Genetic Testing Decision Making: A Game Theoretic Model

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Abstract

Genetic diseases affect around 200,000 people in the United States (Cleveland Clinic, 2021). These are the result of mutations passed down through families leaving a history of disease by inheritance. Several genetic testing kits have become popular in recent years, and have led to positive outcomes for those affected by specific conditions which can be identified and treated before becoming more problematic later in life (e.g. BRCA). However, the decision about whether or not to take a test is not always clear-cut due to financial and psychological implications. For this reason, I have created a model that aids in the decision-making process for someone considering a genetic test. My analysis assumes that patients start with an initial belief about harboring a genetic mutation based on their family history of the disease. As patients receive results for genetic tests, this belief changes. Besides the initial belief, the two other inputs into this analysis are test accuracies and insurance thresholds[1]. At each given test accuracy and insurance threshold, some patients will opt to take the genetic test, and some will not, depending on their initial beliefs. There is a breakpoint[2] in initial beliefs in which the optimal choice switches from *not taking the test* to *taking the test*. As tests become more accurate, patients will become more confident in future health problems arising and more willing to pay for preventive procedures regardless of whether their health insurance will reimburse the costs. These dynamics are captured in the model discussed below.

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Human diseases arise from two primary sources: pathogens and genetics. Genetic diseases account for over one third of human diseases, and generally result from mutations in DNA (Vendette, 2019). The human body contains DNA, the molecule that codes for proteins to be produced. These proteins can perform various functions, which includes preventing hereditary diseases from developing. A mutation in DNA can prevent these preventive proteins from being produced, and therefore result in the disease developing. Since children inherit much of their DNA from their parents, existing mutations in a parent's DNA may be passed on to a child, making them more likely to develop a disease. The inheritable nature of these diseases instills a sense of dread in many inheritors, who are left unsure of whether they may develop the disease or pass the mutation on to their children. In recent years, scientists have developed methods to detect the presence of specific mutations in a person's DNA. Such methods can help patients know how to plan their lives better or undergo preventive treatment to minimize the chances that they develop a disease. However, taking a genetic test may not always be the most rational decision, depending on a variety of factors.

The cost of genetic tests vary, and many patients may not be willing or able to pay the price. Insurance companies don't always financially support the patient in undergoing preventive treatment after discovering mutations from a genetic test (although financial support is more common if the probability of the mutation existing is high enough).[3 4] If a test comes back positive (the test indicates the presence of a mutation in the patient's DNA), a patient may be incentivized to undergo preventative measures (e.g., breast removal for breast cancer). These treatments can be costly, and insurers are hesitant to cover the costs of procedures if the genetic test's results don't indicate a particular DNA mutation is present. A patient's financial standing plays a major role in their decision-making process. Poorer patients will be sacrificing more of their scarce resources to undergo genetic testing or associated preventive procedures. This paper aims to find a path for patients to know whether taking a genetic test is an optimal or suboptimal choice considering patients' varying circumstances.

Project Overview

The decision-making model described below is meant to analyze a patient's expected payoffs while factoring in their family history and financial conditions. Considering these variables, a patient can use this model to make optimal decisions.

The model first considers the most crucial decision: whether the patient should take the genetic test at all. The patient's decision depends on how much the insurance will be willing to support the cost of the genetic test. Next, the patient must decide whether they want to undergo preventative treatment based on the outcome of the genetic test *and* the probability that they may have a particular mutation. Using the terminology of game theory (See Game Theory section), all "players" (patients) start the "game" (series of decisions) with an initial "belief" (confidence) that they have a mutation responsible for developing a disease and that "belief" will change based on the outcome of the test(s). After the patient takes a genetic test, their "belief" that they have the mutation is updated. An insurance company may only support a patient if the insurance company's "belief" that the patient has the mutation is above a certain threshold. As such, the patient must consider whether the insurance company will support the patient's treatment or not. In addition, if a patient is still not confident that the updated "belief" is accurate, they may choose to retake the test. This can cause the "belief" to increase or decrease, potentially moving above or below the threshold. If a patient engages in multiple genetic tests,

the patient can become more certain in their decision making. However, taking genetic tests is not free, and the more times the patient takes a genetic test, the more money the patient will spend, thereby diminishing the total "payoff" the final result will bring.

I found that as the test accuracy increases, patients are more likely to take the test given their new beliefs are higher and the insurance will be more likely to support them. For accurate tests, the threshold[1] the insurance companies set does not change the breakpoint[2]. However, the insurance threshold becomes more prevalent as test accuracy decreases. With less accurate tests, a higher insurance threshold means a higher breakpoint, so fewer people are likely to take a genetic test. For example, if a test has a 90% accuracy, then there is no difference between a 60% insurance threshold and a 90% insurance threshold. However, for a 70% test accuracy, a 90% threshold increases the breakpoint by 3%, meaning fewer people will take the genetic test. To maximize the number of tests taken by people at risk, insurance companies, and any other policymakers, ought to lower the threshold at which they support treatment to incentivize more testing.

Game Theory

Game Theory is the study of how players should approach a situation to come to the optimal solution. This solution can maximize benefits for each player assuming they behave rationally. These games can occur over one step (all players make a single decision and assess the outcome) or multiple steps (both players make a series of decisions). A situation occurring over multiple steps (also called a multi-stage game) can be modeled by a 'game tree.' 'Game Trees' can show how a situation progresses; different people should make decisions based on the benefits that they might receive. At the end of each decision-making process, players receive what is called a payoff. Players will always want to maximize their payoff by the end of a game.

A multi-stage game is analyzed by starting from the end. Each outcome of the game tree is examined, and based on the chance that each outcome occurs, one can discover the average payoff of making certain decisions. By doing this, the optimal decision for each stage of the game can be found by working backwards until finding the set of decisions with the highest payoff. This process is referred to as backward induction. When this process is applied to genetic testing, payoffs are calculated based on what the patient currently knows about how likely it is they have the disease-causing mutation (their current belief).

Every time a patient takes a test, the patient's perceived probability that they have the disease-causing mutation updates. This updated belief is referred to as the posterior. The posterior can be calculated by multiplying the probability of a certain event and the prior belief and dividing that by the probability of the event. For instance, when looking at how the patient's belief changed after a positive test, consider their initial belief in the possibility they had the disease, and the accuracy of the test. The product of multiplying the patient's initial belief and the test accuracy gives the probability that the patient 1) has the mutation and 2) the test comes back positive. This is then divided by the probability that any positive result will return. This can be calculated by, again, multiplying the initial belief that the patient has the mutation and the probability the test was correct (true positive), and adding it to the initial belief that the patient did not have the mutation and the probability the test was incorrect (false positive). Every time an average payoff for a decision is calculated, it is done so based on what the patient currently thinks is the probability they have the mutation and considering that their payoff they undergo preventative treatment.

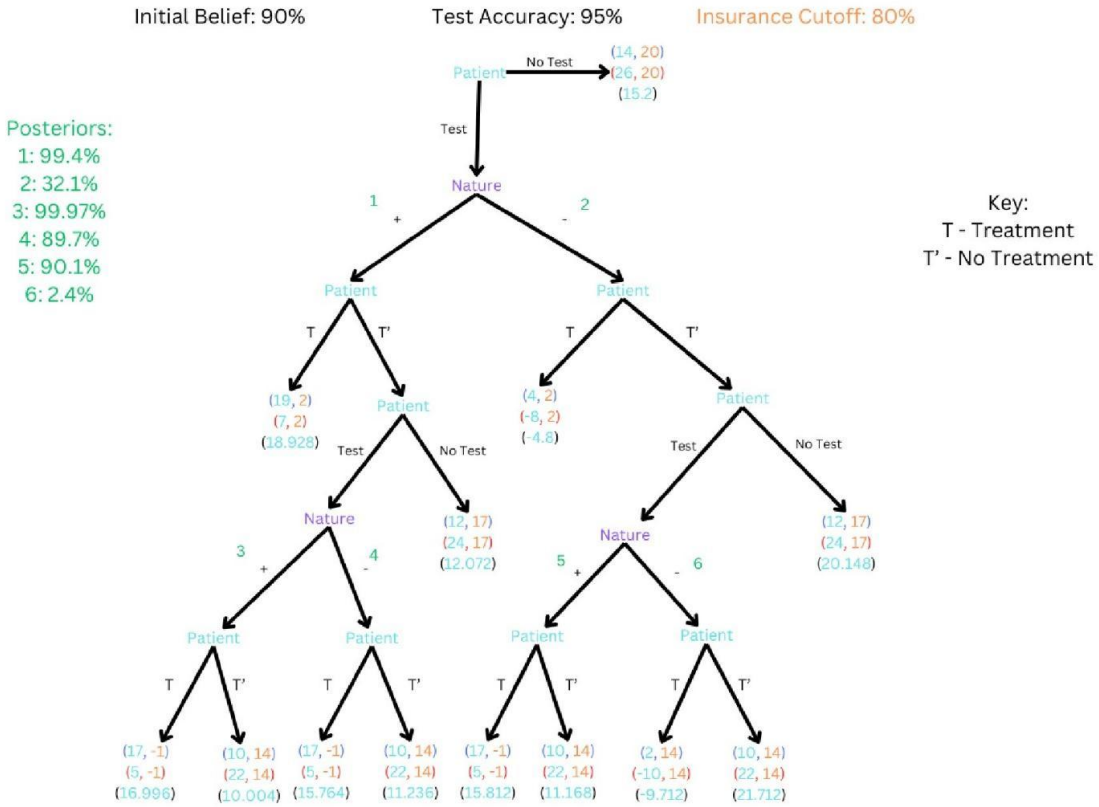
Health Insurance

The patient is not the only person involved in the decision-making. When a patient takes a genetic test, or undergoes preventative treatment, any health insurance the patient may have will be involved in the situation. Regardless of the type of insurance, the health insurance company has a vested interest in supporting the patient, but ideally wants to pay as little as possible to maximize profits. Health insurance companies can support their clients in two ways: through copayments or deductibles. Copayments involve the patient and health insurance company paying a certain percentage of the total cost, while deductibles involve the patient paying a portion of the with the health insurance company covering the rest of the cost.

Theoretically, a genetic test result should not affect chances of insurance coverage or reimbursement. The Genetic Information Nondiscrimination Act (GINA) was passed in 2008 to prevent health insurance from raising rates or dropping coverage based on genetic test results.[5] This law, however, is not always significant, as health insurance companies can still choose to not financially support a patient if they provide a logical reason for not doing so. Reasons may include believing there are safer, cheaper, less invasive, and more effective alternatives and/or believing that such treatments are unnecessary[6]. A genetic test result may lead to the belief that the mutation is present in the patient (the posterior) extremely low, causing the insurance to drop coverage for tests and treatments. For this analysis, I have assumed the insurance will have a threshold for when they will support a patient and when they will not.

Game Tree

The game tree (See below figure for an example) is the model that displays the entire decision-making process for the patient and health insurance company.



The Game Tree Model shows the different payoffs for the patient and the insurance company. Any payoffs in blue parentheses are the payoffs if the patient does have the mutation, and the payoffs in red parentheses are the payoffs if they do not have the mutation. Since there is no way of knowing for sure whether the patient has the disease or not, the average payoff for each branch is calculated, based on the latest posterior (in green). The patient's average payoff for each branch is written in black parentheses.

When considering the game tree, the patient has a choice to ignore taking a genetic test and undergoing treatments completely. This can be the case in the event the patient is not initially certain that they have the mutation. Choosing this will end the game immediately, as I have assumed insurance companies would seldom financially support a patient who has not taken at least one genetic test. Patients who are both well off financially and are sufficiently certain they have the mutation, however, can choose this option and pay for the entire treatment themselves without guarantees of reimbursement from health insurance. If the patient decides to take the first test, then the result will return positive or negative. These different possibilities are modeled by another 'player' called "nature". Nature represents an extraneous 'player' who does not receive payoffs but displays decisions outside of other players' control. Based on the result of the test (positive or negative) a different posterior is calculated, changing the belief on whether the patient has the mutation and whether the insurance would financially support them. After this, the patient can choose to undergo preventative treatment (with or without insurance support). If they choose not to undergo treatment, the game will repeat. The patient can now decide to take a second test if they are unsure of the first test's result. If the patient does not take the second test, the game ends and payoffs are calculated. If the patient takes a second test, a new posterior is calculated using the belief after the first test. From this, the patient can again decide whether to undergo preventative treatment based on if the insurance will support them. When considering the payoffs for the two players (the patient and the insurance), both players are given a starting value of '20'. This can realistically be any number; 20 is just an arbitrary value. People of lower economic status may start with a lower number. With each genetic test, the patient and insurance payoffs will decrease by a certain amount (in this case 2 and 3 respectively) to represent the cost of the genetic test. Genetic tests vary in cost, so the payoffs may need to be altered depending on the cost of the genetic test and the amount a patient must pay for it. The preventative treatments also have a cost and decrease the players' payoffs significantly. In this model, for the preventative treatment, the patient's payoff decreases by 5 if the insurance supports them, and 20 if the insurance does not. The insurance's payoff decreases by 15 if they support the patient, and 0 if they do not. Alongside decreasing the payoffs based on tests and treatments, the payoffs for the patient also change if they make the correct decision. If the patient's decision aligns with the potential result, then their payoff increases by 6. If not, it decreases by 6. This 6 is again an arbitrary value that can be changed. For each outcome, there are two potential payoffs, one in which the patient has the mutation, and one where they do not. For example, if a patient elects to undergo preventative treatment and they have the mutation, then that payoff increases by 6. If a patient chooses to undergo the treatment and does not have the mutation, then their payoff decreases by 6. The two payoffs for that particular outcome (one payoff where they have the mutation, one where they do not) are then averaged based on the probability that the patient believes they have the mutation. This probability comes from the latest posterior or belief.

An alternative method to modeling the payoffs for outcomes is using "Certainties". "Certainties" are increases or decreases in payoffs if the posteriors exceed a certain amount.

For instance, if the posterior is between 80% and 90%, the patient choosing to take the treatment might have a payoff increase of 4, since they are quite certain they have the mutation, and the treatment is worth it. A patient choosing not to take the treatment, however, might have a payoff decrease of 4, since the chance they have the mutation is high and not taking the treatment might have consequences later. Whether the model is done with certainties or averages, however, does not entirely matter, since both models reach the same set of decisions.

Parameter Changes

The game trees involve three variable parameters, an initial belief (the probability everyone thinks the patient has the disease in the beginning), the accuracy of the tests a patient takes, and the threshold the insurance has chosen. Based on the accuracy of the test there is a certain point where the patient's initial belief will change their choice (the breakpoint). For instance, as shown in Table 1 (using the aforementioned arbitrary values), any patients who initially believe there is a 37% chance or lower that they have the mutation will not take a test with a 95% accuracy. Any patients with an initial belief of 38% or higher will take the test. As the test accuracy increases, the cutoff for when the patient decides to take the test decreases. As is shown in Table 1, the most reasonable thresholds for when an insurance company supports a patient (60% to 90%) do not change the point where the patient's decision changes. The insurance threshold has become more important for tests with lower accuracies.

Table 1

Breakpoints for Accurate Tests and Insurance Cutoffs

		Test Accuracy			
		95%	**97%**	**99%**	**99.9%**
Insurance Cutoff	**60%**	38%	34%	33%	30%
	70%	38%	34%	33%	30%
	80%	38%	34%	33%	30%
	90%	38%	34%	33%	30%

In this table, the rows show the breakpoints where a patient chooses to take the test for different insurance thresholds. The columns show the breakpoints where a patient chooses to take the test for different test accuracies.

Posteriors decrease as test accuracy decreases, and the insurance company's threshold then holds more weight. If a patient whose initial belief was around 70% took a test with 70% accuracy (shown in Table 2), then the posterior after a positive test result would be between 80% and 90%. As such, if the insurance has a threshold of 80% or lower then treatment after the first test would usually be supported. If the threshold is at 90%, however, then the treatment after the first test would not be supported. In this case, the insurance's threshold is more important to consider as the breakpoint changes from 72% to 75%.

Table 2

Breakpoints for a Less Accurate Test and Insurance Cutoffs

		Test Accuracy
		70%
Insurance Cutoff	**60%**	72%
	70%	72%
	80%	72%
	90%	75%

In this table, a test is done with a much lower accuracy than normal, that of 70%. In this table, the only insurance threshold to alter the breakpoints is the one of 90%. A 90% insurance threshold increases the point where the patient's decision changes from not taking the test to taking the test.

An increase in the breakpoint indicates that fewer people are taking the genetic test. This can be detrimental as this means people with relatively high initial beliefs that are below 75% are not taking the test. While the difference between 72 and 75 is not a lot, as the test accuracy decreases the insurance's threshold will become more influential, increasing the breakpoint differences. As such, as the test accuracy decreases, it is advised that the insurance threshold also decreases to support more people with relatively high initial beliefs.

Factors Outside Insurance

The matter of taking a genetic test is not always about money. Certain diseases like Huntington's Disease do not have any notable cures or treatments. Taking a genetic test for these types of diseases only provides information on whether the patient may develop the disease or pass it on to their children, helping them prepare for potential life decisions. This information can be very beneficial regardless, however there can also be harmful consequences.

When a patient takes a genetic test, there will almost always be a psychological impact on the patient. If a test comes back positive, then any dread they may have had towards developing the disease may increase, which can negatively impact their lives. Outside of the patient themselves, a positive test result can also affect their family. Family members may experience depression and other negative symptoms due to the knowledge that someone close to them may be living for a limited time. Alongside this, the results of a genetic test also reveal information on family members. For example, a positive test result indicates a sibling or cousin of the patient could also have the mutation.

The knowledge that someone may be a mutation carrier can also be very damaging. Patients may be torn over whether to have a child, and test results can impact their lives for years. False test results, especially, have been noted to have harmful effects on people. From an article from the Genomics Institute at UC Santa Cruz, Katy Mathes and her sister underwent genetic testing in August of 2015 and received results that they were likely to develop breast or ovarian cancer later in their lives. Since their family had a history of the disease, they considered the results seriously and underwent surgery alongside five other family members. Years later, information was received that the mutation variant that they had been diagnosed with had since been reclassified. Initially, the mutation had been identified as pathogenic, or

capable of causing disease. When it was reclassified, however, the classification changed to 'unknown'.[7] This is just one example of how a genetic test was proven unreliable and had significant consequences on not just one patient, but their entire family as well.

When considering a genetic test, it is not just a financial situation that should be considered. There is the type of disease, whether it is treatable, how will it affect family members, or is having a child important to the patient? Depending on the value a patient may place on factors outside their financial status, the payoffs they would receive for each outcome could increase or decrease, thereby changing their decision. When considering if someone should take a genetic test, it is important to personalize the game tree to reflect the values the patient places in outside factors.

Conclusion

To summarize, this paper introduces a model that can help people understand whether they should take a genetic test. There are various tests for different hereditary diseases, and some are more accurate than others. Based on their family history, a patient will have an initial belief on how likely they are to inherit a disease-causing mutation and will have an insurance company that will support preventative treatment if the probability they have a disease reaches a certain threshold. Based on the insurance threshold and the test accuracy, the patient's initial belief will dictate whether they should take the first test. If their initial belief reaches the breakpoint, they will take the test, and if their initial belief falls below the breakpoint, they will not take the test. It was found that with more accurate tests, the breakpoints where the patient's decision changes decrease, so more patients take the test. At high test accuracies, the insurance threshold is mostly negligible. However, with lower test accuracies, a high insurance threshold will increase the breakpoint and fewer people will take the test. As such, insurance companies should lower their thresholds if the patient is taking a test with a low accuracy to ensure that more people are taking the genetic test when they have an appropriately high initial belief.

These models only display the patient's financial payoffs and their relationship with their insurance. If a patient has any factors outside insurance that would change their decision, it is best to change the payoffs of the model to accommodate the patient's circumstances.

Further Research

This model can be further researched by understanding how the second test influences a patient's decision. When a patient is deciding whether to take the second test, another breakpoint can be found on when the patient's decision changes, based on the latest posterior and the initial belief.

Besides better understanding the second test, the model can also be changed to incorporate other players, such as the patient's family. A patient's family members may be just as affected by the results of a genetic test as the patient themselves, and they might also play a role in the patient's decision. The game tree can be improved to incorporate some of the patient's family based on their beliefs and what decisions they might make to influence the patient. This would help model what might happen in real life more accurately.

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Footnotes

[1] A health insurance company may not always provide financial assistance for a patient regarding preventative treatment, such as breast removal for breast cancer, if test results indicate a low probability of the patient having the disease-causing mutation. For the purposes of this analysis, I have assumed that if the belief that the patient has a mutation reaches a certain threshold, the insurance will support the patient. If not, the patient will not receive support.

[2] If a patient with an initial belief of 34% (they believe there is a 34% chance they have the mutation) should not take a test, but a patient with an initial belief of 36% should, then - assuming all other variables are the same between the two patients - there is a breakpoint at an initial belief of 35%. This is the point where, under controlled circumstances, the optimal decision changes based off the initial belief.

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