to set out such an estimate separately with explicit assumptions.

Although all of these measures of indirect cost are subject to criticism, it was felt that in a study such as the present one, which is intended primarily to develop a methodology capable of as broad an application as possible, this flexible approach offers the best hope of arriving at comparable international measures. That is not to say that individual countries or groups of countries should not attempt, in addition, to devise other forms of monetary evaluation based, for example, on notions of the value of reductions in the risk of illness, of distinctions between private and social cost, on the distribution of costs and benefits, and so on. Such calculations however, would supplement rather than replace the basic methodology.

In the case of viral hepatitis B, significant progress might be made by estimating in detail the indirect costs of the disease in particular high-risk groups such as:

- (1) medical and other health care personnel,
- (2) multiple-transfused patients,
- (3) patients with chronic renal failure, with certain malignant diseases, and with other natural or acquired immune deficiency states,
- (4) residents of large institutions.

A possible outline or check-list of headings under which direct and indirect costs might be recorded is set out in Annex I.

3. Further points of discussion

In the discussions which followed the presentations many problems were highlighted, and many participants drew upon the experience of their own countries to illustrate the difficulties which would be encountered in practice when the study got under way. Some of the main points which were made are summarized here.

It was constantly emphasized that, since the main purpose of the study was to develop methodology, it would be foolish to impose too rigid a strait-jacket on the participants in the estimation of costs. Nevertheless, there had to be a basic similarity.

Although it was acknowledged by all that viral hepatitis was a name covering at least two distinct diseases, an attempt should be made to assess the cost of the impact of viral hepatitis as a whole. Type A was declining in importance but was still a major cause of disease in many Member States. It was also realized that in many cases the diseases were not recorded separately in routine figures.

A profound problem was caused by the unreliability of data on the incidence of hepatitis and on the proportion of the incidence accounted for by types B and non-B. It was eventually agreed that, however the participants decided to estimate the incidence of the diseases, the important thing was to describe the assumptions upon which the estimation was based as clearly as possible in order to facilitate comparison between countries. Some participants might choose to confine themselves to published national statistics. Others might wish to correct those figures by reference to specific or local ad hoc statistical studies; it was essential to make it clear what was being done.

Practice in the detection, prophylaxis and care of viral hepatitis clearly differed greatly from country to country. Some countries, for example, hospitalized almost all patients, whereas others hospitalized very few; some countries made extensive use of human immunoglobulin and of screening tests, while others made less use of them. Since the purpose of the study was to estimate actual costs, the main task at that stage was not to decide what should be done, but to calculate the cost of what was actually being done.

It was stressed that the pilot study could provide an opportunity to improve sources of data on viral hepatitis. In any case, the study should make as explicit as possible the effects of viral hepatitis in terms of morbidity and mortality and of its complications and sequelae. When estimating direct and indirect costs, the extent to which type B hepatitis progressed to chronic liver diseases should be made explicit.

The costs should refer to a specific year, but the choice of year should be left to the participants. It was agreed that, in estimating costs, participants could proceed where applicable from the estimation of unit costs¹ to the estimation of total costs.

Although this study is intended primarily to develop methodology as a basis for further studies, it may already provide information which may be used by health planners to compare the relative costs of different practices in respect of hepatitis.

As to future action, it was agreed that participants would discuss with their governments the possibility of carrying out a study of the costs of viral hepatitis as outlined in this report.

It was agreed that a report of the meeting, together with a covering letter recommending the study to Member States, would be sent out as soon as possible. It was hoped that it might be possible to obtain agreement from a significant number of Member States by ~~October 1977~~, and to complete the study by ~~June 1978~~. A review could then be held in ~~October 1978~~. At that time, suitable subjects for cost/benefit or cost/effectiveness studies in hepatitis would be chosen. Common protocols for those studies would be designed and then processed in the same way.

The WHO Regional Office for Europe would act as coordinator at all stages of the present and succeeding studies. The Office was asked to ensure that relevant information on experience gained should be made available to all participants.

¹For example, cost per hospital-bed-day for type B hepatitis; cost per hepatitis B-positive blood donor; average wage lost per month; average income loss per year.