Saliva Diagnostics for Kidney Disease

Project Report

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Submitted to Dr. Miguel Bagajewicz

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ABSTRACT

This project evaluates the development of a saliva-based diagnostic tool analyzing kidney functioning by measuring the concentration of creatinine, a biomarker related to blood filtration. An economic analysis reveals a high expected demand and profitability for this product in comparison to existing blood tests that are currently being used in the medical community.

The test utilizes a reaction between creatinine and picric acid which results in a color change that can be used to determine the concentration of creatinine and therefore the level of kidney functioning. Some compounds, however, are known to interfere with this reaction, creating misleading results. Various product designs were developed in response to this issue, such as adding certain components to the test to reduce or monitor the affects of the interfering compounds.

A consumer satisfaction model was created to determine consumer preference with regard to discomfort level, early diagnosis efficacy, and the likelihood of false results due to interfering compounds. A price and demand model, including consumer preference, as well as consumer knowledge and competition, found that the highest demand was for a product designed to reduce negatively interfering compounds while monitoring the level of positively interfering compounds. However the product cost associated with that design option was significantly higher than others. A net present worth calculation was used to determine the most profitable product design which estimated an NPW of $10 million for a design priced at $4/test which reduces negative interference, but does not monitor levels of positively interfering compounds.

INTRODUCTION

Medical diagnosis currently depends heavily on information gathered from blood tests, urine tests, biopsies, and physical examination. Saliva remains a largely untapped source of medical information that can enhance diagnosis accuracy while saving the patient from some of the discomfort associated with a blood test or other more invasive procedures. Many of blood's constituents make their way into saliva, thus making saliva an indicator of the current state of the blood and the rest of the body. Many biomarkers, or substances used as indicators of biological states, can be readily found in saliva.

The specific goal identified through this project is a salivary diagnostic tool of the kidney. A creatinine clearance test is a typical assay performed upon admittance in order to assess the overall health of a patient. Kidney malfunction can indicate many other systemic problems, therefore a fast, effective, inexpensive, and noninvasive creatinine clearance test would be very beneficial.

The kidney produces urine mainly through passive diffusion, which is the main mechanism at work in the formation of saliva[1]. Therefore, items leaving the blood in the kidneys should be similar to those leaving the blood at the salivary glands. When a physician orders a creatinine clearance test, he is looking for the concentration of creatinine in the blood. The smaller the concentration is, the healthier the kidney is because it is sufficiently removing creatinine from the blood. Because of the parallels between blood and saliva, a creatinine clearance test performed on saliva should provide this same information, but faster and with less discomfort to the patient.

SALIVA

Saliva is composed of many compounds. Saliva is 98% water with some mucus and a wide variety of electrolytes. A detailed list of the compounds found in saliva is given in Table 1, below.

Table 1: Components of Saliva[2,5,14]

Electrolytes	**Concentration**	**Mucus**	**Concentration**
Sodium	32 mmol/L	Mucopolysaccharides	
Potassium	22 mmol/L	Glucose	175 umol/L
Calcium	1.7 mmol/L	**Metabolites**	
Magnesium	0.18 mmol/L	Bilirubin	15 umol/L
Copper	0.4 mmol/L	α-ketoglutaric acid	2.4 umol/L
Lead	0.55 mmol/L	Pyruvic acid	75 umol/L
Cobalt	1.2 mmol/L	**Proteins**	
Strontium	1 umol/L	α-amylase	650-800 ug/ml
Hydrogen Carbonate	20 mmol/L	Peroxidase	5-6 ug/ml
Iodide	10 umol/L	Secretory IgA	96-102 ug/ml
Bromide	14 mmol/L	Lactoferrin	1-2 ug/ml
Hypothiocyanate	1.2 umol/L	Fibronectin	0.2-2 ug/ml
Nitrate	1.1 umol/L	**Cells**	32 mmol/L
Nitrite	178 umol/L		
Fluoride	68 umol/L		
Sulfate	5.8 umol/L		

It has previously been shown that 5 min of rest after eating is sufficient time for a patient's mouth to be free of food particles[8]. A patient with a dry mouth may be asked to chew inert paraffin gum for up to two minutes to stimulate flow. Collecting 5mL of saliva is simple and gives a copious amount for a saliva test.

SCREENING PROCEDURE FOR VALIDATING THE TEST

Before choosing a salivary creatinine clearance test for this analysis, a screening procedure was developed in order to choose the best biomarker candidate. The following questions were asked of each candidate biomarker.

1. Can the biomarker be detected in saliva?
    a. What are normal saliva levels for biomarker?
    b. How do saliva levels compare to plasma levels?
2. Do abnormal levels indicate threat of organ malfunction or disease?
    a. How do we determine baseline concentration?
3. How do you detect abnormal levels?
4. How accurate are detection methods?
5. How widely applicable are detection methods?
    a. Are they too specific?
6. How helpful is result in medical decision making?
7. Is test effective in early diagnosis (compared to serum testing)?
    a. Does test improve treatment?
    b. Does test lead to more cured patients or better managed diseases?
8. Weigh accuracy vs. speed, convenience, portability
9. What is the cost of the detection method?
    a. Is test more economical than serum testing?
    b. Is it economical enough to be used in the home, or can it only be used in clinical settings?

This procedure evaluates ideas on all non-economic aspects of the test, from its accuracy to its actual utility and the usefulness of the information it gives. However, all of these criteria are related to the profitability of this venture, as will be discussed in the market analysis.

The screening procedure is also outlined in the following flowchart, Figure 1.

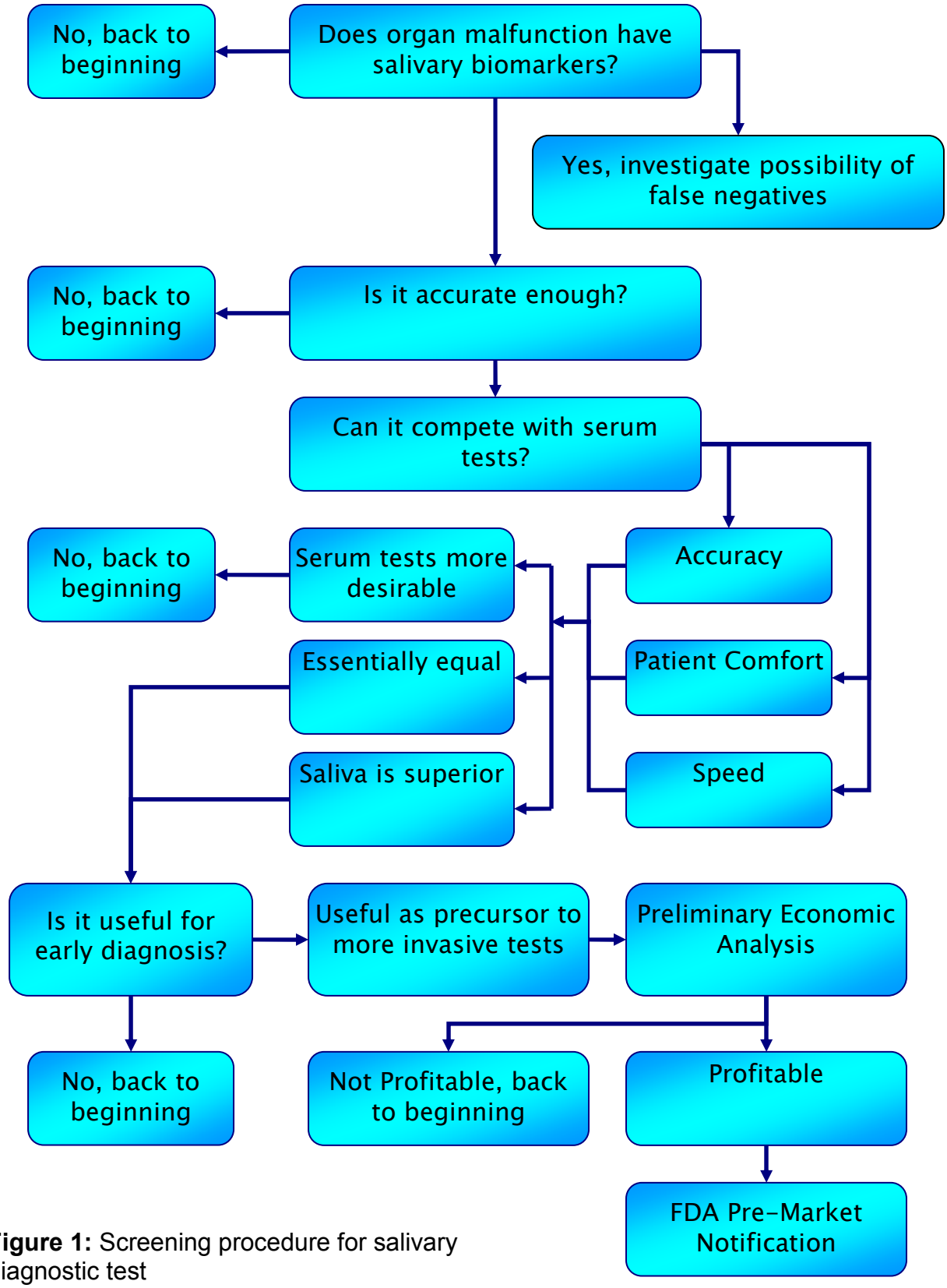

Figure 1: Screening procedure for salivary diagnostic test

THE KIDNEY

Kidney disease currently afflicts about one in twelve Americans. It is to blame for about 80,000 deaths per year making it the ninth killer in the country. Also about a half million Americans depend on dialysis or transplanted kidneys to survive[5]. Any diagnostic tool that could catch kidney disease in its early stages can save these lives and keep people from having to endure dialysis or serious operations.

The kidney's main responsibility is cleaning the blood of waste. Because urine forms mainly through passive diffusion, just like saliva, many of blood's components exchanged at the kidney are also exchanged at the salivary glands.

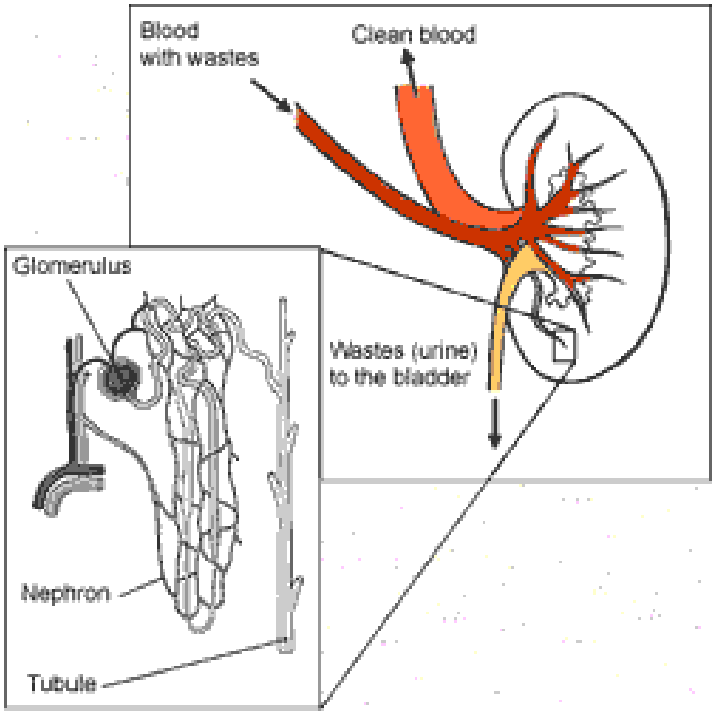

Figure 2: The Kidney[6]

A wide variety of symptoms may call for a kidney test, so physicians call for the tests quite frequently[1]. Any of the following problems may call for a diagnostic test related to the kidney:

- High blood pressure
- Fatigue, less energy
- Poor concentration and appetite
- Trouble sleeping and night time muscle cramps
- Swollen feet and ankles
- Puffiness around eyes, particularly in the morning
- Dry, itchy skin
- More frequent urination

Saliva testing can replace the initial blood in these situations. A positive saliva test may lead to more invasive tests, but a negative one can spare the patient and physician this inconvenience. When tests indicate elevated creatinine levels, patients are then usually asked to submit urine tests. For a 24 hour period, the patient collects and stores all urine they produce and return it for analytical testing. This allows for a very accurate creatinine measurement since the quantity is time dependent and is not contingent on other factors such as hydration.

CREATININE AND GFR

Creatinine, a key in diagnosing kidney disease, is found in both saliva and plasma. Creatinine is a breakdown product of muscle tissue which the kidney normally removes from the blood. The following reaction generates creatinine:

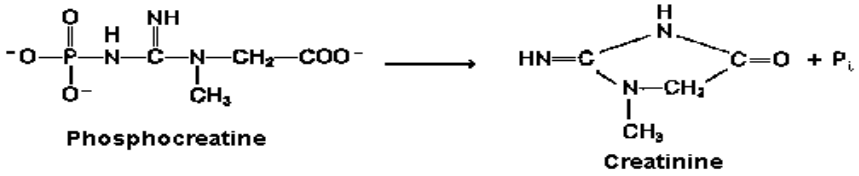

Figure 3: Creatinine Formation

Salivary levels of creatinine share a close relationship with serum levels, with an average concentration 10 times less than serum[9]:

$$P_{cr} = 10 S_{cr} \quad (1)$$

Where P_{cr} is the plasma creatinine concentration and S_{cr} is the salivary creatinine concentration.

An elevated creatinine level in the blood suggests kidney malfunction. The creatinine concentration in the blood is related to the glomerular filtration rate (GFR). GFR refers to the initial urine formation at the glomerulus. The glomerulus is a web of capillaries that functions as the first interface between the blood and the kidney at the Bowman's capsule. Doctors use GFR most frequently to identify the stage of kidney disease progression. A healthy pair of kidneys will have a GFR above 100 mL/min/1.73m^2 [11]. A GFR below 14 is a sign of end stage kidney failure. Simply put, the GFR is the rate at which toxins are removed from the body's blood. Correlations between serum creatinine concentration and GFR are available, and can be used to develop an equation relating GFR to salivary creatinine concentration. The following equation is called the Cockcroft-Gault equation[8]:

$$GFR = \frac{(140 - Age) \cdot Mass}{8150 \cdot S_{cr}} \quad (2)$$

Where GFR is glomerular filtration rate, mass is in kg, and S_{cr} is the salivary creatinine concentration in mmol/L.

The following table shows the relationship between GFR and the stages of kidney disease. The description of the symptoms and the advised treatment is also given.

Table 2: Kidney Disease Stages[11]

GFR	Stage	Description	Treatment
90+	1	Normal kidney function	Observe, control blood pressure
60-89	2	Mildly reduced kidney function, with urine abnormalities, indicates kidney disease	Find out why kidney function is reduced
30-59	3	Moderately reduced kidney function	Make a diagnosis with additional testing
15-29	4	Severely reduced kidney function	Plan for end stage renal failure
14 down	5	End stage kidney failure	Dialysis and/or transplant

THE TEST

The chemistry used in the creatinine clearance test is the Jaffe Reaction which involves the combination of picric acid with creatinine to produce a red color[13]. A spectrophotometer, which most clinical labs already have, tracks the extent of reaction by following the intensity of the red color. The assay also requires NaOH to provide an alkaline environment in which the picrate will form picric acid, the active compound.

A salivary test has many advantages over a serum test. Because there are no blood cells in saliva, a saliva sample does not require centrifugation before testing. The saliva's ease of collection gives it yet another advantage over serum testing in that the tools are cheaper and easier to use. Before a patient can give blood, he must have the area from which the blood is drawn sterilized. The physician or nurse must then go in with a sterile needle and draw the blood. Saliva diagnostics requires a less expensive and less invasive vial.

THE KIT

The kit is to contain the following items which make up 10 tests (with their associated costs in dollars):

Table 3: Kit Breakdown

Product Cost per kit	$
Test Tubes x10	0.5
Syringes x10	1.5
Box	0.16
Bottle	5.21
Picric Acid	0.875
Sodium Hydroxide	0.875
Creatinine Standard	0.5
Total	**9.60**

FDA APPROVAL

A salivary diagnostic device falls under the FDA's regulation. The creatinine assay would be considered a medical device, which is regulated by the FDA's Center for Devices and Radiological Health. The first step in the approval process is to classify the device. There are three different classifications, each with differing amounts of approval required. A salivary creatinine test falls into category II, meaning that Pre-Market Notification is required, but the much more extensive Pre-Market Approval is not.

The main purpose of Pre-Market Notification is to establish substantial equivalence. In the case of this device, the test must compare to a blood test and meet the following requirements:

- Must have the same intended use as the predicate; **and**
- Must have different technological characteristics and the information submitted to FDA:
    - does not raise new questions of safety and effectiveness; **and**
    - demonstrates that the device is at least as safe and effective as the legally marketed device.

Other regulations imposed by the FDA are called Good Market Practices or Quality System Regulation. These criteria must be met, and pertain to issues such as design, process control, employee training, etc.

PRICING MODEL

A comprehensive pricing model was used to determine the optimal selling price as well as the combination of product properties which yields the best return. The most simplified description of this model is illustrated by a classical microeconomics consumer optimization problem[3]. This microeconomics model describes two products, each with a specific demand (d_1 and d_2 for the new and old product respectively). The consumer maximizes his satisfaction in the product subject to the constraints of his budget. This budget constraint can be described as

$$p_1 d_1 + p_2 d_2 \leq Y \qquad (3)$$

Where p_1 is the new product price, p_2 is the old product price, and Y is the total consumer budget.

Many models of consumer utility have been proposed. The function used in this analysis was the Constant Elasticity of Substitution (CES) utility, given by:

$$u(d_1, d_2) = (d_1^{\rho} + d_2^{\rho})^{1/\rho} \qquad (4)$$

Where ρ is a constant which sets the elasticity of substitution to a specific value. For this study, ρ was set to 0.75. Maximizing this utility function yields equation 5.

$$p_1 d_1 = p_2 (Y - p_1 d_1)^{1-\rho} d_1^{\rho} \qquad (5)$$

These equations capture how the consumer reacts to differences in product price. However, there is more to how the consumer maximizes his utility than product price. The consumer preference for the product as well as the consumer awareness of the new product both need to be taken into account for an accurate modeling of demand. To do this, utility can be maximized by considering consumer satisfaction functions, which are still a function of demand:

$$u(d_1, d_2) = (h_1^{\rho} + h_2^{\rho})^{1/\rho} \qquad \text{with } h_i = h_i(d_i) \qquad (6)$$

These satisfaction functions can then be associated with consumer awareness and consumer preference as follows:

$$h_1 = \alpha d_1 \qquad (7)$$

$$h_2 = \beta d_2 \qquad (8)$$

Where α is the consumer awareness function and represents how aware the consumer is of the superiority of the new product. β is the consumer preference function and describes how much the consumer prefers the old product over the new. If the utility function is differentiated and set equal to zero, the following equation is derived:

$$\Delta d_2 = \left(\frac{\alpha}{\beta}\right)^{\rho} \left[\frac{d_2}{d_1}\right]^{1-\rho} \Delta d_1 \qquad (9)$$

The maximization of the consumer utility function is then given by :

$$0 = p_1 d_1 - \left(\frac{\alpha}{\beta}\right)^{\rho} p_2 \left[\frac{Y - p_1 d_1}{p_2}\right]^{1-\rho} d_1^{\rho} \qquad (10)$$

This model was used to solve for the demand for various scenarios with different new product prices, values for α, and values for β.

AWARENESS FUNCTION

The awareness function, denoted by α in equation 7, describes how aware the consumer is of the superiority of the new product. Awareness is a function of time, advertising, and professional education. Figure 4 gives an example of how α varies with time, ultimately reaching a value of one which indicates perfect knowledge of the new product.

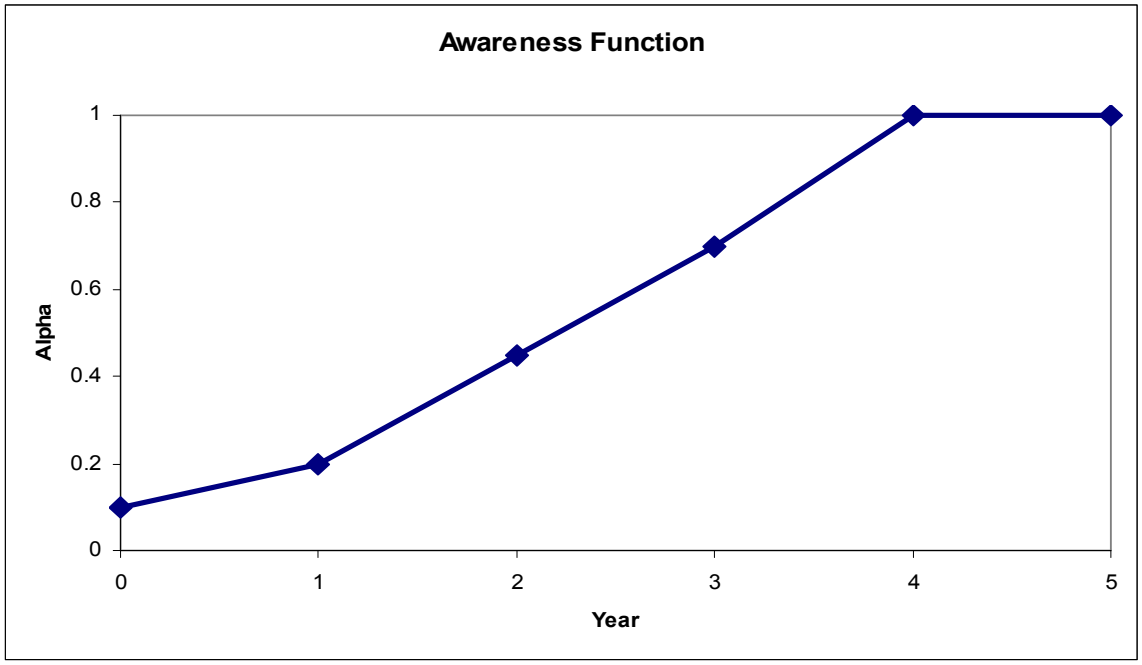

Figure 4: Consumer Awareness versus Time

Through advertising, α can be shifted to the left, increasing the demand for the new product. Additionally, actively spreading knowledge of the test to medical professionals will shift α even further to the left. The following figure represents the change in α with increased advertising and education.

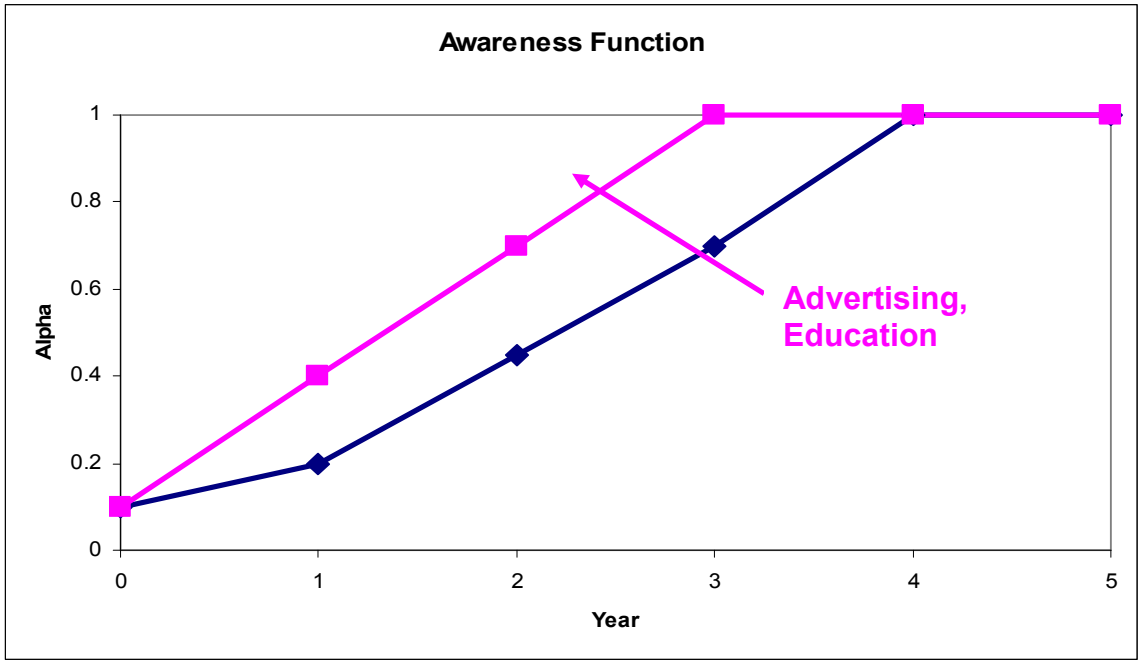

Figure 5: Expected Change in α with Advertising and Education

CONSUMER PREFERENCE MODEL

To use the pricing model developed previously, a function for β (the consumer preference function) was developed. β is the ratio of the consumer satisfaction with the old product to the consumer satisfaction with the new product.

$$\beta = \frac{H_2}{H_1} \tag{11}$$

The consumer satisfaction function is defined as the sum of the products of the weights and the property scores for each of the product characteristics.

$$H_i = \sum_j w_{i,j} y_{i,j} \tag{12}$$

The first step in developing the β function for product design is to determine the characteristics that a consumer would find important. These consumer properties can then be related to physical properties of the product. The consumer properties chosen for this analysis were patient discomfort, sensitivity, false positive rate, and false negative rate.

Discomfort

Discomfort is a consumer property related to the invasiveness of the test. For the consumer satisfaction model, D is a constant dependent on whether or not blood is drawn. If blood is drawn, it is assumed that the consumer satisfaction is 0.5, and for no blood drawn, the consumer satisfaction is 1.

D = 0.5 if blood is drawn
D = 1 if no blood is drawn

Sensitivity

The consumer parameter sensitivity describes the ability of the test to detect very low levels of the target compound. The lower the detectable levels, perceivably the better the diagnosis ability. Figure 6 indicates how consumer satisfaction would be expected to change with the sensitivity of the testing device. The sensitivity of the device is described by the patient's disease progression at diagnosis. In this way, consumer satisfaction can be related to the ability of the test to detect early stages of kidney failure.

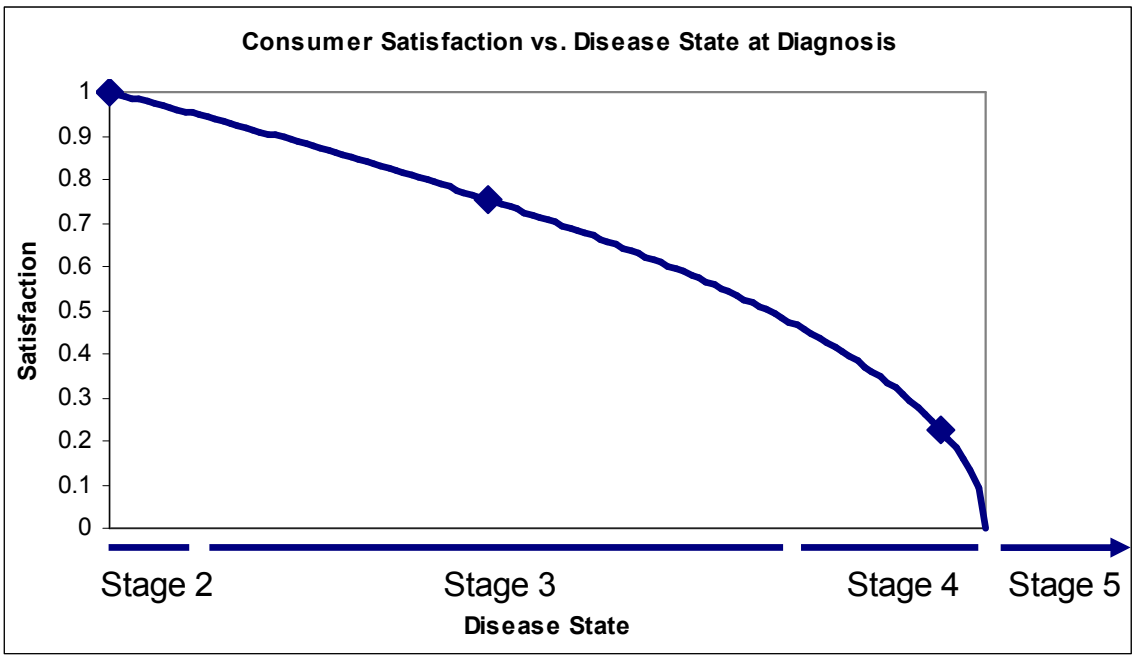

Figure 6: Consumer Satisfaction versus Disease State at Diagnosis

The sensitivity of the diagnostic device can be related to the detectable concentration limit of the test. By relating sensitivity to concentration, a qualitative measure of consumer satisfaction can be quantified and related to a physical property of the product. Figure 7 shows the way in which kidney disease state varies with minimum detectable concentration.

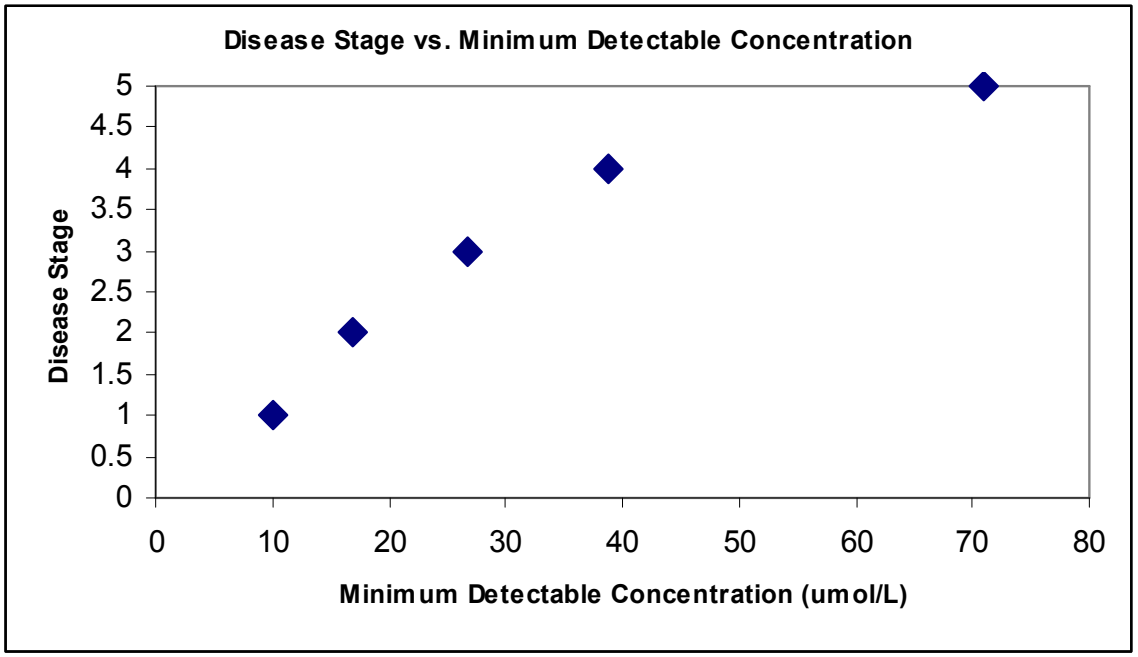

Figure 7: Relationship between disease stage and minimum detectable concentration[9]

Using this relationship, consumer satisfaction can be related to the minimum detectable concentration of the diagnostic test. This produces a curve as shown in Figure 8, on the following page. The equation for this curve is given below.

$$y_C = \sqrt{\frac{C - C_{max}}{C_{min} - C_{max}}} \qquad (13)$$

Where y_c is the property score for detectable concentration, C is the concentration (umol/L), and C_{max} and C_{min} are the minimum and maximum concentrations for the given range (umol/L).

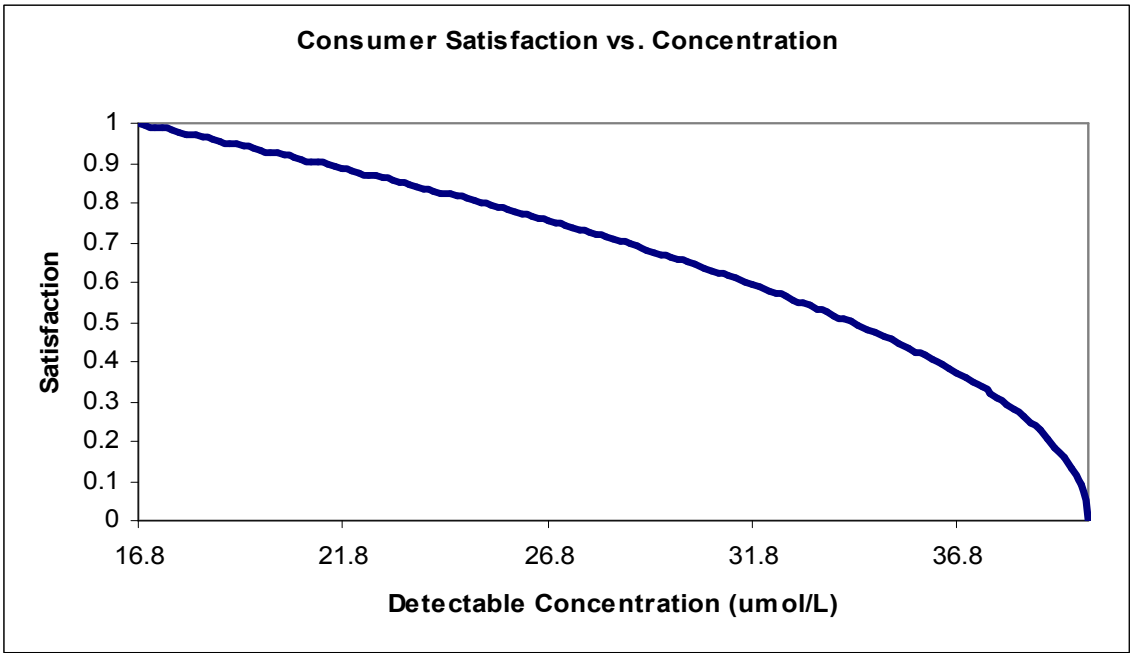

Figure 8: Consumer Satisfaction versus Minimum Detectable Concentration

False Negatives

False negatives are an important parameter to evaluate for consumer satisfaction as well as consumer safety. False negatives are test results that indicate the patient is healthy when they are actually unhealthy. The following figure shows the expected consumer response to the percentage of tests that give a false negative. It is anticipated that consumer satisfaction will decrease rapidly with increasing percent false negative.

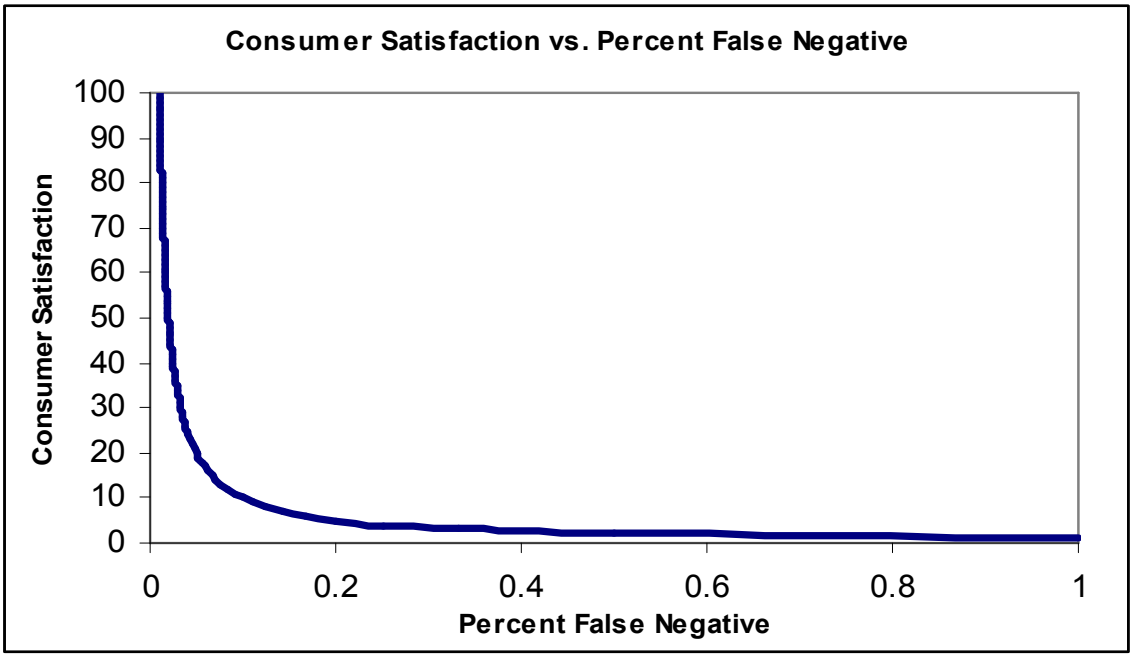

Figure 9: Consumer Satisfaction versus Percent False Negative

False negatives can occur due to the influence of a compound called bilirubin[16]. Bilirubin causes the apparent concentration of creatinine to decrease, so that a patient with a high concentration of creatinine (indicating problems) might be told that they are healthy.

In order to quantify the percent false negatives that would occur through the use of a saliva creatinine test, it is important to determine the percentage of patients at each stage of kidney failure and the amount of bilirubin present in saliva. The following figure shows the distribution of patients having specific salivary creatinine concentrations. These concentrations correspond to glomerular filtrations rates, which correspond to the stages of kidney disease.

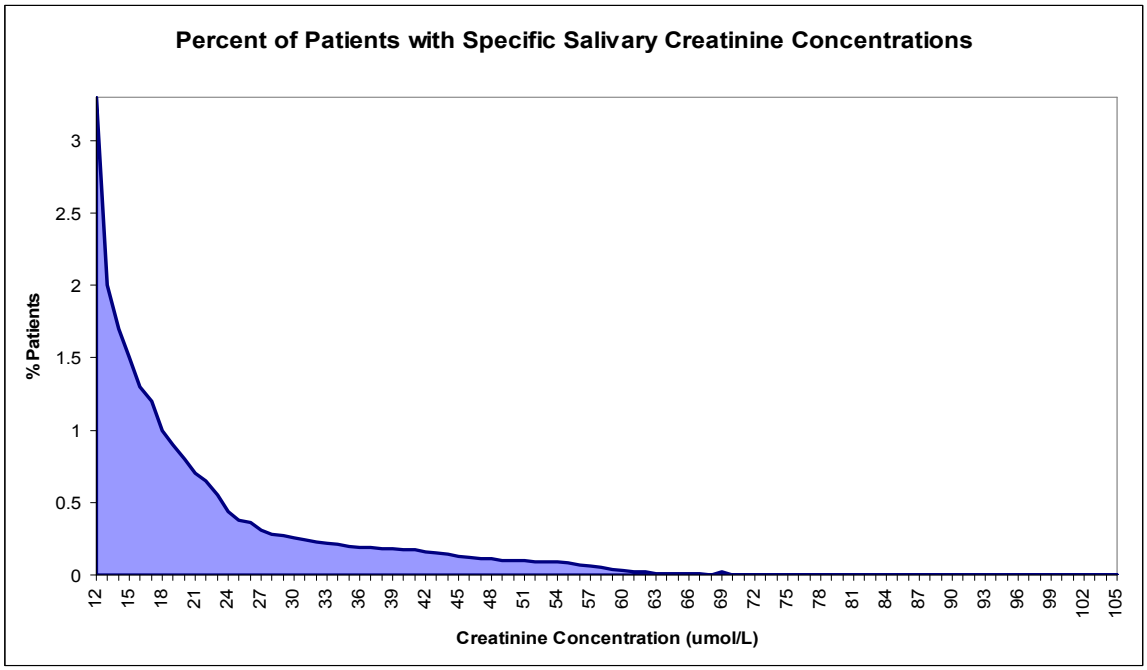

Figure 10: Distribution of Patients with Specific Salivary Creatinine Concentrations[15]

The average concentration of bilirubin in saliva was found to be 15 ± 5 umol/L[5]. Using a normal distribution, the percentage of patients with 10, 15, and 20 umol/L was determined.

Using data from the literature, the interference of bilirubin was found as a function of the bilirubin to creatinine concentration ratio[16]. The following figure shows the ratio of apparent creatinine concentration to actual creatinine concentration versus the bilirubin/creatinine ratio. From this figure, it can be seen that a bilirubin/creatinine concentration ratio of 4, for example, would yield a test result that is only 20% of the actual creatinine concentration present.

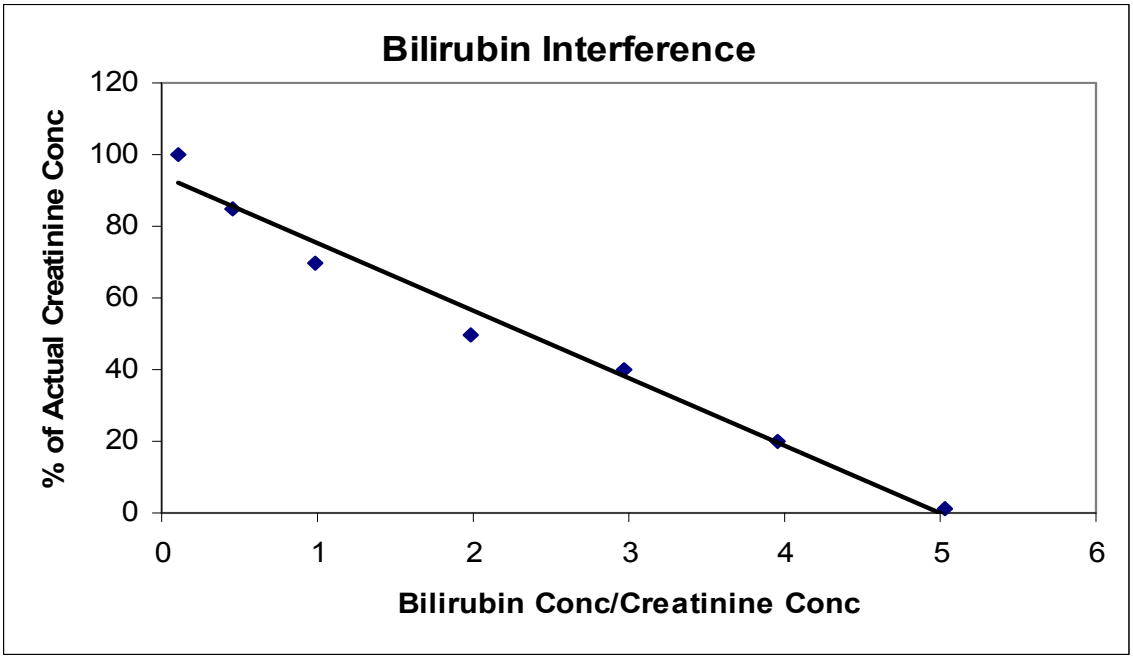

Figure 11: Bilirubin interference for a given [bilirubin]/[creatinine] ratio[16]

Using this data, the creatinine concentrations that would yield false negatives for the average and the average ± the standard deviation salivary bilirubin concentrations were determined. Once it was known what creatinine concentrations would give a false negative result, the percentage of patients that would generate a false negative was found using the distribution of patients previously mentioned. This gave the total percent false negative expected for this test.

It has been found that the addition of sodium dodecyl sulfate (SDS) to the reaction solution decreases the interference of bilirubin[10]. An equation for the interference of bilirubin as a function of SDS concentration was found, so that the percent false negative could be related to the SDS concentration. Figure 12 shows the percent false negative versus SDS concentration. The percent false negative decreases linearly with increasing SDS concentration until a concentration of 140 mmol/L where the usefulness of SDS levels off[10].

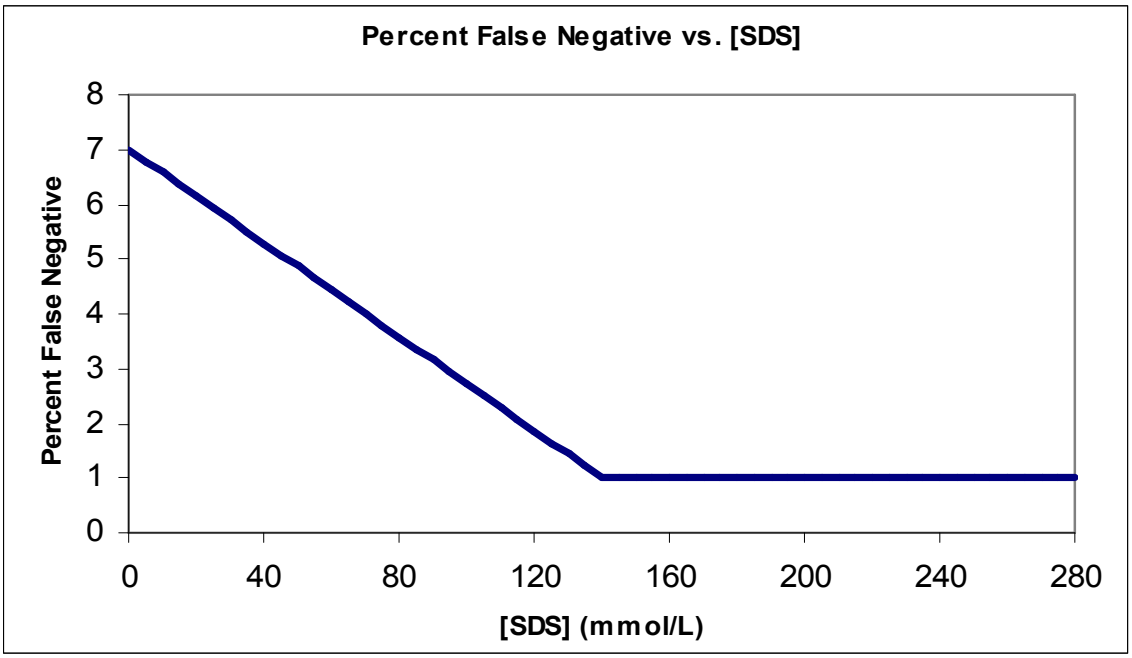

Figure 12: Reduction of false negative rate due to presence of SDS

Using this relationship, the consumer satisfaction was related to the concentration of SDS added to the reaction solution. Figure 13 shows how consumer satisfaction varies with SDS concentration.

The equation relating consumer satisfaction to the concentration of SDS is given below:

$$y_{neg} = \left(0.1181e^{0.0125 \bullet [SDS]}\right) \qquad (14)$$

Where y_{neg} is the property weight for the percent false negative, and [SDS] is the concentration of SDS added to the test.

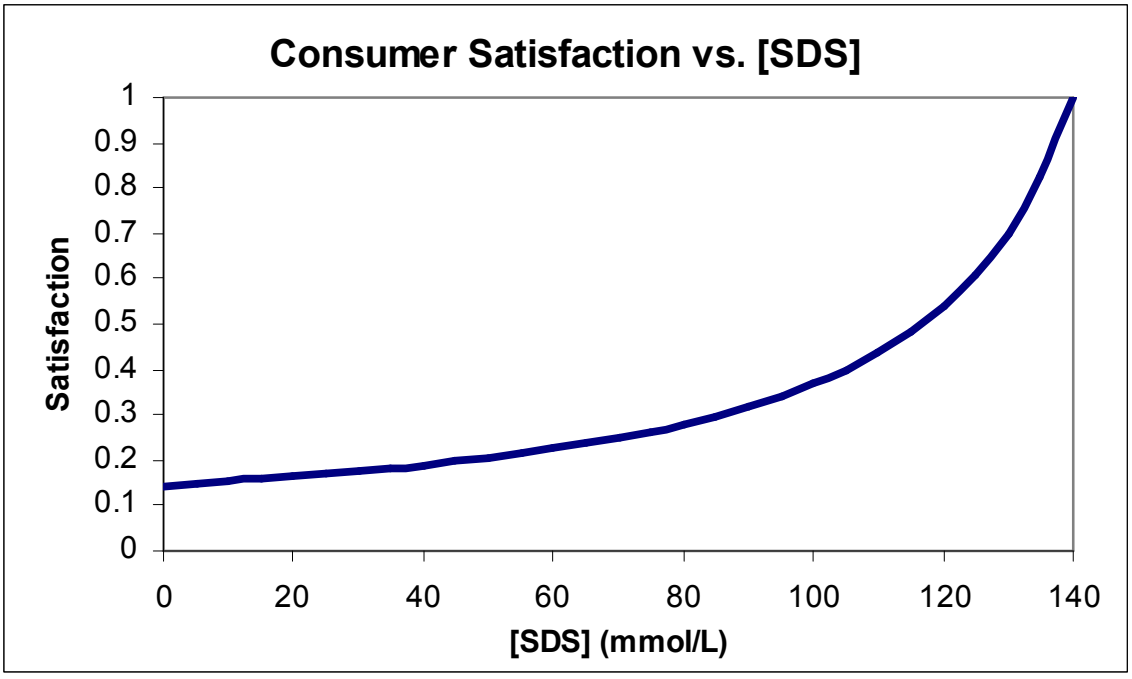

Figure 13: Consumer Satisfaction versus Concentration of SDS

False Positives

False positives are another concern when evaluating a diagnostic test. It was assumed that the consumer reaction to the percent false positive would be as shown in the following figure. The response would be similar to that for false negatives.

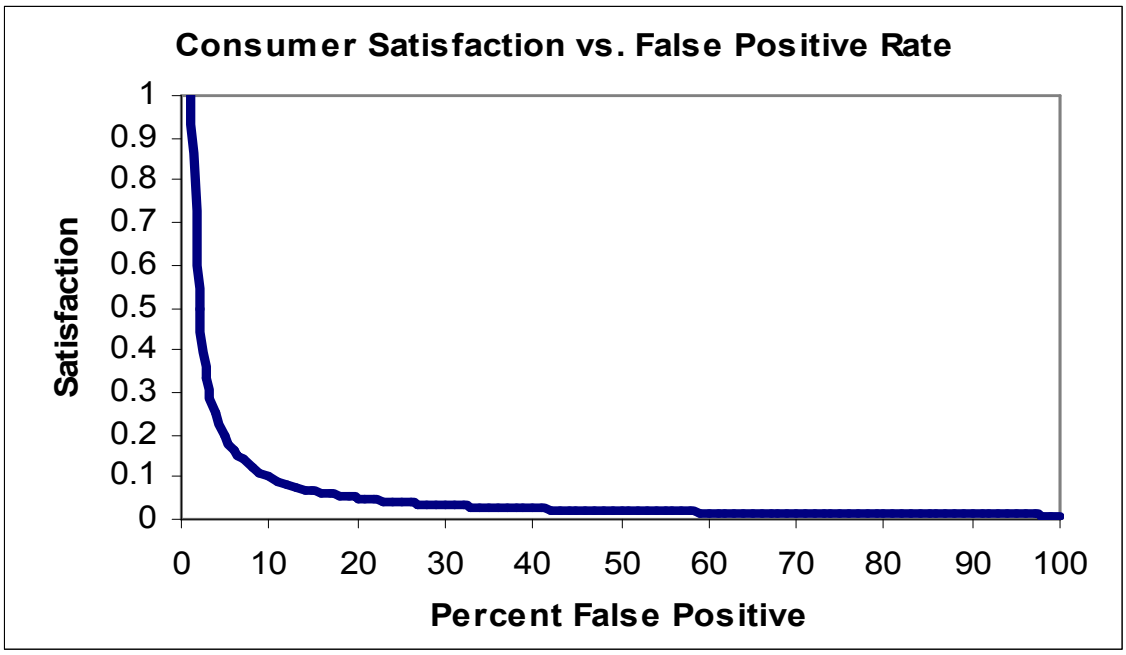

Figure 14: Consumer Satisfaction versus Percent False Positive

Interference leading to false positive test results is known to occur due to the presence of ketoacids and aromatic compounds[4]. From the literature, the apparent increase in creatinine concentration due to the presence of these compounds can be determined. Using the average salivary concentrations and the same data on the distribution of patients with specific salivary creatinine concentrations, the percentage of patients with the concentration of interferons required to produce a false positive result was determined. The percent false positive associated with the test turned out to be much smaller than the false negatives associated with the test. The following plot of percent false positive versus total concentration of interfering compounds shows the linear relationship of interference to concentration of interferons.

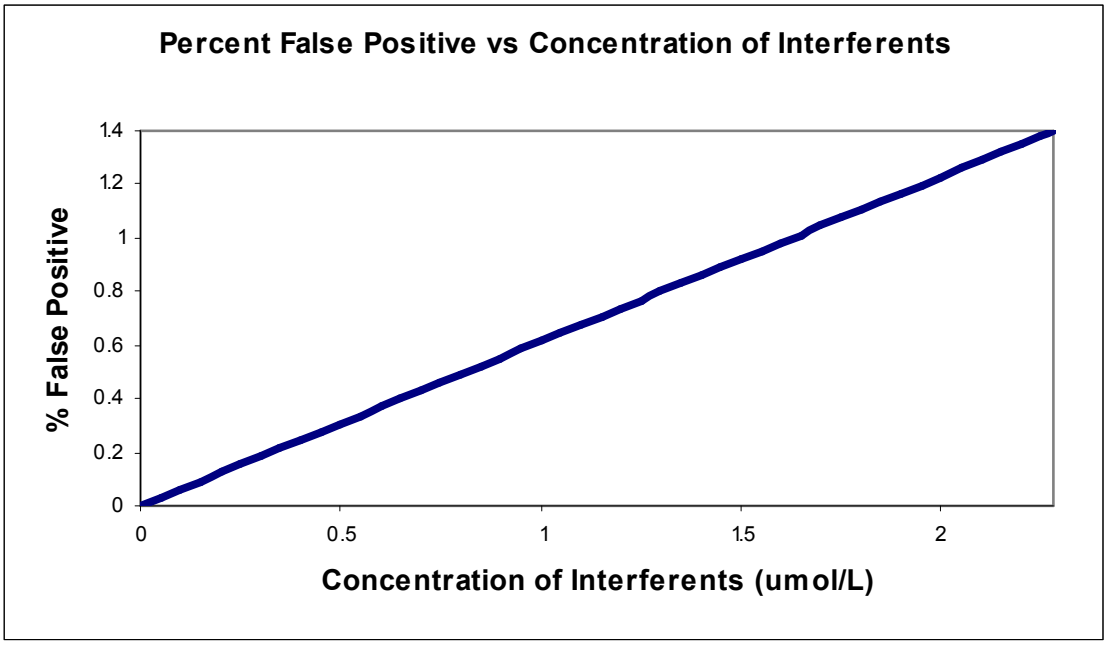

Figure 15: Percent False Positive versus Concentration of Interferents[4]

Using this relationship, a plot of consumer satisfaction versus concentration of interferents was created.

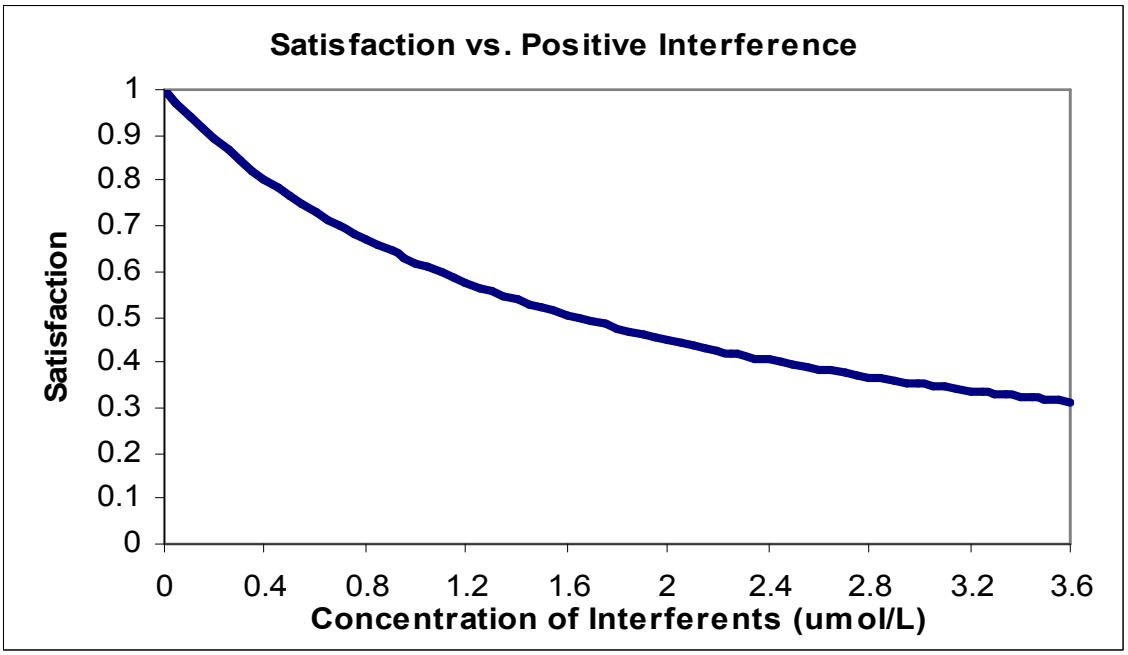

Figure 16: Consumer Satisfaction versus Concentration of Interferents

The equation used to quantify the consumer satisfaction as a function of the concentration of interfering compounds is given below.

$$y_{pos} = \left(0.05 \cdot I^2 - 0.36 \cdot I + 0.9\right) \qquad (15)$$

Where y_{pos} is the property score for false positives and I is the total concentration of positively interfering compounds. It was proposed that the addition of a glucose meter to the test kit would decrease the positive interference by allowing the user to differentiate between the concentration of glucose and creatinine.

CONSUMER SATISFACTION MODEL

Using these consumer satisfaction relationships, the consumer satisfaction model was created. The equation (equation 16) for this model is shown below, and is simply the summation of the products of the property functions and the weights for each variable.

$$H = w_c \sqrt{1 - \frac{[C] - [C_{max}]}{[C_{min}] - [C_{max}]}} + w_{neg}\left(0.1181 e^{0.0125 \bullet [SDS]}\right) + w_{pos}\left(0.05 \cdot I^2 - 0.36 \cdot I + 0.9\right) + D$$

Using this model, consumer satisfaction for different levels of interference was plotted for various detectable concentrations. These plots were created for 4 interference scenarios. The first was with nothing added to decrease interference, the second with only SDS added to reduce negative interference, the third with a glucose meter used to quantify the positive interference, and the forth with both SDS and a glucose meter.

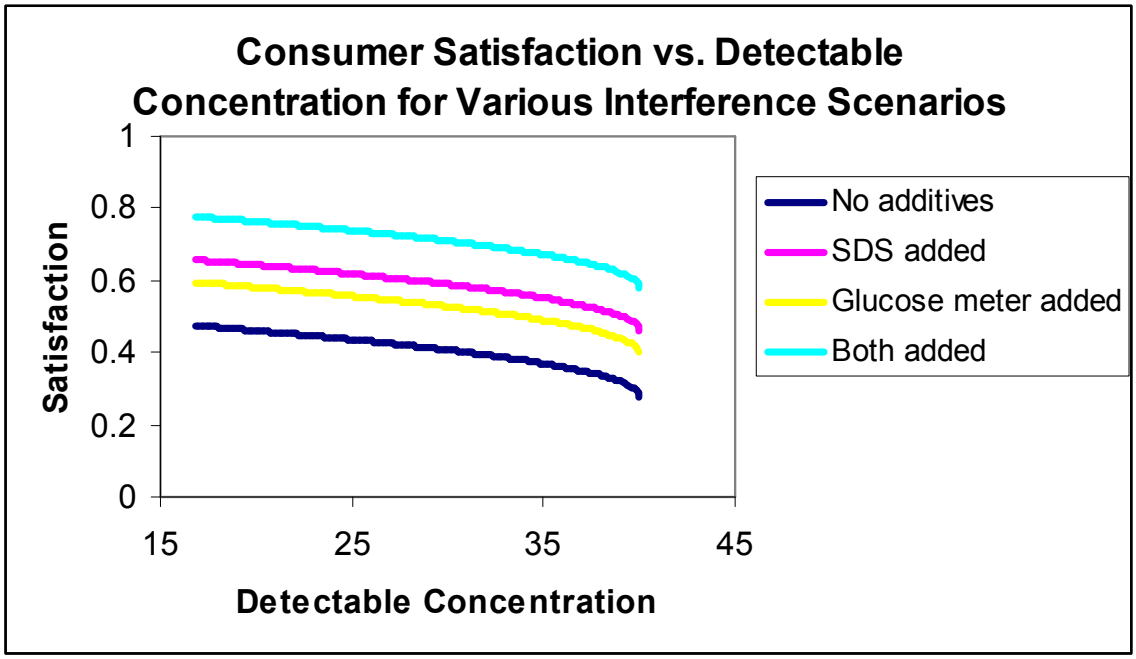

Figure 17: Consumer Satisfaction for Various Test Scenarios

As can be seen from this plot, consumer satisfaction is maximized for the test with the minimum detectable concentration and both SDS and a glucose meter. Also, the test with SDS added has a higher consumer satisfaction than with just the glucose meter because the negative interference has a larger effect than the positive interference. Clearly, the test with no additives yields the lowest consumer satisfaction, because it has the most interference.

CONSUMER PREFERENCE

The consumer preference for the saliva test compared to the serum test was determined by calculating the consumer satisfaction with the serum test and dividing that value by the various satisfaction values for the saliva test. The consumer preference value (β) is plotted versus minimum detectable concentration for various product options.

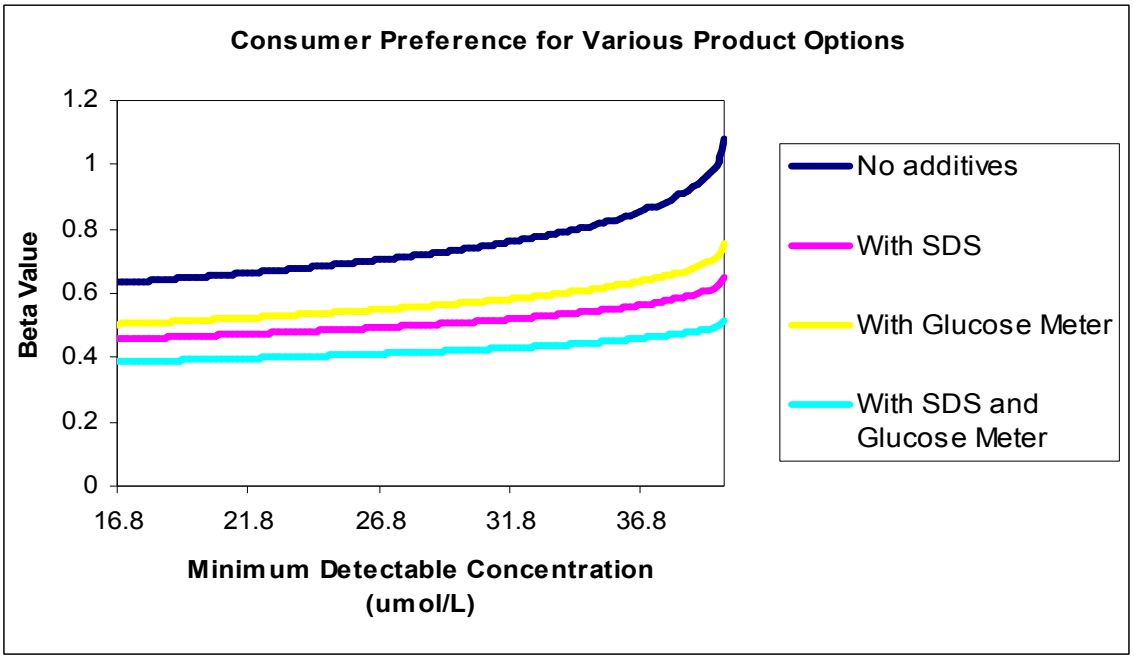

Figure 18: Consumer Satisfaction for Various Product Scenarios

The values of β used for the economic analysis were first chosen at the highest and lowest minimum detectable concentration, and then for the four interference scenarios.

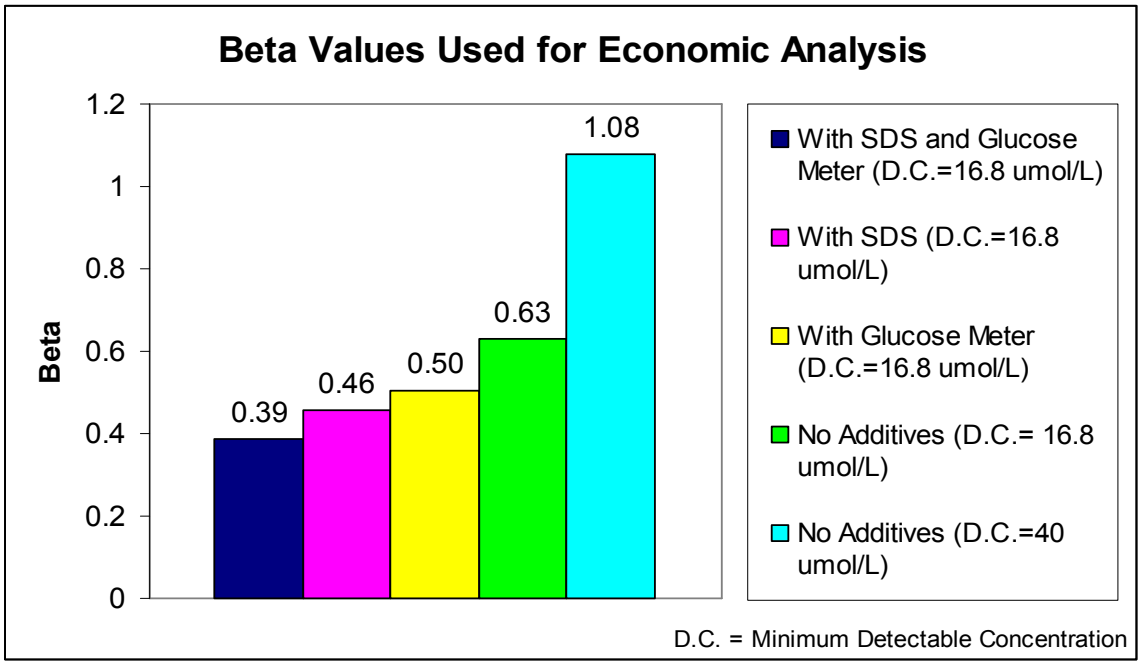

Figure 19: Values of β for Various Product Scenarios

PRODUCT DESIGN

Various product designs were investigated to determine optimum product features. Two sets of criteria were used as a basis to classify the designs. One was used to determine how the level of minimum detectable concentration relates to both demand and NPW. The other deals with including/excluding certain components which help to counter the affects of interfering compounds in saliva and observing how each one affects the profitability.

Minimum Detectable Concentration

To find how the minimum detectable concentration affected the demand for the product, two cases were created. One case set a low minimum detectable concentration of 16.8 umol/L, while the other was set at a high minimum detectable concentration of 40 umol/L. The product able to detect low concentrations of creatinine is to be used with a spectrophotometer and therefore includes standardization material. It is designed to provide information precise enough to indicate Stage 2-Stage 5 kidney failure. The second case, in which only high concentrations of creatinine are able to be determined may be observed visually and does not need standardization material for spectrophotometry. However, this test is not sensitive enough to determine the lower stages of kidney failure.

Inclusion of Anti-Interference Components

To deal with the interference of certain components, four options were considered which addressed the issue in different ways. The first option was to add nothing to the test to counter the negative or positively interfering components. The second option includes SDS to counter the negatively interfering bilirubin, but does nothing to deal with the possibility of positively interfering compounds. A glucose meter was included in the third option so that consumers may test their glucose level in the event that they receive a positive test result and wish to check if it may be due to abnormally high levels of

glucose. The third option does not include any additives to counter negatively interfering components. The fourth option includes SDS and a glucose meter to manage both positive and negative interference. The various costs and satisfaction parameters associated with each option were included in the economic analysis to determine the best one.

DEMAND

The demand as it varies with price is shown in figure 20 for both high and low minimum detectable concentrations. The test able to detect low concentrations of creatinine has a lower beta value due to the more appealing aspects of a test that can indicate earlier stages of kidney failure, causing the demand to be higher than that for the high minimum detectable concentration product.

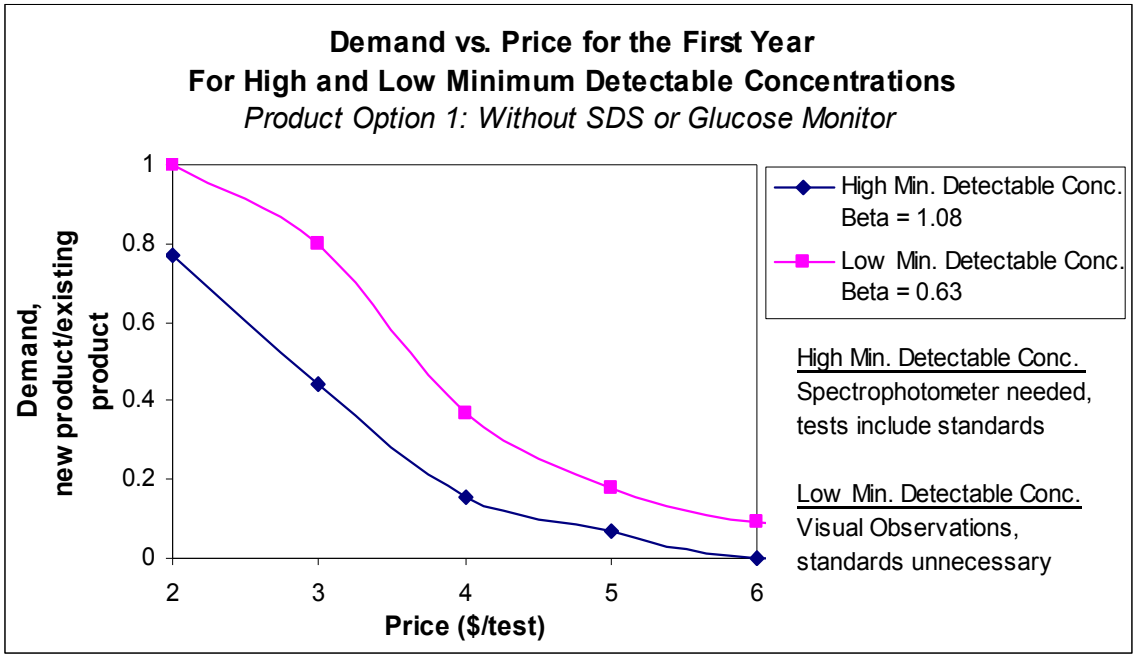

Figure 20: Price and Demand for Different Minimum Detectable Concentrations

While the demand was higher for the low minimum detectable concentration product, it was also more expensive to manufacture because of the need to

include standards. Because of the cost difference, it was important to determine the net present worth by including both demand and product cost. This is described in the following net present worth section, but for now we will consider the low minimum detectable concentration product to be superior.

Demand was calculated for the first three years of the project for scenarios with low minimum detectable concentrations and various options for dealing with interference. The figure below shows the case in which SDS was added to the product; the ratio of the demand for the new product over the demand for the existing product is plotted vs. the set price per test. Demand is plotted separately for the first three years to show the affect of time. The demand is higher in years two and three due to the increase in consumer awareness as time passes. At a demand of 1, it is assumed that all consumers will choose the new product and at a demand of 0 it is assumed that all consumers will choose the existing product.

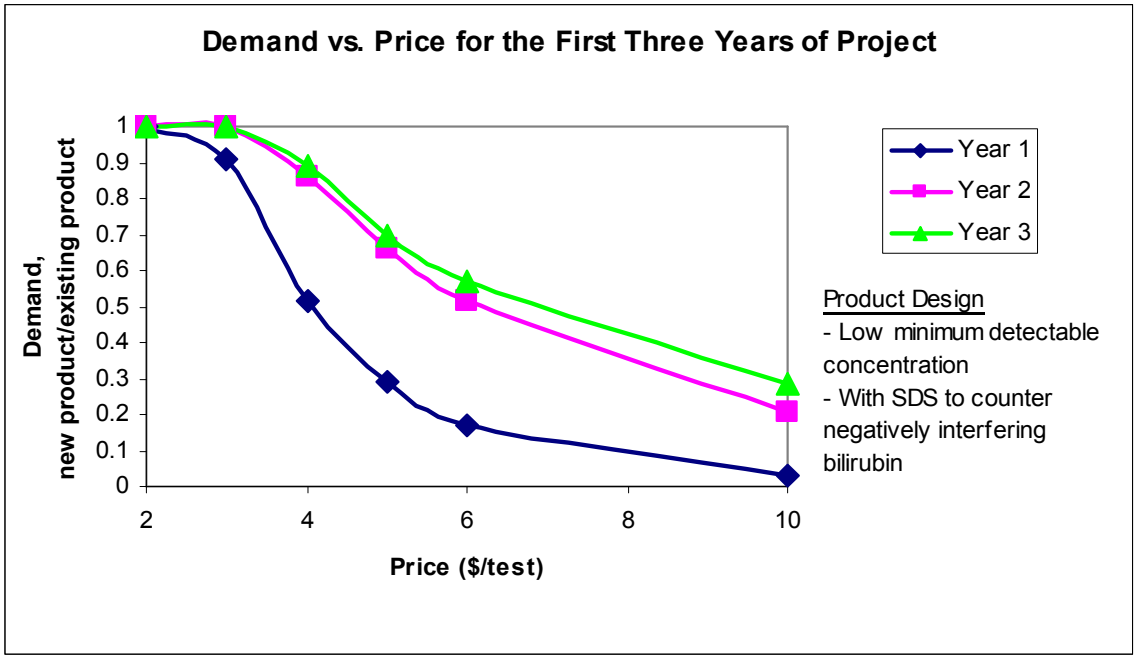

Figure 21: Price and Demand for First Three Years for One Product Option

The decreasing trends show that consumers are less willing to choose the new product over the existing product as the price of the new product increases. This

indicates that even though consumers may prefer the new product because of its appealing qualities such as its less invasive sample collection, they may opt for the existing product due to its lower cost.

Figure 22 shows how demand varies with price in the first year for each of the four anti-interference options. Each option was analyzed for a low minimum detectable concentration design.

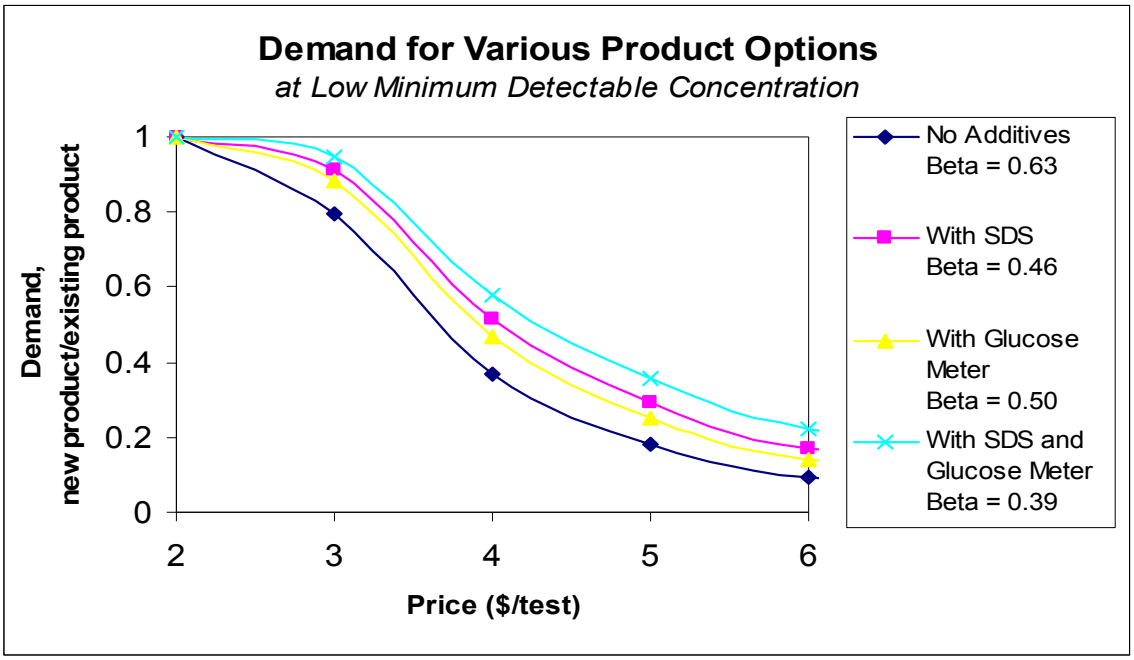

Figure 22: Price and Demand for Various Product Options

The lowest demand is for the product that has no additives to manage the interfering compounds. The glucose meter is seen to be less important than the addition of SDS as indicated by the lower demand. The option with the highest demand is the one including SDS to counter the negative interference from bilirubin and also includes the glucose meter to monitor glucose levels. Lower beta values result in higher demands. However, it is again important to realize that the option with the highest demand does not necessarily correspond to one that is the most profitable due to the costs associated with adding components to the design.

NET PRESENT WORTH

As previously mentioned the most profitable scenario must be determined by net present worth (NPW) and not demand alone. While the demand for the product able to detect low concentrations of creatinine was higher than that of the product only able to detect creatinine concentrations above 40 umol/L as seen in figure 20, the manufacturing costs were also higher. NPW accounts for both cost and demand and is plotted at different selling prices for both the high and low minimum detectable concentration scenarios in figure 23. The decision to use a high or low minimum detectable concentration test was made before anti-interference options were investigated.

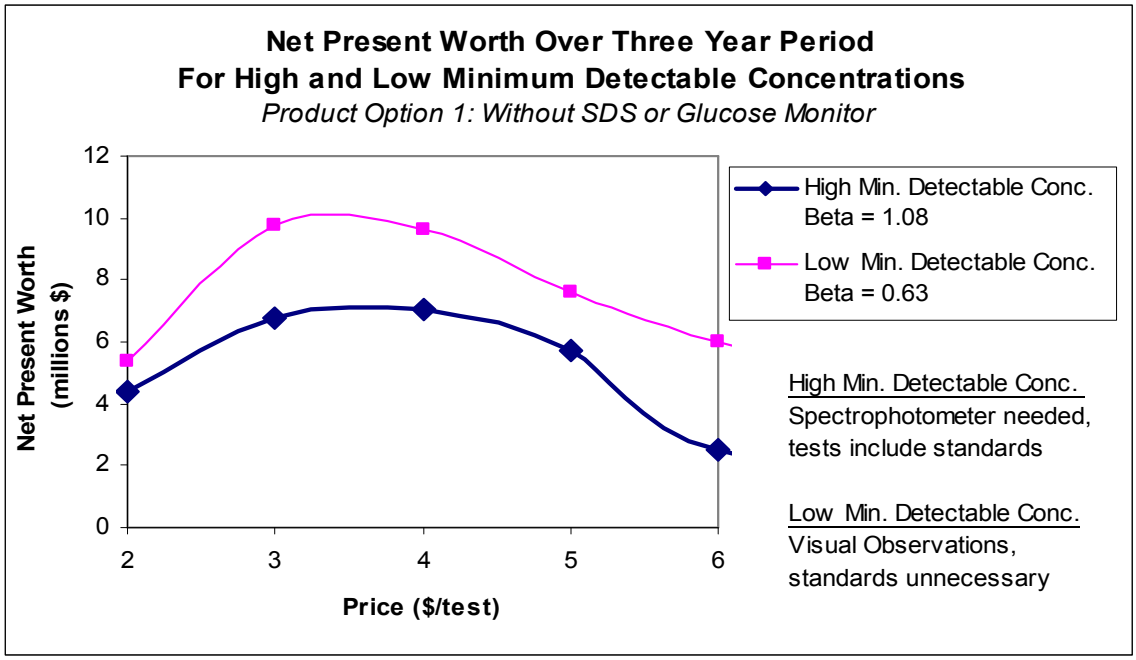

Figure 23: NPW Over Three Years for Different Minimum Detectable Concentrations

In this case, the higher demand for the product detecting lower concentrations was a larger contributing factor to the NPW than the higher manufacturing costs that accompanied the product. This NPW calculation determined that a product detecting lower concentrations of creatinine was more profitable.

The four anti-interference options were then applied to the low minimum detectable concentration scenario and their NPWs were determined. Figure 24 shows how NPW for each option changes with the selected selling price. The maximum in each trendline indicates the best price for each option. Prices set too low will not bring in enough revenue to create a profit, but prices that are too high will lower the number of consumers willing to purchase the product.

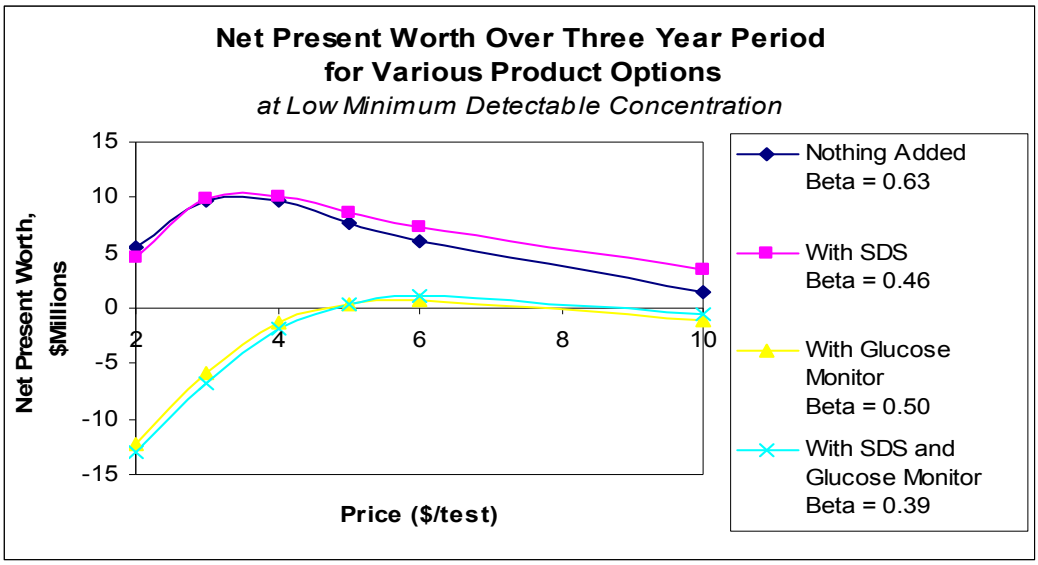

Figure 24: NPW Over Three Years for Various Product Scenarios

As seen before, lower beta values, which indicate an increased consumer satisfaction, correspond to greater demands. However, lower beta values do not necessarily mean more profitable products. When factoring in the expense associated with the various options, it was determined that the most profitable option was that of the product with SDS to counter negative interferences, but without glucose monitoring. While including a glucose meter increases demand by reducing the likelihood of false positive readings, it is not the best option because the increased demand is not substantial enough to justify the large added expense. The optimum selling price is $4/test and results in a NPW of $10 million for an ROI of 10%. Only slightly less profitable is the product with no

additives sold at either $3 or $4/test and also the product with SDS sold at $3/test, all of which have NPWs above $9.6 million.

CONCLUSIONS

The development of new, less invasive diagnostic tests is a worthy goal. The use of saliva as a diagnostic fluid as opposed to blood is an obvious alternative, and has previously been shown to be applicable towards diagnosis of various diseases. The use of creatinine to diagnose kidney health is an established practice that translates well into the development of a salivary assay. In this study, it has been shown that the development and marketing of a salivary creatinine test would be a profitable venture.

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