Chapter 10

Prospects and Problems for the Economic Evaluation of Genetic Testing

Contents

Table

Chapter 10

Prospects and Problems for the Economic Evaluation of Genetic Testing

Introduction

Genetic testing in the workplace has potential benefits and costs to workers, employers, and society as a whole. The magnitude of those benefits and costs and their distribution among the sectors of society will help determine the desirability of this approach to improving occupational health. The techniques of economic evaluation—cost-benefit and cost-effectiveness analyses—are methods for collecting, organizing, and presenting evidence about the benefits and costs of alternative courses of action. They are systematic approaches to examining the tradeoffs among the different kinds of consequences—for example, dollar outlays today versus improved levels of health 5 years hence—stemming from a decision.

The usefulness of economic evaluation rests on its ability to improve decisions. Even when economic analysis is severely limited by uncertainties about the magnitude, direction, or value of certain consequences—as is the case with genetic testing—it can still be a useful exercise. The very identification of key areas of uncertainty, for example, can be used to set priorities for further research, It can also show how sensitive the results of an analysis are to changes in assumptions concerning these uncertain elements of the decision.

This chapter considers the fundamental principles and limitations of economic evaluation and proposes a general framework for economic evaluation. Then, the specific issues and problems that arise in applying the framework to genetic testing are discussed. The goal is to illustrate the kinds of information that are currently available to support such analysis and the present level of knowledge about the costs and benefits of these approaches to occupational health.

Economic evaluation in health

The analytic pillars of economic evaluation are cost-benefit and cost-effectiveness analyses. They share a common purpose—to help decisionmakers understand the consequences of the choices before them. This objective is approached from different perspectives under the two techniques. Consequently, each technique has strengths and limitations that make it more or less acceptable to analysis of particular problems.

General principles

In theory, a cost-benefit analysis identifies, quantifies, and places a value on all consequences, both positive (benefits) and negative [costs) arising from each possible alternative course of action. If all such consequences are valued in the same unit of measure (for example, dollars), the decisionmaker would merely have to tally these values and compare them across all possible alternatives. The alternative with the highest level of net benefit (or lowest net cost) would be preferred to all others.

In practice, no cost-benefit analysis is ever completely comprehensive or accurate in measuring consequences, and the valuation of such consequences, even when they can be measured, is replete with conceptual and methodological difficulties. Consequently, in practice a cost-benefit

98-986 0 - 83 - 11

analysis is not a definitive decisionmaking tool but rather a useful framework for arraying information (11).

Indeed, the Achilles' heel of cost-benefit analysis is its need to assign a monetary value to all measured consequences of each alternative. This value is generally accepted as the sum of the values of the consequence to each affected member of society. But how does one assess the value that a person places on a reduction in the probability of early death, pain, or discomfort associated with illness, especially when the changes may occur at different times in the future? The question of how to value consequences has been addressed at length in the cost-benefit literature (11). Methods do exist (some of which are discussed below) that are generally accepted by economists as reasonable for assigning monetary values to some important consequences. None, however, is completely satisfactory, and the technique of cost-effectiveness analysis was developed to sidestep the valuation problem.

In cost-effectiveness analysis, the monetary costs of an alternative are compared with one or more measures or indexes of effectiveness, such as "number of lives saved,"" number of life-years saved, " or "quality-adjusted life-years saved" (11,16). The effectiveness measure must act as a surrogate for all of the nonmonetary consequences that are otherwise unmeasured. Only those alternatives whose consequences are well represented by the selected effectiveness measure should be compared with one another. Consequently, cost-effectiveness analysis can be used to compare only a narrow range of alternatives. Whereas cost-benefit analysis is theoretically powerful enough to compare widely different alternatives, such as occupational health programs versus housing programs, cost-effectiveness analysis can be used only to compare alternatives with the same or a very similar range of nonmonetary consequences, such as different approaches to reducing workers' exposure to a particular industrial carcinogen.

Economic evaluation does not require the aggregation of all benefits and costs into a single index. Recently, some scholars have advocated a social accounting approach in which all of the important dimensions of benefit and cost are arrayed and, to the extent possible, their magnitude estimated (11,17). Some dimensions would be measured in dollars, some in physical units, and some in constructed scales. The decisionmaker would have a balance sheet showing the performance of each alternative on each dimension. The advantage of this disaggregated approach is that important but hard-to-measure consequences of an alternative will not be ignored. However, if many dimensions of outcome are important but cannot be measured precisely, the enumeration of effects can obscure rather than clarify the differences among alternatives.

Identifying and measuring consequences

What are the consequences of alternative strategies for achieving occupational health? Such strategies typically reduce exposure to illness- or injury-causing hazards. This exposure reduction presumably lowers the incidence or severity of occupational illness. These positive health effects are bought at the price of the occupational health program expenditures. But the positive health effects of the program also mean reductions in the cost of illness. The cost of illness has three components, each of which maybe altered by the program's health effects. First, the reduction in the incidence and severity of illness over workers' lifetimes will mean fewer expected expenditures for health and medical care at various points in the future. The discounted value* of these immediate and future monetary outlays is called the direct cost of illness.

The consequences of a strategy do not end with these direct costs. When a worker dies or falls ill, his or her productivity is lost or diminished. This productive activity has a value in the market place, and its loss is referred to as the indirect cost of illness. Thus, a program that improves worker health will reduce the indirect cost of ill-

*An outlay in the future cannot be compared directly with one made today because the postponement of the expenditure allows for the investment of those funds in alternatives and because people prefer a benefit today to one in the future. The value of the future expenditure must therefore be discounted by a rate equal to the return from those alternative investments.

ness as we]]. But the consequences of illness go still further. Quite apart from its effect on productivity, illness brings about pain, suffering, anxiety, emotional distress, and grief in patients, their families, friends, and others. The value of these losses are the psychosocial costs of illness (l).

The "benefit" of an occupational health strategy is the value of changes in these costs of illness due to the program, The goal of cost-benefit analysis is to measure the impact of a program or strategy on the cost of illness and to compare this benefit with the cost of the program. If the difference between benefit and cost is positive, society would be better off if it were to implement the strategy. If the net benefit is negative, however, the program is not worth its cost. The assumption underlying these conclusions is that all of the costs and benefits can be quantified.

The challenges to measurement and valuation of the cost of illness are great, even when the health effects of a program are known with precision. There are two different conceptual approaches to measuring the cost of illness: human capital and willingness to pay, Illness is something that people are clearly willing to pay to avoid, and in theory, this willingness to pay is the value of the health benefits resulting from a program. But for a variety of reasons it is not easy to determine how much people would be willing to pay to reduce, say, the probability of contracting a given disease at some point in the future. * Consequently, most cost-benefit analyses employ the human capital approach to valuing benefits.

The human capital approach measures only those benefits that have a value in the market place: the direct and indirect costs of illness. Psychosocial costs are left to be considered in some other way. Under this method, the value of lost production due to illness or death is measured by the market price for workers' labor. Occupational health strategies directed toward those members of society with lower wages or lower rates of participation in the work force, such as women, minorities, and the elderly, therefore would be valued at less than those aimed at others.

*For a discussion of the willingness-to-pay concept, and the difficulties of measuring it, see ref. 6.

Cost-effectiveness analysis typically does not involve the valuation of either the indirect or psychosocial costs of illness. The effectiveness measure (such as life-years saved) presumably acts as a proxy for both of these. The net costs of a program are defined as the sum of the direct program cost and the change in the direct cost of illness-that is, present and future medical care costs. If this net cost is negative, the program is cost-saving without even considering effectiveness. But if program expenditures outweigh the discounted value of savings in direct medical care costs, ratios of net cost to effectiveness then are constructed for each alternative under study.

The cost-effectiveness approach also contains built-in value judgments, For example, the "life-years saved" measure would treat 10 extra years of life to a 45-year-old patient the same as 10 extra years of life to a 70 year old, There is substantial evidence from survey research that the value of these outcomes is not the same in most people's minds (4), but a cost-effectiveness analysis using the life-years measure would not be able to account for such differences.

problem of value judgments

Biases and value judgments are inherent in all economic evaluations, no matter how comprehensive. Value judgments creep in through the framing of the question, the choice of measures of benefit, effectiveness, and cost, the choice of data sources, and the design of measurement instruments, A value judgment also is present in the general neutrality of economic evaluation toward the winners and losers of a decision, Each alternative will affect the distribution of benefits and costs among segments of the population. These differences generally are netted out in economic evaluations under the assumption that if the winners could more than compensate the losers, society as a whole would be ahead, whether or not the compensation actually takes place. * In reality, of course, such compensation rarely occurs; consequently, economists increasingly have come to view the analysis of distributional consequences of alternatives as a fundamental element

*For a discussion of the compensation test, see ref. 7.

of economic evaluation, especially when they are major (17).

Perhaps the most important value judgment in any economic evaluation is the definition of alternatives, Relevant alternatives can be easily excluded from consideration simply because they are not recognized at the time the study is designed. In genetic testing, the definition of a strategy must include not only the testing protocol and procedures, but also the followup and enforcement activities that follow testing. Minor modifications in the definition of a genetic testing strategy, such as the inclusion or exclusion of counseling services for employees, can have major effects on program costs, anticipated health effects, and psychosocial consequences. Yet, available funds may limit the number of alternative strategies that can be compared, so choices must be made as an analysis is designed. Often, one cannot be certain that the best strategy has been included as an alternative in the study.

Framework for economic evaluation

There are five critical elements of any economic evaluation, be it cost effectiveness, cost benefit, or some hybrid of the two. This section identifies and discusses the five components.

Alternatives compared

The most important characteristic of an evaluation is the set of alternatives chosen for study, since the usefulness of an analysis for any decision depends on the choice of relevant alternatives. There are two entirely different kinds of relevant alternatives for genetic testing in the workplace. The first involves strategies for research on genetic testing, including development and refinement of the testing technology and epidemiological and clinical research on the relationship between occupational exposure and disease in various human populations.

The second set of alternatives involves the use of these tests to screen or monitor specific worker populations with the purpose of following up on the test results with strategies to reduce exposure. These are strategies of intervention, as opposed to research.

It is possible to structure the research question as one for economic evaluation on the rationale that limited research resources should be allocated to projects that can promise the highest ratios of benefit to research cost. But the measurable benefits of research rest largely on the benefits of the interventions subsequently made possible by it. Thus, even economic evaluations of alternative research strategies must consider interventions. To date, the use of economic analysis as a guide for biomedical research has been limited. This is primarily the result of the inherent difficulty of predicting the outcomes of research projects, their timing, and even their probability of occurring. Consequently, the discussion in subsequent sections will concentrate on alternative strategies for implementation of genetic testing.

Population studied

The definition of the population to which the alternatives apply is also an important attribute of any analysis. A comparison of two alternatives can have widely different results depending on the characteristics of the population. For example, the potential importance of age as a factor in susceptibility to exposure argues for separation of populations into age groupings. Narrowly defined populations have an advantage in that the interpersonal variation in measured costs and benefits is low. On the other hand, if the worker population is defined so narrowly that few fall into each category, the analysis may lack the statistical power to identify differences among alternatives even when they actually exist.

The population also may be defined so narrowly that the benefits and costs associated with a strategy cannot be achieved in actual practice, Consider, for example, the costs and benefits of genetic screening for thalassemia trait in workers. If the study were to compare alternatives only for workers in specific high-incidence ethnic or racial groups, the results might be irrelevant for the actual operation of an occupational health program, where it may not be ethical or lawful to require the test on the basis of race or nationality. In other words, an economic analysis might show the desirability of screening for thalassemia trait if the procedure were limited to blacks and Mediterraneans, whereas in reality no screening program could be limited to that population.

The consequences considered

As discussed earlier, an economic evaluation may be characterized by the range of consequences (costs and benefits) included in its purview. It is possible to consider only the direct costs of a program. If, for example, a screening program can be shown to reduce net direct costs (consisting of the sum of the cost of administering the program and the net reduction in the discounted costs of present and future health care), consideration of other consequences, such as the indirect and psychosocial benefits, may be unnecessary. However, a usual precondition to the accurate estimation of the net direct costs of a strategy is the ability to estimate the impact of the program on the health of workers and therefore on their need for medical care. Thus, even ignoring the indirect and psychosocial costs, economic evaluation generally cannot evade the need for some estimate of a strategy's health effects.

Inclusion of indirect cost impacts into an economic assessment adds an additional degree of complexity to the evaluation problem. Even when it is possible to assess the impact of a program on the incidence of disease, it may be difficult to assess its impact on the person's ability to work at his or her level of productivity.

Methods for aggregating consequences

The consequences of any action will be distributed over time and among the members of society. These effects must be aggregated into coherent summary measures if the analysis is to be useful to decisionmakers.

The usual approach for dealing with effects occurring through time is to discount future costs or benefits by an appropriate rate. The further away in the future that a consequence will occur, the less importance or value it will have when discounted, There is no generally accepted '(correct" rate at which future consequences should be discounted to their present value. Discount rates of 3, 5, and 10 percent per year are common, Even nonmonetary effectiveness measures such as '(lives saved" are often discounted in economic evaluations, though it is difficult to determine the appropriate discount rate for these kinds of effects. Estimates of lifetime direct and indirect costs vary widely with the choice of discount rate (3,6).

Aggregating consequences across individuals also is necessary. Two issues are pertinent to the aggregation methods employed. The first is the statistical issue of the best measure to represent a potential distribution of impacts. Commonly accepted measures such as the mean or median may obscure important effects occurring in a subset of the population. The direct and indirect costs of large changes in health status may be quite different from those of smaller changes, and measures such as the mean may not reflect these important differences.

The second issue is one of equity. Consequences are likely to be differentially distributed among sectors of the society, Exposed workers comprise one affected group, the industrial employer another. Workers in other industries and the general public are other affected sectors. Analyses can be, but rarely have been, structured to show how the costs and benefits of a program are distributed among these groups.

Study design

All analyses ultimately rest on estimates of the expected effect of each alternative on the consequences of interest. How these estimates are derived will determine their validity and, hence, the validity of the economic evaluation itself. *Thus,* the issues inherent in study design in general—internal and external validity-are important in economic evaluation as well (2).

Most economic evaluations contain one or more estimates that are based on assumptions or rules of thumb. Estimates are often necessary because of a lack of data. When such estimates are included in the analysis, however, validity necessarily suffers. An accepted procedure for dealing with uncertainty is to conduct a sensitivity analysis, a study of the impact of changes in assumptions on the findings of the evaluation. If the results of the analysis are insensitive across the entire reasonable range of correct values (that is, the most preferred alternative remains so regardless of asgumptions), then its findings can be considered valid.

Using the framework

The five components of economic evaluation described above define the analysis. In structuring an evaluation, it is necessary precisely and fully to define the alternative strategies, specify the population to which the alternative strategies will apply, determine the consequences to be included and the methods of measurement, select methods of aggregating consequences over time and across individuals, and identify those estimates whose validity is sufficiently suspect to warrant sensitivity analysis. These steps will be applied in the next sections as the use of economic evaluation for analysis of genetic screening and cytogenetic monitoring is explored,

Economic evaluation of genetic screening

To carry out an economic evaluation of genetic screening in the workplace, the following kinds of information must be available:

- a detailed description of the proposed testing strategy, including followup procedures,
- estimates of the prevalence of the genetic trait in the worker population under study, and
- estimates of the differential effect of worksite exposure on the incidence and severity of disease in the target population.

Genetic screening programs consist of a family of strategies for identifying and reducing exposure of workers with particular genetic traits. A strategy may or may not include counseling of workers with positive test results. The costs and benefits of any such program will depend not only on the type of screening test but also on the followup actions associated with positive and negative test results. For example, a preemployment screening test might result in job denial, whereas a program for employed workers could result in transfer or termination. Alternatively, the choice might be left to the employee, who could remain in the position, request a transfer, or resign. Each of these strategies has different implications for costs and benefits and for the distribution of these consequences among the sectors of society.

The definition of the strategy also depends on the configuration of the screening program itself. Since the tests for detecting genetic conditions are rarely perfectly sensitive or specific but involve some false positive and false negative results, the testing strategy may well include retesting of all those with initial positive results, Or, when two or more different tests, one more costly than another, are available to detect a condition, the testing strategy might consist of a broad screening with the less costly procedure and using the more expensive test to retest positives. Program costs will depend on the configuration selected,

The prevalence of genetic traits in worker populations also may vary. Some susceptible workers may self-select themselves out of high-risk environments. Therefore, reliable data on the prevalence of a trait in given populations is not always available.

The benefits of a genetic screening strategy presumably are manifested in the reduced incidence of the disease associated with the genetic trait.

A necessary condition for such an impact is that the person with the condition be truly at enhanced risk because of exposure to hazardous substances found in the work environment, and the followup action must reduce the probability of the disease. Thus, the complicated chain of relationships between the existence of a genetic trait, occupational exposure to a hazardous agent, and disease onset must be known if the effects of a strategy on worker health are to be estimated. At present, the evidence is generally inadequate to assess the relationship between genetic traits and increased susceptibility to industrial exposure. Yet, even lacking data on these basic relationships, economic evaluation can provide some insights that may assist in decisionmaking regarding the use of genetic screening.

As an example of how economic evaluation might proceed, consider screening for heterozygous serum alpha$_1$-antitrypsin (SAT) deficiency in work environments containing respiratory irritants. This condition has been selected as an example because estimates of its prevalence in the general population are available and some work has been done to estimate the economic costs of the illness it may provoke-emphysema. Evidence has accumulated that people who display an intermediate deficiency of SAT are at increased risk of developing emphysema. Assume for the purposes of this example that a correlation has been shown between intermediate SAT deficiency and an increased risk for respiratory disease in work environments containing respiratory irritants. About 3 to 4 percent of the population in the United States is thought to have this genetic condition. Tests for SAT deficiency are relatively inexpensive. Suppose a large-scale screening program could be implemented for $20 per person. The cost of screening 1,000 workers, then, would be $20,000. Assume also that a worker with a positive test result is removed from an environment containing respiratory irritants. The following question can be asked: How many cases of emphysema would have to be prevented or delayed by such an action to make the test program pay for itself in direct and indirect benefits? The direct and indirect costs of emphysema in 1979 were estimated at $1,300 per person* (10). If this estimate is accepted as accurate, the screening program would have to prevent 15.3 cases of emphysema (in the 1,000 workers screened) in order to pay for itself in direct and indirect cost savings. This implies that emphysema would have to be prevented in 37 to 50 percent of the SAT-deficient workers detected in the screening program.

Since estimates of the average cost of a SAT screening test and the direct and indirect costs of emphysema are uncertain, an analysis of the sensitivity of the break-even point to different values of these parameters is shown in table 17. The practical lower limit of the average cost of a genetic screening test is about $5. * * At this unit cost, the break-even number of cases declines to 8 to 16 percent of the SAT-deficient population. Although there are no epidemiological studies relating different levels of exposure to respiratory irritants in work environments with increased risks of emphysema in SAT-deficient individuals,

*This estimate is only a rough approximation of the discounted lifetime costs associated with a new case of emphysema. It is an estimate of the costs incurred in 1979 by all then-extant cases of emphysema, These "prevalence costs" overestimate the lifetime costs of a new case because they are not discounted. Conversely, to the extent that the incidence of emphysema has been growing, the total costs in 1979 disproportionately represent the early and presumably less costly stages of the illness. The extent to which these sources of overestimation and underestimation compensate for one another is unknown. Good data on the incidence of emphysema in the United States do not exist; hospitalization rates have been decreasing since 1970, but the prevalence of the condition has been on the increase (9).

* *The average unit cost of a worksite hypertension screening program was recently estimated at $6 (13), Since hypertension screening involves minimal equipment and technician time, it is likely that it represents a lower bound on other types of worksite screening tests as well.

Table 17.—Hypothetical Break-Even Number of Cases Averted by SAT Testing per 1,000 Workers
(break-even percent of SAT-deficient workers)

Direct and indirect cost of emphysema	Cost per test: $20	Cost per test: $5
$1,040	19.2 (49-64%)	(12-41 %)
$1,300	15.3 (37-50%)	(10-31%)
$1,560	12.8 (32-430/o)	3.2 (8-10°/0)

SOURCE: Office of Technology Assessment.

it is known that only 10 percent of all SAT heterozygotes will develop the disease (8) and that emphysema may be brought on by multiple causes (5,8). Thus, the likelihood is low that a SAT deficiency screening program can be justified in terms of its impact on direct and indirect benefits. Moreover, additional research into the relationship between exposure and disease is unlikely to change this conclusion, given what is already known about the potential impact of screening on the incidence of emphysema,

This conclusion does not suggest, however, that the SAT screening issue should be put to rest. Psychosocial consequences have not been included in the analysis; these can be extremely important in a debilitating disease like emphysema. Suppose, for example, that a program of screening and subsequent removal of susceptible individuals from exposure is able to prevent emphysema in only 5 percent of SAT-deficient workers who would otherwise be exposed. This implies that society would incur a net direct and indirect cost of $1,460 to $11,800 for each case of emphysema prevented, depending on assumptions about screening costs, direct and indirect illness costs, and the frequency of SAT-deficient heterozygotes in the population tested. Is it worth up to $10,000 to prevent the psychosocial consequences of a case of emphysema? And how do these psychosocial costs compare to the psychosocial costs of a positive finding on a genetic screening test? Positive test results, whether correct or incorrect, may cause anxiety and disruption to people's lives (that is, psychosocial costs). This is especially true if workers are denied jobs or lose self-esteem because they are labeled as "susceptible. " Thus, the $1,460 to $11,800 net direct and indirect cost per case averted cannot be measured against only one type of psychosocial cost.

Note also that the different categories of cost would be borne by different actors. The costs of screening might be incurred by the employer (and ultimately in part by the public in higher prices) or by the government. The direct and indirect benefits would be shared by the individual worker and the public (through impacts on health insurance and disability programs), The psychosocial costs and benefits primarily accrue to workers themselves. Thus, the immediate monetary costs of a screening program are borne by the employer and the public, while the worker and the general public stand to gain monetary benefits in the future and workers may gain psychosocial benefits in the future at the expense of monetary and psychosocial costs in the near term,

It is interesting to compare the principles of economic evaluation with a set of criteria suggested by Stokinger and Scheel for applying genetic screening to the workplace (14). These investigators listed the following conditions that should be met for a genetic screening to be appropriate:

- the condition detected by the test should have a relatively high prevalence in the worker population;
- people with the condition should be susceptible to agents commonly occurring in industry;
- the genetic condition should be compatible with an apparently normal life until exposure occurs; and
- the test should be simple, inexpensive, and amenable to large-scale use.

These conditions are consistent with but more rigid than economic analysis. For example, it might be highly cost effective to screen for a rare condition if the testing cost is low and the health effects of exposure reduction are very large. The conditions of Stokinger and Scheel do not make such tradeoffs explicit, whereas an economic evaluation does.

The prevalence of a trait can be so high that genetic screening becomes impractical. A program consisting of genetic screening with subsequent removal of the worker from the high exposure environment must then be compared with other strategies for reducing exposure levels of all workers. If, for example, 70 percent of all workers are susceptible, it may be more cost effective to take general action to reduce exposure of all workers. How high the prevalence must become before screening is eclipsed by more general exposure reduction strategies depends on the particular situation. For example, slow acetylation rates have been linked to aromatic amine-induced cancer. Approximately 12)000 workers were exposed to these chemicals in the workplace in 1974

(15). Yet, about 50 percent of the U.S. population have slow rates of acetylation. Thus, it may be more effective to reduce exposure levels to all workers than to remove about half of the workers from the potential labor pool. The feasibility of either alternative would depend on the pervasiveness of exposure to the offending chemicals and the technical barriers to reducing ambient exposure levels. Of course, much more information would be needed before such an hypothesis could be accepted or rejected, but the question could be addressed through economic evaluation of the relelvant alternatives.

Whether one sees the SAT example given above as informative or misleading depends on expectations about the use to which the information will he put in decisionmaking. Critics of cost-benefit and cost-effectiveness analyses claim that incomplete analyses such as that provided above are given too much attention merely because the results are in a quantified form. Moreover, the unquantified effects, despite their importance, tend to be ignored because they are bothersome. Supporters of the approach Would claim that the analysis clarifies the central tradeoff between net direct and indirect costs to society and psychosocial benefits and costs to workers. Both sides would agree, however, that economic evaluation is severely, perhaps fatally, flawed when substantial uncertainty is present in the central estimates of effectiveness or benefit. Sensitivity analysis can remove some of the limitations, but when the results of the analysis are highly sensitive to estimates of cost or effectiveness, as they are in the case of SAT testing, economic analysis is of limited usefulness.

Economic evaluation of cytogenetic monitoring

The case for using cytogenetic studies to monitor workplace exposure to hazardous material rests on the hypothesis that exposure to mutagenic or carcinogenic agents is related to somatic chromosomal damage, which is in turn correlated with an increased risk of disease. If this hypothesis is accepted, and particularly if the relationship between exposure level, degree of chromosomal damage, and risk of disease is known and quantified, then cytogenetic tests might be used as biological monitoring devices for workplace hazards.

The potential uses of cytogenetic monitoring are to identify carcinogenic agents and to identify populations at risk due to overexposure to these agents. Ultimately it might be possible to use the tests to develop standards for safe levels of occupational exposure to chemicals and radiation.

It is difficult to lay out a specific strategy for evaluation of a cytogenetic monitoring program because of the profound lack of knowledge about the relationships between occupational exposure, chromosomal damage, and disease in human populations. For the sake of discussion, however, let us suppose that the research evidence were sufficient at this time to justify the use of cytogenetic monitoring to identify carcinogenic agents. Suppose that it has been established that there is a high correlation between chromosomal damage in a group and subsequent cancer rates. Then, employers might establish programs for periodic monitoring of workers who are routinely exposed to industrial chemicals. The cost of such a program would be highly sensitive to features such as the frequency of testing (that is, monthly, quarterly, yearly), the sample size in each testing period, the methods of recordkeeping and quality control, and the actual cytogenetic procedures employed. Cytogenetic studies are relatively expensive laboratory procedures. The estimated cost is between $100 and $300 per test, depending on a laboratory's volume and organization, although testing costs may be reduced in the future with the development of automated methods. At an average cost per test of $100, however, the features of the monitoring program make an enormous difference in program costs. For example, testing 500 workers once each year would cost $50,000, whereas a quarterly testing program of the same number of workers would cost $200,000 annually.

Both the costs and benefits of a monitoring program depend on the actions taken on the basis of its results. If significant chromosomal damage were followed by removal of the chemical from the workplace or some other method of exposure reduction, the major hypothesized benefit would be a reduction in the rate of exposure-induced cancer. The costs of exposure reduction would depend on the technical and economic relationships in the production process. If no action were taken, neither benefits nor additional costs would ensue. It is reasonable to assume that an expensive monitoring program would be undertaken only if some benefits could be expected; therefore, a program for exposure reduction must be assumed to be a natural sequel to cytogenetic monitoring.

To estimate the economic benefits of cytogenetic monitoring programs, it is necessary to know, or at least to estimate, the probability that the agents found in the monitored workplaces will be found to produce chromosomal damage, Further, precise analysis would demand that the impact of exposure on cancer rates be estimated with reasonable certainty. But if the latter were known, the need for a monitoring program of the type outlined above is questionable. Thus, the prospects are poor for reasonably accurate a priori estimates of the health effects, and hence benefits, of cytogenetic monitoring.

Though it is not possible now, and may never be, to estimate the benefits of cytogenetic monitoring with any precision, it is useful to consider the order of magnitude of the economic benefits that would result from each case of cancer that might be prevented by such a program. The direct and indirect costs per case of cancer were estimated in 1978 at about $22)000, consisting of $5,000 in direct and $17,000 in indirect costs* (12). These costs vary with the age of onset and the type of cancer, but they can be taken as a general guide to the order of magnitude of the monetary benefits associated with each case of cancer prevented. In a pioneering but highly speculative study, Abt attempted to estimate the combined indirect and psychosocial costs of cancer (1). These costs were estimated at $137,000 per case. Thus, even though this estimate is based largely on assumptions and rules of thumb, it illustrates the overwhelming importance of psychosocial costs in the consequences of cancer.

The stakes are clearly high on both sides of the issue. The costs of cytogenetic monitoring are potentially high, but the costs of cancer are also high. At present there is insufficient evidence to assess the value of cytogenetic monitoring because the relationships between chromosomal damage and clinically relevant effects have not been demonstrated. Yet, the magnitude of the costs involved argues for increased research into these relationships.

*These are prevalence costs. Possible sources of inaccuracy in these estimates are discussed in an earlier footnote,

Conclusion

Cost-benefit and cost-effectiveness analyses are economic methodologies that can be useful in structuring the analysis involved in decisionmaking and in assessing the desirability of alternative outcomes. The significant uncertainties associated with genetic testing, particularly the limited evidence of an association between endpoints and risk of disease, preclude the rigorous application of these tools to this technology. However, these tools can help identify the uncertainties involved and provide a rough sense of the benefits, burdens, and tradeoffs associated with genetic testing programs.

Chapter 10 references

1. Abt, C., "The Social Costs of Cancer, " *Social Indicators Research* 2:1 75-190, 1975.
2. Campbell, D., and Stanley, J., *Experimental and Quasi-Experimental Designs for Research* (New York: Rand McNally, 1963).
3. Hodgson, T., "The State of the Art of Cost of Illness Estimates, " draft paper(Hyattsville, Md.: National Center for Health Statistics, 1982).
4. Kalish, R., and Reynolds, D., *Death and Ethnicity: A Psycho-Cultural Study* (Los Angeles: University of Southern California Press, 1976).
5. Kazazian, H., "A Geneticist's View of Lung Disease)" *American Review of Respiratory Disease* 113:261-266, 1976.
6. Landefeld, J. S., and Seskin, E. "The Economic Value of Life: Linking Theory to Practice, " *American Journal of Public Health* 72(6):555-565, *1982.*
7. Mishan, E. J., *Cost-Benefit Analysis: An Introduction* (New York: F. A. Praeger Publishing Co., 1971).
8. Mittman, C., et al., "The PiMZ Phenotype, " *American Review of Respiratory Disease* 113:261-266, *1978.*
9. National Center for Health Statistics, Health Interview Survey, 1980.
10. National Heart, Lung, and Blood Institute, personal communication with Dr. Hannah Peavy, 1982.
11, Office of Technology Assessment, U.S. Congress, *The Implications of Cost-Effectiveness Analysis of Medical Technology* (Washington, D. C.: U.S. Government Printing Office, August 1980), OTA-H-126.
12. Rice, D., and Hodgson, T., "Social and Economic Implications of Cancer in the United States, " a paper presented to the Expert Committee on Cancer Statistics of the World Health Organization, June 20-26, 1978.
13. Ruchlin, H., and Alderman, M., "Cost of Worksite Hypertension Treatment, " U.S. Department of Health and Human Services, Public Health Service, NIH-81-21 15, November 1980.
14. Stokinger, H., and Scheel, L., "Hypersusceptibility and Genetic Problems in Occupational Medicine—A Consensus Report, " *Journal of Occupational Medicine* 15:7, *1973,* pp. 564-573.
15. U.S. Department of Health and Human Services, National Institute of Occupational Safety and Health, *Quarter@ Hazard Summary Report,* Aug. 6, 1980.
16 Weinstein, M., and Stason, W. "Foundations of Cost-Effectiveness Analysis and Medical Practices, " *New England Journal of Medicine* 296(13):716-21, *1977.*
17. Weisbrod, B. A., "Benefit-Cost Analysis of a Controlled Experiment: Treating the Mentally Ill," *Journal of Human Resources* 16:523-48, fall 1981.