An introduction to cost-effectiveness and cost–benefit analysis of pharmacogenomics

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Methods of economic evaluation, especially cost-effectiveness analysis and cost–benefit analysis, are widely used to examine new healthcare technologies. However, few economic evaluations of pharmacogenomics have been conducted, and pharmacogenomic researchers may be unfamiliar with how to review or conduct these analyses. This review provides an overview of the methods of economic evaluation and examples of where they have been applied to pharmacogenomics. We discuss the steps in conducting a cost-effectiveness or cost–benefit analysis, demonstrating these steps using specific examples from the pharmacogenomics literature.

Introduction

Methods of evaluating the costs and benefits of healthcare have become increasingly important due to the rising costs of healthcare, and the number of economic evaluations of healthcare has increased dramatically [1-3]. Economic evaluations assess the trade-offs of scarce resources that result from utilizing health technologies by comparing competing healthcare alternatives. Cost-effectiveness analysis (CEA) and cost–benefit analysis (CBA) in particular provide decision-makers with a framework whereby they can make decisions regarding healthcare provision, insurance reimbursement, and drug development given a fixed budget and competing choices. By comparing the relative value of interventions, CEA provides a way to illuminate the lost health benefits – longer life or decreased morbidity – of not selecting the next-best alternative [4,5]. Several articles have noted that pharmacogenomics has the potential to influence not only health outcomes but also the delivery and cost of healthcare. However, there have been few studies to empirically evaluate this impact [6-9].

To ensure that pharmacogenomic technologies can be implemented in an efficient and cost-effective manner, it is critical that the methods of economic evaluation in healthcare are applied to pharmacogenomics [10-13].

The objectives of this review are to:

- Provide an overview of the methods of economic evaluation in healthcare, particularly cost-effectiveness and CBA, and how they apply to pharmacogenomics.
- Discuss the steps in conducting economic evaluations, using specific examples from a systematic review of the pharmacogenomics literature.

Several guides to conducting economic evaluation and CEA have been developed [4,5,14-16]. We previously developed a framework for evaluating the potential cost-effectiveness of pharmacogenomic technologies [3]. This study expands our previous work to include a more detailed review of the methods of economic evaluation as applied to pharmacogenomics by discussing the specific steps in conducting CEA and CBA of pharmacogenomics. We use specific examples identified from a systematic search of the literature. The methodology used for our systematic search is discussed in detail elsewhere [17].

Our literature search identified six studies that examined the cost-effectiveness of pharmacogenomics [18-23]. We used a broad definition of pharmacogenomics that included the use of genetic information to target drug therapies based on either inherited (host) or acquired (e.g., tumor or viral) mutations. Two studies were on genotyping for deep vein thrombosis (DVT) and two of the studies evaluated genotyping hepatitis C virus (HCV) compared to an array of alternative pretreatment strategies to determine subsequent drug treatment. Another study evaluated genotyping HIV-1 to identify variants with drug resistance [18] and the final study conducted a CEA of screening for thiopurine S-methyltransferase polymorphism (TPMT) prior to treating patients suffering from rheumatological conditions with azathioprine [23]. Four of the six studies found genotyping to be relatively cost-effective [18,21-23], while two studies found it to be less cost-effective than other options [19,20].

Methods of economic evaluation

Methods of economic evaluation provide a quantitative framework for evaluating the
complex and often conflicting factors involved in the evaluation of healthcare technologies [3]. Importantly, it helps ensure that all costs and benefits resulting from a healthcare intervention have been properly evaluated. There are several types of economic evaluation that are used in healthcare: cost-minimization analysis, cost-consequences analysis, CBA, CEA, and cost–utility analysis (CUA) (Table 1). These methods vary primarily in the way they measure health outcomes, for example, in monetary terms, natural units such as life-years gained or lives saved, or quality of life adjusted life expectancy, or in the case of cost-minimization analysis the assumption that health outcomes are identical.

Although CEA is a specific type of economic evaluation that measures cost in relationship to tangible outcomes gained, such as life-years saved, the term is commonly used (sometimes mistakenly) to refer to all types of economic evaluation in healthcare. CUA is a specific type of CEA, which has become widely accepted in healthcare because it measures benefits in patient-oriented terms (quality of life) and permits comparison between different interventions by standardizing the denominator. CBA values both costs and effects (benefits) in monetary terms, presented either in the form of a ratio or net benefits. To illustrate, if we conducted a cost-effectiveness study comparing genotyping versus not genotyping prior to the administration of a drug for individuals with a known mutation A, our result might be US$10,000 per life-year saved. On the other hand, a CUA might obtain a result of US$9,000 per quality-adjusted life years and a CBA might obtain a result of net benefits of US$500.

In this study, we focus on the methods relevant to CEA, CUA, and CBA because these are the most commonly used and accepted approaches for evaluating healthcare technologies. However, the steps we discuss apply generally to all forms of economic evaluation. For the purposes of this review, we do not distinguish between the use of the terms ‘pharmacogenetics’ and ‘pharmacogenomics’.

Steps in conducting economic analyses
The US Panel on Cost-Effectiveness in Healthcare provided general recommendations for

<table>
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<tr>
<td>Cost-minimization</td>
<td>Used when effects are identical; compares costs only</td>
<td>Easy to perform</td>
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<td>Cost-consequences</td>
<td>Values costs and benefits of each comparison program separately and often with an array of outcome measures without comparing the benefits or indicating their relative importance</td>
<td>Data presented in straightforward fashion</td>
<td>A ratio is not calculated, thus making comparisons of health interventions difficult</td>
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<td>Cost–benefit</td>
<td>Values all costs and all benefits in monetary terms</td>
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<td>Less commonly accepted by healthcare decision makers. Evaluation of benefits methodologically challenging</td>
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<td>Cost-effectiveness</td>
<td>Values all costs in monetary terms while effects of comparison programs are valued with a relevant health outcome, such as, ‘mmHg drop in diastolic blood pressure’ that is common to all comparison programs</td>
<td>Relevant for clinicians. Easily understandable</td>
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<td>Cost–utility</td>
<td>Values all costs in monetary terms while effects of comparison programs are valued with quality adjusted life years (QALYs)</td>
<td>Incorporates quality of life by adjusting changes in life-years for differences in health benefits/effects. Comparable across disease areas and interventions</td>
<td>Quality of life requires evaluation of patient preferences. Can be difficult to interpret</td>
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In this study, we focus on the methods relevant to CEA, CUA, and CBA because these are the most commonly used and accepted approaches for evaluating healthcare technologies. However, the steps we discuss apply generally to all forms of economic evaluation. For the purposes of this review, we do not distinguish between the use of the terms ‘pharmacogenetics’ and ‘pharmacogenomics’.

Steps in conducting economic analyses
The US Panel on Cost-Effectiveness in Healthcare provided general recommendations for
Step 1: Define research question and study framework

- Develop concise, clear, and answerable research question
- Conduct literature review to determine what is currently known
- Define current and potential interventions; state perspective for analysis (societal, payer, insurer etc.); define population (including prevalence of the relevant disease and mutation); define time horizon to include all relevant future effects of intervention

Step 2: Assess costs, benefits/effects, and outcomes

- Determine data sources and type of model to be used
- Develop estimates for costs, benefits/effects, and outcomes
- Adjust costs and benefits/effects for time (discounting)
- Describe the conceptual model using an event pathway (decision tree)

Step 3: Calculate and present results

- Calculate and present primary results
- Conduct sensitivity analyses to assess the impact of changing the data inputs and model

Step 4: Interpret results and place into context

performing cost-effectiveness analyses [4]. These general recommendations, together with other key guides (e.g., [5,14-16]), provide the framework below.

Box 1 summarizes the steps to conduct an economic evaluation. Each step includes several illustrative points, which may be relevant to specific analyses. We illustrate these steps using examples gathered during a systematic review of the literature of economic evaluations of pharmacogenomics [17].

Step 1: Define research question and study framework

a) Develop concise, clear, and answerable research question
In general, defining the research question involves steps that are not unique to pharmacogenomics studies and is similar with respect to demonstrating any question’s significance. A description of the basic problem underscores the pharmacogenomic strategy’s significance and describes the relevant alternative drugs or therapies. This step is particularly important to pharmacogenomics because it includes the prevalence of the disease and/or mutation, and the known morbidity and mortality, as well as detailing the current known costs of disease and/or mutation effects. It has been noted that most single-gene mutations are uncommon, most mutations do not have a phenotypic effect, and mutations may contribute to but not necessarily cause diseases [24]; thus creating potential barriers to developing the pharmacogenomic research question.

b) Conduct literature review to determine what is currently known
Because the field is rapidly changing, locating relevant literature on economic evaluations of pharmacogenomics is particularly important but also problematic. For example, PubMed does not include a medical subject heading (MeSH) term for pharmacogenomics, and thus the term pharmacogenetics has to be used. In addition, the available MeSH term for economic evaluations is cost–benefit analysis. Specific types of economic evaluations (e.g., cost-effectiveness analyses) are included underneath this broader term, with the result that it is more difficult to identify specific types of studies.

Another major barrier is that it does not appear that all relevant studies can be located using the MeSH term pharmacogenomics. Thus, in our comprehensive search, of cost-effectiveness evaluation of pharmacogenomics, we included the MeSH headings drug resistance/drug effects, drug resistance/genetics, genotype, and mutation as well as MeSH terms for the most relevant examples of genetic variations that effect drug therapy known to us at the time of our review. In summary, comprehensively locating the literature on economic evaluations of pharmacogenomics requires multiple search strategies using both MeSH subject terms and keywords.

c) Define current and potential interventions; state perspective for analysis (societal, payer, insurer etc.); define population (including prevalence of the relevant disease and mutation); define time horizon to include all relevant future effects of intervention
Initial decisions, such as the interventions to be examined, study perspective, and time horizon, are important for economic evaluations of pharmacogenomics to clearly frame and define the scope of the study. The study perspective is the determination of what group affected by the intervention will be considered in the evaluation. What will be considered relevant costs and benefits for evaluation can vary greatly according to the perspective chosen. Study perspective options include societal, insurer, payer, industry, and government, and are particularly important with respect to the costs that will be included in the analysis. For example, from the perspective
of the pharmacogenomics company, patient time costs such as lost wages may not be relevant while from the societal perspective the wages lost due to receiving healthcare or due to illness may be substantial. The time horizon is the period for which costs and benefits/effects will be collected for the analysis.

Such decisions will depend on the nature and purpose of the study but should be explicit at the start of the study to ensure that the appropriate model and data are collected. When the purpose of the study is to examine the broad allocation of health resources, and when comparability to other studies is important, the US Panel on Cost-Effectiveness in Health and Medicine developed guidelines for a typical or ‘reference case’ analysis [4]. For reference case analyses, the recommendations are to:

- use a societal perspective
- estimate costs and benefits or effects over a relevant long-run time horizon
- use as a comparison program/treatment the current standard of care and/or where appropriate a ‘do nothing’ approach
- use quality-adjusted life-years as the outcome measure
- use a discount rate of 3%

Of particular interest to pharmacogenomics is the specific population to be evaluated. First, as noted by Veenstra and colleagues [3], the prevalence of the gene mutation can greatly affect the resulting cost-effectiveness and net benefits of relevant interventions. Second, in the case of inherited mutations, a positive finding for a mutation in the proband may suggest testing for family members. The costs and benefits of such testing will differ from those of the proband but should be considered.

Underscored in the introduction of this review is the critical step of determining the proposed intervention’s effectiveness relative to an alternative. When conducting cost-effectiveness analyses, the proposed intervention is always compared to a comparison program. For example, a genotyping strategy prior to drug therapy might be compared to a phenotyping strategy instead of a ‘do nothing’ strategy. The choice of comparison program is very important in determining the validity and usefulness of the CEA results. The program chosen should be the one most likely to be replaced by the new program. When clinical trial data are not available comparing the proposed and current program, care needs to be taken to evaluate the use of indirect comparisons. In an economic evaluation of pharmacogenomics, there are essentially two effectiveness components: first, the effectiveness of the genetic test to identify the mutation carrier, and second, the effectiveness of the subsequent changes in drug therapy for the mutation carriers. As discussed further in the next section, these are critical aspects.

Example from systematic literature review
Weinstein et al. conducted a study to assess the cost-effectiveness of genotypic resistance testing for patients acquiring drug resistance through failed treatment (secondary resistance) and those infected with resistant virus (primary resistance) [18]. This study carefully defined the two research questions (secondary and primary resistance), the interventions (genotypic resistance testing and clinical judgment versus clinical judgment alone), perspective (societal), population (HIV-infected patients in the US with baseline CD4 counts of 0.250 x 10^9 cells/l), and time horizon (lifetime). Further, the authors specifically noted that they followed the ‘reference case’ recommendations to ensure comparability to other analyses.

Step 2: Assess costs, benefits/effects, and outcomes
a) Determine data sources and type of model to be used

Data can be obtained from a variety of sources including primary data collection as part of a clinical trial and secondary data obtained from the literature. Most economic evaluations also employ mathematical or simulation modeling to provide estimates for incomplete or unavailable data. Modeling is acceptable in cases where neither primary nor secondary data are available to estimate the effectiveness of the intervention. Models, however, should be based on realistic assumptions about the data and when possible, validated against other data. There are two main groups of models: decision-analytic models and epidemiological models. Decision-analytical models are most commonly used in economic evaluations, and would include models such as decision-trees and state-transition models such as Markov models. Epidemiological models have been used to model chronic diseases such as heart disease [25].

b) Develop estimates for costs, benefits/effects, and outcomes

The next step is to assess the data on costs, benefits/effects, and outcomes in order to incorporate
costs of the genetic test and of subsequent drug therapy, costs might include to initiating drug therapy, costs might include comparing genotyping versus not genotyping prior to initiating drug therapy, costs might include costs of the genetic test and of subsequent drug therapy as well as costs of genetic counseling (direct costs) and patient time costs to attend testing, counseling, and/or follow-up (indirect costs). The major cost components relevant in cost-effectiveness analyses are typically cost of healthcare services, costs of patient time, costs associated with care-giving, other costs associated with illness, and costs associated with the non-health impacts of the intervention.

Effects are measured in a variety of ways. A commonly reported approach is quality-adjusted life years (QALYs). QALYs incorporate the concept that alternative health interventions do not prolong a year of life equivalently. Using QALYs in economic evaluations allows for comparing health states associated with similar life-years but different morbidity. A second advantage of QALYs is that the relative value of programs across disease can be compared because the effectiveness outcome measure is the same.

QALYs are calculated by multiplying a 'quality' number between 0 (worst imaginable health) and 1.0 (ideal health) for various health states by the life-years saved by the intervention. In general, the utility numbers represent the satisfaction or happiness for different health states associated with either the disease and/or the drug. For example, suppose a drug to prevent disease X is given to an individual with mutation A but that drug X has as a side effect, daily nausea. If the individual gains one life year as a result of the drug but also suffers from nausea, the health state, daily nausea, might be valued less than ideal health and thus the QALY would be some value <1.0. On the other hand, it is possible that the individual does not take the drug and lives in a health state that is preferred over daily nausea but for less time. Given these two situations, it is entirely possible that QALYs will be the same or even greater for those not taking the drug. These quality values for the alternative health states, also known as utilities, are either estimated as part of the study or gathered from the existing literature.

A commonly used approach to measuring benefits in dollar terms for CBA is the willingness-to-pay (WTP) approach, which uses quantitative approaches to estimate how much people are willing to pay for a good, service, or reduction in health and well-being. Similar to obtaining utility values for health states, WTP values may be assessed directly (asking), indirectly (observing behavior), or obtained from the literature. Direct approaches use specific techniques, such as contingent valuation, to determine the individual's WTP. As a consequence of the time and expense required to collect WTP values and indeed the difficulties associated with asking people to value life in dollar terms, fewer CBAs have been conducted than other evaluation types for healthcare services.

Several aspects of measuring costs and benefits should be considered in pharmacogenomics studies. As noted by Higashi and Veenstra [1], one important consideration in pharmacogenomics studies is that the cost of a genetic testing strategy includes much more than the cost of the test itself. There are also potential induced costs such as long-term follow-up, testing of family members to assess heritable traits, and the costs of treatments pending the results of genetic tests. However, other potential uses of the genetic information obtained from testing can provide long-term benefits. This is most likely to occur when the genetic variation affects more than one drug, as with the P450 metabolic enzymes, for example. Thus, economic evaluations of pharmacogenomics will need to consider a wider range of possible effects and longer-term outcomes than analyses of some other healthcare interventions.

c) Adjust costs and benefits/effects for time (discounting)
It is generally agreed that both costs and benefits/effects should be discounted to net present value to take into account costs and benefits being realized at different times. Discounting the costs of a pharmacogenomic strategy adjusts for the perception that a dollar spent in the future is worth less than a dollar spent today. To help understand discounting costs, Gold et al. (1996) likened discounting to the interest paid for a loan received today (e.g., if I borrow US$100 today I might have to pay US$110 in the future), where a dollar paid in the future is worth
less than a dollar paid today. Although historically a 5% discount rate has been most commonly used, the US Preventive Services Taskforce recommended 3% as the primary rate with 5% used in sensitivity analyses [4].

d) Describe the conceptual model or event pathway
The conceptual model outlines an event pathway stemming from the use of the intervention to health outcomes. It includes both the series of health events and costs associated with those events. For this step it is often useful to draw a 'picture', such as a decision tree or flow diagram, that follows the patient from the relevant decision point (e.g., take genetic test or not take genetic test) through to the relevant end point (e.g., death). For example, Figure 1 shows a simple event pathway that could be the core of a larger decision analysis model that would include the associated probabilities and outcomes. A genetic screening program as a pretreatment strategy for prescribing drug XYZ might require that the patient agree to the test, adhere to any prescreening requirements (e.g., fasting), show-up to take the test, obtain a test result, and adhere to treatment and follow-up (Figure 1). Each of these steps is associated with costs such as the cost of the test and the cost of drug treatment and monitoring. Each step is also associated with effects such as changes in the probability of disease progression if the treatment is not followed or the adverse effects of a drug.

Such models can be analyzed using 'decision analysis', a systematic, quantitative approach for assessing the relative value of different decision options. Decision analysis is used for economic evaluations as well as other types of complex decisions where information is uncertain. Three commonly used software programs include using Decision Analysis by TreeAge (DATA 4.0™), Precision Tree® for MS Excel, and SMLTREE, which have been developed to simplify drawing and analyzing decision trees.

In the case of pharmacogenomic analyses, a key issue will be the effectiveness of the genetic test. Therefore, the researcher should consider characterizing genetic test performance according to its analytic validity (i.e., sensitivity and specificity), clinical validity (i.e., penetrance, positive and negative predictive values, and attributable risk), and clinical utility [26].

Example from systematic literature review
Marchetti [21] developed a decision analytic model using DATA 4.0 to compare two intervention strategies for patients with a first episode of DVT. Specifically, they used a Markov simulation model to trace events over time, and costs and effects were discounted at 3%.

Step 3: Calculate and present results
a) Calculate and present primary results
Results should generally include tables of the costs and benefits/effects for each intervention considered. Most importantly, these should include the relevant incremental cost-effectiveness ratios (ICER) (e.g., cost per QALY gained). Incremental ratios compare each intervention to the next most effective option after eliminating options that are dominated (i.e., have higher cost and lower effectiveness). It is also often useful to report total costs and benefits/effectiveness in addition to incremental costs and benefits/effectiveness, so that readers can understand how the overall results were calculated. For a CEA of pharmacogenomics comparing genotyping (1) versus not genotyping (2) prior to initiating drug therapy, incremental costs are calculated by subtracting the costs of the genotyping (C1) from the costs of not genotyping (C2). Similarly, incremental effects are determined by subtracting the effects of genotyping (E1) from the effects of not genotyping (E2). Thus, the incremental cost-effectiveness ratio represents "the difference in costs between the two alternatives to the difference in effectiveness between the same two alternatives (p 399)" [4]. Mathematically the ICER is given as:

\[
\text{ICER} = \frac{C_1 - C_2}{E_1 - E_2}
\]

In cost-effectiveness studies, incremental rather than average CEA ratios should usually be reported. Average cost-effectiveness ratios are typically determined with respect to the 'no-cost/’no-effect’ alternative and are mathematically given as:

\[
\text{Average cost-effectiveness ratio} = \frac{C}{E}
\]

Average cost-effectiveness ratios have the potential to confuse the reader and incorrectly misrepresent the cost-effectiveness of the alternatives. For example, suppose we are conducting a CEA to screen for gene X prior to initiating drug therapy. The total cost of not screening is US$5000 and the total effectiveness is 10 QALYs. For the alternative, screening, the total
cost is US$8000 and the total effectiveness is 12 QALYs. Therefore, the ICER for screening is \( \frac{(5000 - 8000)}{(10 - 12)} = \text{US$1500}. \) However, if the average cost-effectiveness for the screening program were presented, the reader might mistakenly think that the cost-effectiveness of screening compared to not screening was lower at \( 8000/12 = \text{US$667}. \) This simple example highlights how the average ratio might be confused with the ICER; in reality, the no screening alternative is often not associated with no-costs or no-effects.

b) Conduct sensitivity analyses to assess impact of changing the data inputs and model

There are two key sources of uncertainty in economic analyses: (1) parameter uncertainty, which is uncertainty about the true numerical values of the parameters used as inputs, and (2) model uncertainty, which is both uncertainty about the model structure and uncertainty about the combination of decisions made in the analysis. In a sensitivity analysis, critical components of the calculation should be varied and the results recalculated to determine how sensitive the results are to a specific input. For example, sensitivity analysis can show how the cost-effectiveness would differ if the genetic test were to decrease in price or if the prevalence of the mutation in the population was found to be greater than the best estimate. Sensitivity analysis can be conducted by varying the assumptions about one variable and assessing the effect on the evaluation of the decision (one-way analysis) or by simultaneously allowing assumptions about multiple variables to vary and reanalyzing the decision (multi-way analysis). The value of multi-way analyses is that they take into account interaction among the variables as well as the impact on the cost-effectiveness calculation.

Example from systematic literature review

Younossi [22] provides a table with total costs, incremental cost, total effectiveness, incremental effectiveness, and the incremental cost-effectiveness ratio for each of the six chronic hepatitis C treatment strategies. This study also provides a table that compares the incremental cost-effectiveness ratio with other accepted interventions. One-way sensitivity analyses, as well as best-worst case analyses and model validation, were also reported.

Step 4: Interpret results and place into context

The final step of a CEA of a pharmacogenomic strategy is to put the results into context for the reader and to clarify their meaning. This final step includes explaining the generalizability of the results from the study population to other groups and interpreting the external validity of the results. Other important discussions may include a review of results from other relevant studies and the distributive implications (i.e., who will gain and who will lose if a new strategy is implemented). As with other research studies, limitations that influence favorable cost-effectiveness should be explained to the reader. For example, suppose a clinical trial finds that a strategy to genotype both the proband and the first-degree relatives of the proband are cost-effective compared with no genotyping. While the positive result of the CEA is encouraging, a limitation to the cost-effectiveness might be that in a general population, as opposed to a study population, first-degree relatives of the proband would have to agree to genotyping. To generalize
the result might therefore require knowing the percentage of first-degree relatives for whom this could be expected.

Outlook and conclusion
In summary, we have provided an overview of the steps generally required to conduct and interpret an economic evaluation, and we have provided specific examples of published economic evaluations of pharmacogenomics for the reader to consider. This review is intended to provide the reader who may be unfamiliar with economic evaluation with a general guide that will assist with not only analyses of the cost-effectiveness of pharmacogenomics but also with the ability to understand and evaluate the published literature. However, the reader is cautioned that the general guidelines shown are neither exhaustive nor detailed with respect to calculating costs or defining the outcomes of interest. Important components of conducting economic evaluations are not discussed here. Readers embarking on their own economic evaluation of pharmacogenomics may find more detailed discussion in recommended texts [4,5,14].

In the future, economic evaluation will become increasingly important to assess the costs and benefits of pharmacogenomics. However, there are currently few economic analyses of pharmacogenomics, and studies cover a limited number of genetic mutations and diseases. Although the lack of cost-effectiveness evaluations of pharmacogenomics undoubtedly reflects the currently limited use of these technologies, it is important to systematically evaluate their likely costs and benefits before they are widely implemented. Previously [3,27], we identified key factors that are likely to determine the cost-effectiveness of pharmacogenomics, which need to be confirmed with empirical analyses:

- Prevalence of the genetic mutation and the disease in the population.
- Severity and cost of the disease or outcome the test is designed to predict or diagnose.
- Strength of the association between the genetic mutation and clinical outcomes (penetration).
- Availability of effective interventions that can be implemented on the basis of genetic information that provide a reduction in the relevant event rate over standard care.
- Cost, turn-around time, and accuracy of the test.

In conclusion, the expanded use of pharmacogenomics offers many potential clinical benefits but also many economic challenges. It will thus be essential that systematic, evidence-based technology assessments and economic evaluations be used to guide the incorporation of pharmacogenomics into clinical practice.

Bibliography
Papers of special note have been highlighted as either of interest (+) or of considerable interest (++) to readers.

   • Provides details on how to apply cost-effectiveness analysis to genetic testing.
   www.aapspharmsci.org.
   • Provides details on how to apply cost-effectiveness analysis to pharmacogenomics.
   • Widely used guide.
   • Widely used guide.
   • Provides overview of economic issues relevant to pharmacogenomics.


