Two Dimension Threshold Model for Medical Decision Making

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Abstract

Two previous threshold approaches to medical decision making, one using the clinician's estimate of the probability that the patient has the disease and the other using the patient's utility for his/her current health state, were combined. We derived a two dimensional threshold space for deciding to treat or not treat. The case where an additional diagnostic test was available was also explored. The situation where more than one treatment choice is available, which is more interesting with a two dimensional space than with the traditional one dimensional threshold, was also explored.

It is generally agreed that the best way to make medical decisions is through the application of normative, mathematical models that have been developed in the field of decision science.[1] However, the application of such in clinical practice is often too complicated and time consuming. Pauker and Kassirer proposed an elegant solution to this problem.[2] Their method, which they named the threshold approach, allowed the clinician to apply a normative model, but all that was required in clinical practice was for the physician to use clinical skills to assess the probability that the patient had a specified disease. This probability is then compared with a predetermined value called the threshold probability. If the assessed probability exceeded the threshold probability, the decision would be to give the treatment, and to not treat otherwise. This threshold probability for each disease was to be determined using the normative decision making models prior to seeing patients. Utilities of costs, risks, benefits, and their likelihoods needed to calculate the threshold could be estimated from population norms. Equations for this were given by those authors.

Pauker and Kassirer later extended this to the case where there was a further diagnostic test available.[3] Two probability thresholds were established. If the clinically assessed probability of disease exceeded the first threshold but not the second, the test would be preformed and the treatment administered if and only if the test outcome was positive. If the probability exceeded the second threshold, the test would be skipped and the treatment administered. If the probability failed to exceed the first threshold, neither the test nor the treatment would be administered. Again, these thresholds were to be determined using normative models from population norms of the utilities of costs, risks, benefits, and their likelihoods of untreated disease, treatment, cure, as well as those associated with using the test. Again, these authors derived the equations.

Nease and Bonduelle argued that the probability of disease is not the most likely parameter to vary for each patient.[4] They argued that the utility to the patient of his/her current health state was more likely to vary more for each patient. They derived a threshold model that requires the physician to estimate this utility with the patient and compare it against the threshold utility to make the decision of whether to treat or not. This utility would depend upon the subjective impact to the patient of the severity of the symptoms and their impact. The probability that the patient has the disease is one of the parameters estimated by population norms used prior to seeing patients to set the value of the utility threshold. These authors derived the equations for determining this threshold. They also derived a version of this threshold model with two threshold values for when an additional diagnostic test was available.

We think that both the probability threshold and the utility threshold approach have merit, but both have a major problem. Many of the parameters required to calculate either threshold can best be estimated globally, and it would not be feasible for a physician to estimate them specifically for individual patients. However, the probability that this patient has the disease, which is one the physician is trained to estimate from this patient's particular clinical presentation, can often be expected to vary a great deal with each patient. Likewise, the utility to this patient of a cure versus the patient's current utility for the present state of symptoms can often be expected to vary a great deal. A disease can cause widely varying distress due to symptoms for different patients. The physician interacting with the patient can assess this. Therefore, we have developed a two dimensional threshold model that uses both the probability of the disease and utility of a cure for the patient. In this paper, we first present the model where the decision is to treat or not and then the model where there is an additional test available. We also consider the case where there are two or more different treatments available.

Two Dimensional Threshold Model of Treat versus Not Treat

The Decision Space

The first axis is the physician's estimate of the probability that the patient has the disease. We choose to make this the abscissa. Of course it has a range of zero to one. The other axis, the ordinate, is the patient's subjective utility. The utility variable is a little more complicated. Utility is an interval variable, and as such is invariant under a nonsingular affine transformation.

It is customary to scale it so that it has a range of zero to one. Typically, the utility is a measurement of the patient's subjective valuation of or preference for his or her condition and ranges from 1, perfect health and happiness, to 0, death. As Nease and Bonduelle noted, this produces an axis where treat is the decision at the lower range and don't treat is at the upper end. This is opposite of the probability axis. We choose to use 1 minus the utility to give it the same range and direction as the probability variable because this greatly simplifies the conception of the two dimensional decision space. The value can be thought of as the gain in utility the patient would realize if restored to perfect health. Thus it is a measure of the severity of the symptoms, the patient's utility for those symptoms, and the problems associated with them. A value of 0 would indicate that the patient is experiencing no problems at all, while increasing values indicate worse distress. We further discuss the issues of the range for utility and other issues associated with it in the discussion.

The Model

The decision space defined above is the unit square. We now use the principles of decision analysis to derive the equation that divides this space into treat and not treat regions. The curve will be where the expected utility of treating is equal to the expected utility of not treating. The treat region is where the expected utility of treating is greater than the expected utility of not treating. The do not treat region is just the opposite. First we define the variables.

P Probability the patient has the disease using information the physician has such as from a routine physical, history, symptoms and any tests that have been performed. This variable is the abscissa axis in the present threshold space.

U^* The patient's utility for his/her present disease state on a scale where 0 is the worst possible and 1 is the best possible. This is the utility measure used by Nease and Bonduelle in their utility threshold model[4].

U The gain in patient's utility if a perfect cure. That is the difference between the patient's utility for his/her present health state and a perfect health state (i.e., $U=1-U^*$). *U* could be called the disutility for the patient's current state of health or the potential utility gain. This variable is the ordinate axis in the present threshold space.

C The utility of the cost of treatment. Includes all costs (e.g., pain, loss of work and other time, financial, morbidity, risk, etc.). As further discussed in the discussion section, it must be noted that *C* has to be on the same scale as *U*. That is, a delta gain or reduction in *U* must be equivalent to the same delta gain or reduction in *C*.

E The utility of the expected outcome (i.e., the expected value of U^*) of the treatment, given the disease is present. This is the efficacy or benefit of the treatment. If the treatment is perfectly efficacious, then it should always result in an outcome of 1 for the patient's utility for his or her present health state. However, if the treatment sometimes produces complete relief and sometimes somewhat less, or if the treatment always produces somewhat less, then *E*, which is the average outcome, is less than 1. *E* must be scaled so that it is in the same units as *U*.

We now proceed to derive the equation. The expected utility for doing nothing is the current health state of the patient which is:

$$1 - U. \tag{1}$$

If one treats and the disease is present, then the outcome will be the efficacy of the treatment as defined above. On the other hand, if one treats and the disease is not present, then the outcome will still be the current health state. The cost of treating must be subtracted in either case because the treatment was applied. Multiplying these two possible outcomes by the probability of each state (disease present or not) and adding them gives the expected utility for treating:

$$P\,E + (1 - P)\,(1 - U) - C. \qquad (2)$$

When equation 1 is equal to equation 2, the expected utility of not treating is equal to the expected utility of treating This result is given by equation 3.

$$U = \frac{C}{P} + (1 - E)\,. \qquad (3)$$

Equation 3 is an equation of the indifference curve that divides the two dimension threshold space into the treat/don't treat regions. An example is shown in Figure 1. The curve from equation 3 is shown with example values of C and E. The curve divides the space into the treat area, shaded, and the do not treat area, unshaded. A patient, the pair of values (probability and utility), would be a point in this space. Four possible patient points are presented in this example. The point “patient 1" represents a patient with a low probability of disease and low symptom severity. Patient 2 has high probability of disease, but low potential utility gain (low symptom severity). Patient 3 shows low probability of disease, but high symptom severity, and patient 4 is high on both variables. One should note that utility and probability are compensatory. In general, a higher probability will move the point into the treat region as will a higher utility. One would treat with a lower value on one variable provided the other variable had a high enough value. However, there are some values of both probability and utility that are so low that no matter how high the other variable is, treatment would not be recommended.

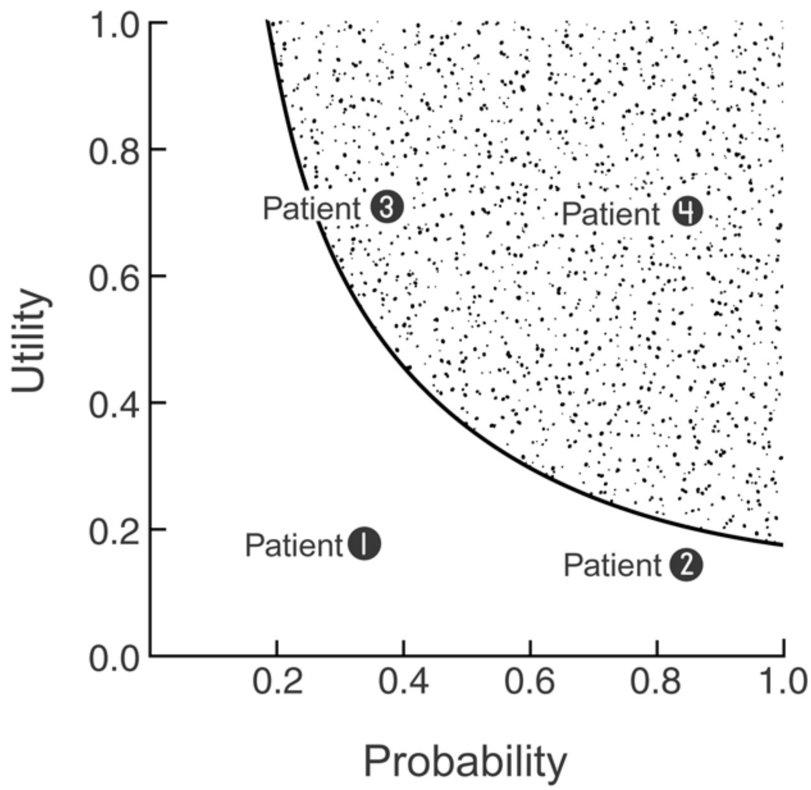

Figure 1: The two dimensional threshold management space is shown with an example indifference curve dividing the space into treat (shaded) and do not treat regions and four example patient points.

Effects of the Parameters

The location of the indifference curve in the decision space is a function of two parameters, cost (C) and efficacy or benefit (E) of the treatment, whose values are determined globally. As the cost increases, the indifference curve rises up in the space so that one would require a higher probability of disease or more severe symptoms, or both, to decide to administer the treatment. As the cost goes to zero, the curve approaches the axes. Indeed, if there were no cost at all for a treatment, then one would apply the treatment no matter what the probability or utility were. As the cost increases, the indifference curve continues to approach the upper corner of the graph, with less and less area in the treat region. For sufficiently high cost, the treatment is never given. As the efficacy decreases, the curve becomes flatter and moves to the upper right-hand corner of the graph but with a rotation.

The case where there is more than one treatment available can be more interesting with the two dimensional threshold model than with the one dimensional threshold models. In the probability threshold model of Pauker and Kassirer,[2] the treatment with the smaller threshold value is always preferred and is administered if the patient's probability exceeds the threshold. In the utility threshold model of Nease and Bonduelle,[4] the treatment with the larger threshold value is always preferred and is administered if the patient's utility is less than the threshold. (Recall that in their utility model, utility is one minus that in the present two dimensional model.) In the present model, if there is more than one treatment available, the choice may not be trivial. If efficacy is constant and only cost varies or if cost is constant and only efficacy varies, the indifference curves will not intersect in the threshold space. The treatment with the lower indifference curve is always preferred and is applied if the patient's (P,U) point is above its indifference curve. However, the situation is more interesting if the treatments' indifference curves cross. It can be shown that the i-th and the j-th treatments' indifference curves will intersect at the point:

$$P = \frac{C_i - C_j}{E_i - E_j}, \quad U = \frac{C_i - C_j + C_j E_i - C_i E_j}{C_i - C_j}. \tag{4}$$

One will be indifferent between treatment i and treatment j, if:

$$P = \frac{C_i - C_j}{E_i - E_j}. \tag{5}$$

It should be noted that this is not a function of U and, thus, is a vertical line in the threshold space.

Figure 2 presents an example with three available treatments with different values of C and E such that their indifference curves intersect. Shown are the treat/don't treat indifference curves for each treatment (Equation 3) and two treatment indifference lines (Equation 5). We did not extend these treatment indifference lines below the treat/don't treat indifference curves, because it is irrelevant which treatment is preferred if no treatment is to be administered. We omitted the indifference line for treatments 1 and 3, as this one would fall in the region where treatment 2 is the preferred treatment and thus be irrelevant. In each case the lowest treat/don't treat indifference curve in the region is of the treatment that is preferred and is used to determine if the treatment is administered. If the patient's (P,U) point lies to the right of the indifference between treatments 1 and 2 line (the vertical line from where the indifference curves for treatment 1 and treatment 2 intersect) and above the indifference curve of treatment 1, then treatment 1 is administered. If the patient's (P,U) point lies to the left of the indifference between treatments 2 and 3 line (the vertical line from where the indifference curves for treatment 2 and treatment 3 intersect) and above the indifference curve of treatment 3, then treatment 3 is administered. If the patient's (P,U) point lies between the two treatment indifference lines and above the indifference curve of treatment 2, then treatment 2 is administered, Of course, the area below all the indifference curves is the do not treat region, and if the patient's (P,U) point falls in there, no treatment is given.

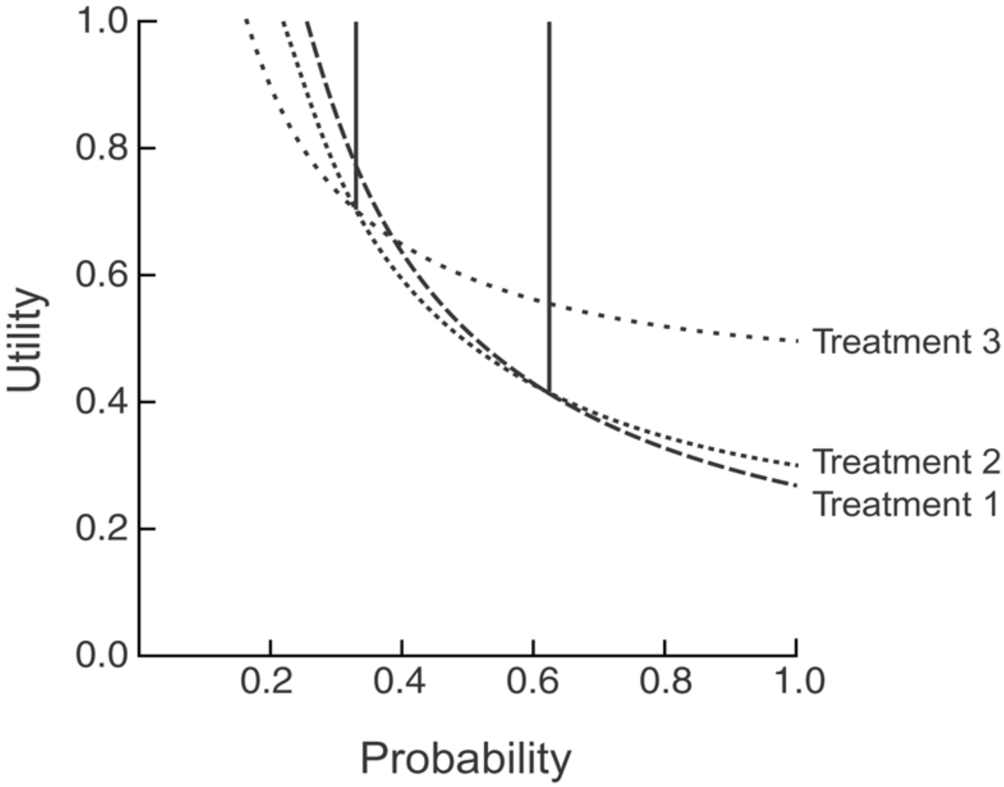

Figure 2. An example two dimensional threshold space with three different possible treatments.

The Possibility of an Additional Diagnostic Test

Both previous threshold models considered the case where an additional diagnostic test was possible. Two thresholds were derived. The decision situation then was to do nothing, to treat without performing the test, or to perform the test and treat if and only if the outcome of the test was positive. We now derive the two dimensional model for this case. First, it is necessary to introduce additional notation.

T The cost of testing. This includes all the costs for testing the same as *C* includes all the costs for treating. Also, *T* is a utility in the same sense as *C* is and must be scaled to be equivalent.

S The sensitivity of the test, that is the probability the test will be positive given the disease is present.

F The specificity of the test, that is the probability the test will be negative given the disease is not present.

The expected utility for testing and treating, if and only if the test is positive, is:

$$(E - C)\, S\, P + (1 - U)\, P\, (1 - S) + (1 - U - C)\, (1 - P)\, (1 - F) + (1 - U)\, F\, (1 - P) - T. \qquad (6)$$

One would be indifferent between performing this test and treating if and only if the test is positive and doing nothing whenever Equation 6 is equal to Equation 1. That will be the case whenever:

$$U = \frac{\left(\dfrac{C - CF + T}{S}\right)}{P} + \left(C + 1 - E - \frac{C}{S} + \frac{CF}{S}\right) \qquad (7)$$

It should be noted that Equation 7 has the same form as Equation 3. That is, *U* is a function of a constant term multiplied by the inverse of *P* plus another constant term. The constant terms in Equation 7 are just more complex than those in Equation 3. Of course these two equations give similar graphs.

To completely define the situation where a further test is an option, one not only needs Equation 7, but also an equation to decide between doing the further test and treating without doing the further test. One would be indifferent whenever Equation 2 is equal to Equation 6.

That will be the case whenever:

$$U = \frac{\left(\frac{CF - T}{1 - S}\right)}{P} + \left(\frac{1 + C - E - CF - S - CS + ES}{1 - S}\right) \tag{8}$$

When equality holds, this defines the line that separates the treat without testing region from the test first region. Again, notice that Equation 8 is of the same form as Equations 3 and 7. It can be shown that Equations 3, 7, and 8 will intersect at the point:

$$P = \frac{-C + CF + CS - T}{C(-1 + F + S)},$$
$$U = \frac{C + C^2 - CE - CF - C^2F + CEF - CS - C^2S + CES + T - ET}{C - CF - CS + T} \tag{9}$$

Unlike Equation 5, which separates the treat region into different treatments, Equation 8, which separates the treat region into treat and test first regions, is not a vertical line, but rather a curve. An example of Equations 3, 7, and 8 is shown in Figure 3. This figure presents an example of treating versus test and treat if and only if the test is positive versus do nothing. The management space is divided into these three regions. If the patient's (P,U) point is below and to the left of all the threshold lines, nothing would be done. If it is in the space at the upper right side and above the treatment indifference curve, treatment would be recommended without a test. If it is to the upper left and above the testing indifference curve, the diagnostic test would be performed and treatment administered if and only if the results of the test were positive. It should be noticed that, as in the case of two possible treatments, the indifference curve that is lower dominates.

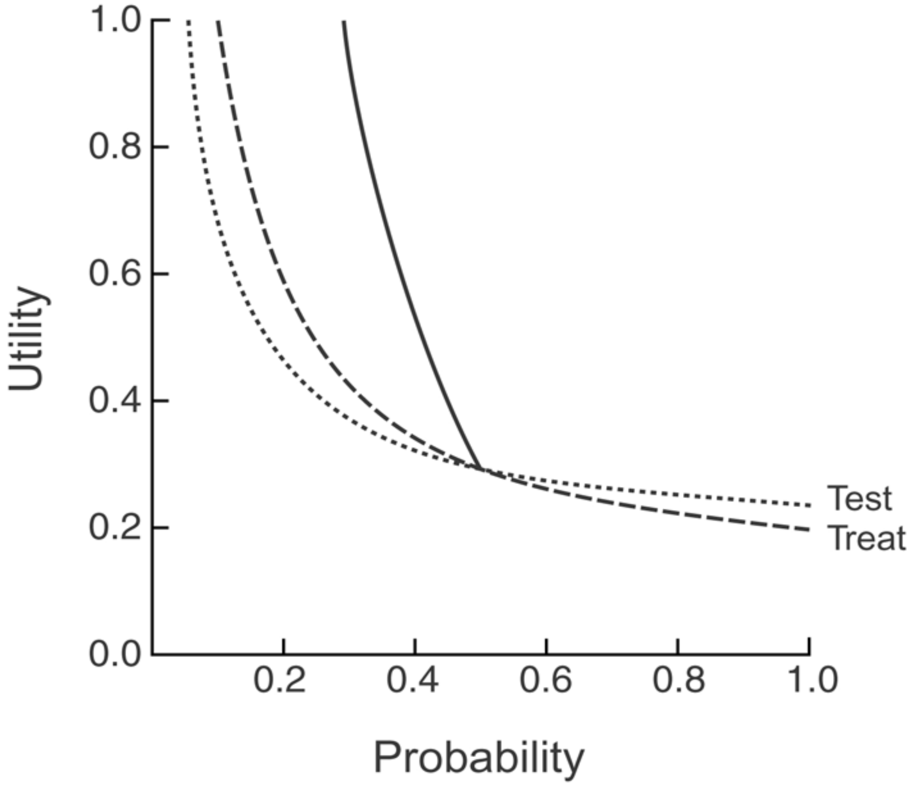

Figure 3. An example two dimensional threshold space with the possibility of an additional diagnostic test.

Discussion

We have derived the equations that define the threshold curves in a two dimensional threshold space combining the previous approaches of a probability of disease threshold and a patient's utility for his/her current health state. Which of these three threshold models should be applied, depends on the disease being considered. For some diseases the probability of the disease will dominate the decision making. The utilities are generally the same across the population. In some diseases the probability of disease will be certain and it is the utility that will be determinant. Prostate cancer is an example. The pathology is clear (P = 1 or close to it) from routine tests, but the individual's utility is important. For diseases like carpal tunnel syndrome[5], where, the probability of disease and the severity and effect of the symptoms vary widely with patients, the two dimensional approach is useful. The choice of method defers to a single dimension when there is limited variability among patients in either utility or probability. However, variability across the population on utility and probability is an indication that the two dimensional approach may be helpful to conceptualize the decision making.

We derived equations which define the threshold curves in the two dimension space for the cases of treating versus not treating, the case where alternative treatments are available, and the case where an additional test is available. If more than one treatment is available and also there is an additional test available, it is straight forward to combine these in the threshold space. The lower indifference curve in each region of the threshold space dominates in that region.

The ordinate of the two dimension space is a utility as are several of the parameters involved in the equations. As noted before, utility is measured on an interval scale. It can be rescaled by a nonsingular affine transformation (U' = AU + K, where A is positive). All the utility measures must be scaled to be on the same scale. We set the range, as is customarily done, to be from 0 to 1. However, what these endpoints (the 0 and 1) are must be set and must be equivalent for all the utilities. Pauker and Kassirer, in their probability threshold model, only required that they all be the same. This is sufficient with a model where the utilities are all parameters. Nease and Bonduelle, in their utility threshold model, set them to 0, death, and 1, perfect health. It is possible to use these same end points for the two dimension model. However, this may well, for some diseases, produce a severe restriction of the range for the variable U. That is, all the patients may have nearly the same values for U. This would make it extremely difficult to access this variable and use it in the threshold space. For any particular application to a particular disease, different assignments to 0 and 1 may be chosen such that 0 is the worst possible and 1 is the best possible. All the utility parameters for this application must then be scaled to have these same end points.

Of course, clinicians use the likelihood of the disease and the patient's reaction to the severity of the symptoms along with efficacy and cost in making decisions about treatment. We quantified this in a form useful to them using the principles of normative decision making. As such, it can be expected that the two dimension threshold model will reflect the decision making of expert clinicians. Our model can be used to understand variations and changes in medical care. An interesting clinical example of this situation occurred when endoscopic cholecystectomy was developed. The endoscopic and traditional removals of the gallbladder were equally efficacious, but the endoscopic method had lower morbidity and shorter time in hospital. The anticipated savings in dollar cost for the procedure was not realized on a population scale because there was an increase in the number of procedures performed.[6] We believe this is a shift in the population of surgical patients to include those with less severe symptoms and less probability of disease in keeping with a transition of the threshold curve to the lower left as predicted by our model. We believe our model can predict the behavior of the medical system when changes in management are suggested, and we advocate its use as a step in introduction of new management strategies. This would include, but not be limited to, new diagnostic tests, new technology, new surgical procedures, and continuous quality improvement activities.

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