WIGTON

Medical Decision Making

Analyzing Diagnostic Tests: A Programmed Text

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This tutorial will show you how to analyze diagnostic tests. It covers only tests with only two outcomes, positive or negative.

This is a programmed text. You don't read it from front to back like a usual text. Rather, you follow the directions given in each frame. Your path depends on the answers you choose.

The three units are separate. When you have finished unit 1, go on to unit 2, which starts at frame 200. Unit three starts at frame 300.

The tutorial has been updated from previous versions. I would appreciate your suggestions for improvement for next year. The last page is an evaluation sheet. When you are done, please fill it out and send it to me.

To start, go to frame 100.

100

Unit I

This unit explains how to analyze the power of a diagnostic test. You will learn to calculate sensitivity, specificity, predictive value and prevalence. Start at frame, 101, and work through the unit by following the directions given with the answer you select or at the end of the frame.

101

The SENSITIVITY of a test is the likelihood the test will be positive in patients who have a particular disease. It measures the ability of the test to correctly identify patients with the disease.

The AST (SGOT) is a test for a liver enzyme in the blood. What is the sensitivity of the AST if 70 out of 100 people with viral hepatitis have a positive test and 160 of 200 people who do not have viral hepatitis have a negative test?

- 0.80 Go to 111
- 0.20 Go to 121
- 0.70 Go to 131
- 0.30 Go to 141
- 1.43 Go to 151

102

Right. Go on to 129.

103

Here are the calculations for the lipase.

	Pancreatitis yes	Pancreatitis no	
Positive lipase	80	250	330
Negative lipase	20	750	770
	100	1000	1100

Sensitivity = 0.8
Specificity = 0.75
PVP = 0.24
PVN = 0.97
Prevalence = 0.09

If you had no problems with these calculations go on to 152. If you would like some help, turn to 136.

104

Right. The sensitivity of the test is higher than the specificity. The test is better at identifying those who have the disease. Go to 115.

105

The SPECIFICITY of a test is the likelihood the test will be negative in patients who do not have a particular disease. It measures the ability of the test to correctly identify well patients.

As before, 70 out of 100 people with viral hepatitis have a positive AST and 160 of 200 people who do not have viral hepatitis have a negative AST. What is the specificity of the AST for viral hepatitis?

- 0.80 Go to 114
- 0.20 Go to 124
- 0.70 Go to 134
- 0.30 Go to 144
- 1.43 Go to 149

106

No. Return to 135 and try again.

107

No. Return to 140 and try again.

108

Wrong. Prevalence is the number with disease divided by the total number. Try again. Go to 125.

109

Right. Specificity is the number of negatives among all those who don't have the disease. Go on to 125.

110

If the sensitivity of a test is 0.8 and the specificity is 0.6, then.

- The test is better at identifying patients with the disease than those who do not have it. Go to 104
- The test is better at identifying those who do not have the disease than those who do. Go to 122

111

Wrong. This answer is the specificity of the test. The sensitivity is the number of patients with a positive test divided by the number of patients with the disease. Return to 101 and pick another answer.

112

Wrong. Specificity is the number of negatives among all those who don't have the disease. You're partly right. The false positives are part of the denominator. Return to 120 and choose another answer.

113

Wrong. Sensitivity is the number of positives among those with the disease. True negatives are patients who do not have the disease. Return to 115 and choose another answer.

114

Correct. The specificity is the number of patients without the disease who have a negative test divided by the number of patients without the disease. Go to 110

115

True Positive: Positive test in a patient who has the disease.
False Positive: Positive test in a patient who does not have the disease.
True Negative: Negative test in a patient who does not have the disease.
False Negative: Negative test in a patient who has the disease.

Define SENSITIVITY.□

- Sensitivity = true positives / true negatives: Go to 113
- Sensitivity = true positives / (true negatives + false positives): Go to 123
- Sensitivity = true positives / false positives: Go to 133
- Sensitivity = true positives / (true positives + false negatives): Go to 143
- Sensitivity = true positives / false negatives: Go to 148

116

Right. Go on to 140.

117

No. Return to 140 and try again.

118

Right. Prevalence is the number with disease divided by the total number. Go to 150.

119.

No. Return to 135 and try again.

120

It helps to think of the four outcomes as a 2 x 2 table.

	Disease Yes	Disease No
positive test	TP	FP
negative test	FN	TN

Define SPECIFICITY in these terms.

- Specificity = true negatives / false positives: Go to 112
- Specificity = true negatives / (true negatives + false positives): Go to 109
- Specificity = false negatives / true negatives: Go to 132
- Specificity = false negatives / (false negatives + true negatives): Go to 142
- Specificity = true positives / false negatives: Go to 147

121

Wrong. The sensitivity is the number of patients with a positive test divided by the number of patients with the disease. Return to 101 and pick another answer.

122

Wrong. The sensitivity of the test is higher than the specificity. The test is better at identifying those with the disease. Go to question 110.

123

Wrong. Sensitivity is the number of positives among those with the disease. True negatives and false positives are patients who do not have the disease. Return to 115 and choose another answer.

124

Wrong. The specificity is the number of patients without the disease who have a negative test divided by the number of patients without the disease. Return to 105 and pick another answer.

125

Prevalence is the fraction of all patients who have the disease. Thus, it is the number of patients with the disease divided by all patients with and without the disease.

If you are considering a group of patients, 16 of whom have viral hepatitis and 48 do not, what is the prevalence of viral hepatitis?

- 0.33 Go to 108
- 0.25 Go to 118
- 0.20 Go to 128
- 20 Go to 138

126

No. That is the false positives divided by those with a positive test. The numerator in the PVP is the true positives. Return to 135 and try again.

127

No. That is the predictive value negative. Return to 140 and try again.

128

Wrong. Prevalence is the number with disease divided by the total number. Try again. Go to 125.

129

The serum amylase is a useful test for diagnosing pancreatitis. In analyzing the tests done in his laboratory, a physician found the following results.

	Pancreatitis yes	Pancreatitis no	
Positive amylase	85	300	385
Negative amylase	15	700	715
	100	1000	1100

Test your mastery of the 5 test characteristics you have learned. Write your answers below, then check your results at 139.

- Sensitivity =
- Specificity =
- PVP =
- PVN =
- Prevalence =

130

The table below gives the answers.

	Hepatitis Yes	Hepatitis No	
positive AST	14	20	34
negative AST	6	80	86
	20	100	120

Sensitivity = 0.70
Specificity = 0.80
Prevalence = 0.17

Go to 135.

131

Correct. Sensitivity is the number with a positive test divided by all those with the disease. Go to 105.

132

Wrong. Specificity is the number of negatives among all those who don't have the disease. The false negatives are not involved in specificity since they have the disease. Return to 120 and choose another answer.

133

Wrong. Sensitivity is the number of positives among those with the disease. False positives are patients who do not have the disease. Return to 115 and choose another answer.

134

Wrong. The specificity is the number of patients without the disease who have a negative test divided by the number of patients without the disease. Return to 105 and pick another answer.

135

The test characteristic we often want the most is not given by either sensitivity or specificity. When a patient has a positive test, we want to know what that means. How likely is it that the patient has the disease given that the test is positive? This characteristic is called the predictive value of a positive test, or predictive value positive (PVP).

The PVP is the likelihood of having the disease given a positive test. PVP = TP/(TP+FP)

What is the predictive value of a positive AST in hepatitis calculated from the observations below?

	Hepatitis Yes	Hepatitis No	
positive AST	14	20	34
negative AST	6	80	86
	20	100	120

- 0.07 Go to 106
- 0.41 Go to 116
- 0.59 Go to 126
- 0.70 Go to 119
- 0.93 Go to 146

136

In calculating test characteristics, we don't need all the values; many can be inferred. Refer to the 2 X 2 table below as we go through the lipase problem.

There are 1100 patients. Place this marginal total in the lower right corner. 100 had pancreatitis; put this number at the bottom of the leftmost column. 330 had a positive lipase; put this total at the far right of the top row. 80 of these were positive (true positive); place this number at the top of the left column.

Although this information seems insufficient, we can derive all the other values from these. The false positives (top of 2nd column) are equal to the total with a positive test minus the true positives (330 - 80 = 250). The total who don't have pancreatitis is the total number (1100) minus the total with disease (100) or 1000. The true negatives can be inferred by subtracting the false positives from the number without disease (1000 - 250 = 750).

	Pancreatitis yes	Pancreatitis no	
Positive lipase	80		330
Negative lipase			
	100		1100

	Pancreatitis yes	Pancreatitis no	
Positive lipase	80	250	330
Negative lipase	20	750	770
	100	1000	1100

When you are done, go on to unit 2 (200).

137

No. That answer is the false positives divided by those with a positive test. The numerator in the PVN is the true negatives. Return to 140 and try again.

138

Wrong. Prevalence is the number with disease divided by the total number. Try again. Go to 125.

139

Results from 129.

	Pancreatitis yes	Pancreatitis no	
Positive amylase	85	300	385
Negative amylase	15	700	715
	100	1000	1100

Sensitivity = 0.85
Specificity = 0.70
PVP = 0.22
PVN= 0.98
Prevalence= 0.09

Go on to 145

140

Similarly, specificity doesn't measure what we often want to know when our patient gets a negative test result. What is the likelihood of disease now that the test is negative?

The predictive value of a negative test is just that: the likelihood of disease given a negative test. PVN = TN/(TN+FN).

In the hepatitis example, what is the PVN?
Hepatitis

	Yes	No	
positive AST	14	20	34
negative AST	6	80	86
	20	100	120

- 0.07 Go to 117
- 0.41 Go to 127
- 0.59 Go to 137
- 0.70 Go to 107
- 0.93 Go to 102

141

Wrong. You picked the fraction of patients with a negative test. The sensitivity is the number of patients with a positive test divided by the number of patients with the disease.. Return to 101 and pick another answer.

142

Wrong. Specificity is the number of negatives among all those ~~who don't have the~~ disease. The false negatives are not involved in specificity since they have the disease. Return to 120 and choose another answer.

143

Right. Sensitivity is the number of positives among all those with the disease, the false negatives and the true positives. Go to 120.

144

Wrong. This is the sensitivity. Return to 105 and pick another answer.

145

The serum lipase also is useful in diagnosing pancreatitis. The same physician analyzed the performance of the serum lipase in patients with pancreatitis. The same 1100 patients were considered. 100 had pancreatitis. 330 had a positive lipase, of whom 80 had pancreatitis.

Make up a 2 X 2 table for lipase as a test for pancreatitis and calculate the sensitivity, specificity, predictive value positive, predictive value negative and prevalence. Some of the values in the table were not given, but you will find they can be calculated with a little thought. When you are done, go to 103 to check your answers.

	Pancreatitis yes	Pancreatitis no
Positive lipase		
Negative lipase		

146

No. That is the predictive value negative. Return to 135 and try again.

147

Wrong. Specificity is the number of negatives among all those who don't have the disease. The true positives are not involved in specificity since they have the disease. Return to 120 and choose another answer.

148

Wrong. Sensitivity is the number of positives among all those with the disease. False negatives are only part of the patients who have the disease. Return to 115 and choose another answer.

149

Wrong. The specificity is the number of patients without the disease who have a negative test divided by the number of patients who do not have the disease. Return to 105 and pick another answer.

It is often easier to look at the behavior of a test with two outcomes (e.g. positive or negative) by making a table. The results of the AST (SGOT) test in viral hepatitis can be plotted as follows.

	Hepatitis Yes	Hepatitis No
positive AST	14	20
negative AST	6	80

These patient numbers represent the numbers of false positives, false negatives, true positives and true negatives as shown here.

	Hepatitis Yes	Hepatitis No
positive AST	TP	FP
negative AST	FN	TN

By totaling the columns and rows, we have enough information to find sensitivity, specificity and prevalence.

	Hepatitis Yes	Hepatitis No	
positive AST	14	20	34
negative AST	6	80	86
	20	100	120

Calculate the sensitivity, specificity and prevalence from this table. Then go on to 130 to check if you got the right answers.

- Sensitivity =
- Specificity =
- Prevalence =

151

Wrong. The sensitivity is the number of patients with a positive test divided by the number of patients with the disease. Return to 101 and pick another answer.

152

In this unit you learned to calculate all the important characteristics of a dichotomous test. Test yourself on the problem below. Then go on to unit II.

A positive EKG is seen in 70% of patients with acute myocardial infarction (AMI) while 5% of patients who do not have an AMI have a positive EKG. See if you can construct the 2X2 table and calculate the test characteristics for a patient whose likelihood of AMI (before you know the EKG results) is 50%.

	AMI	no AMI
Positive EKG		
Negative EKG		

Sensitivity =
Specificity =
PVP =
PVN =
Prevalence =

Go to 153 to check your answers, then go on to Unit II.

	AMI	no AMI	
Positive EKG	70	5	75
Negative EKG	30	95	125
	100	100	200

Sensitivity = 0.70
Specificity =0.95
PVP = 0.93
PVN = 0.76
Prevalence = 0.5

When you are done, go on to Unit II (200).

200

Unit II.

The prevalence of a disease affects the predictive power of a test. This unit will show you how to calculate that effect.

You will also learn the concepts of prior probability and posterior probability.

201

The serum lipase has a sensitivity of 0.8 and a specificity of 0.75 in diagnosing pancreatitis. If the prevalence of pancreatitis is 0.50, as in the example below, what is the probability of pancreatitis given that the serum lipase is positive?

	Pancreatitis yes	Pancreatitis no	
Positive lipase	80	25	105
Negative lipase	20	75	95
	100	100	200

- 0.21 Go to 206
- 0.75 Go to 216
- 0.76 Go to 221
- 0.79 Go to 226
- 0.80 Go to 240

202

Right. The probability of disease before doing the test (the prior probability) is the same as the prevalence of the disease in that population. Go on to 220.

203

Right. This is the posterior probability for a negative test = 1-PVN. Go on to 205.

204

No. This answer is 1-PVN, you want the PVP. Go back to 225.

205

If you ordered a serum amylase rather than serum lipase on the same patient, what would be the posterior probability if the test were positive (PVP)?

Serum amylase has a sensitivity of 0.85 and specificity of 0.70. Before any tests are done, you think the chance of pancreatitis is 10%. Complete the table below to get the answer.

	Pancreatitis yes	Pancreatitis no	
Positive amylase		270	
Negative amylase	15		
	100		1000

What is the likelihood of pancreatitis given a positive amylase?

- 0.24 Go to 211
- 0.31 Go to 219
- 0.38 Go to 229
- I don't see how to get the missing values. Go to 238

206

No. The probability of disease given a positive test is the PVP. (PVP = TP/(TP+FP)). Go back to 201.

207

Wrong. Specificity is the probability of a negative test given the disease is absent. You want the probability of disease given a negative test. Go back to 220.

208

No. The sensitivity is the likelihood the test will be positive if the patient has the disease. Go back to 215.

In the previous example, we calculated that 76% of patients with a positive test have the disease (PVP= 0.76).

	Pancreatitis yes	no	
Positive lipase	80	25	105
Negative lipase	20	75	95
	100	100	200

Sensitivity = 0.8
Specificity = 0.75
PVP = 0.76

In the example below the PVP is different:

	Pancreatitis yes	no	
Positive lipase	80	250	330
Negative lipase	20	750	770
	100	1000	1100

Sensitivity = 0.8
Specificity = 0.75
PVP = 0.24

What has happened?

- The sensitivity and the specificity are the same, so the power of the test should remain the same. There may be a mistake in the calculation. Go to 222.

- The laboratory techniques for performance of the test must have changed. This affected the true negatives and false positives. Go to 227.

- The prevalence of disease has changed. This changed the percent of those with a positive test who have the disease. Go to 232

211

Correct. Since the test is positive, posterior probability = PVP = TP/(TP+FP). This kind of problem can be solved if you know three things: sensitivity, specificity and prevalence. Go on to 241.

212

Wrong. (1 - Specificity) is the probability of a positive test given no disease. You want the probability of disease given a negative test. Go back to 220.

213

No. This is the PVP. You want the posterior probability for a negative test which is 1-PVN. Go back to 230.

214

Correct. You know the true negatives are 675 since this is (specificity * all with no disease) or (.75 * 900). Good work. Go to 230.

215

The table below shows how the predictive value of the serum lipase changes as the prevalence of pancreatitis changes.

Prevalence of Pancreatitis	Predictive Value Positive
.001	.003
.01	.03
.05	.14
.1	.26
.2	.44
.3	.58
.4	.68
.5	.76

You can see that a positive test always improves the chances that the patient has the disease, but the resulting likelihood of disease depends on the prevalence.

The likelihood that a patient has the disease before a test is performed is called the prior probability and the likelihood of disease after the test results are known is called the posterior probability.

In a clinical test, the prior probability is the same as the,

- prevalence: Go to 202.
- sensitivity: Go to 208.
- predictive value positive: Go to 224.
- specificity: Go to 231.

216

No. This answer (0.75) is the specificity. The probability of disease given a positive test is the PVP. (PVP = TP/(TP+FP)). Go back to 201.

217

Hardly. Go back to 230.

218

No. You must be guessing. Go back to 225 and pick d. if you need some help.

219

No: .31 is TP/FP. What you want is the PVP, (TP/(TP+FP). Go back to 205.

220

The posterior probability is the likelihood of having the disease after the test results are known. In this case, it is the likelihood the patient has pancreatitis after you know the serum lipase. If the test is positive, the posterior probability is the same as the predictive value positive. If the test is negative, the posterior probability of having the disease is the same as

- specificity: Go to 207.
- 1 - specificity: Go to 212.
- predictive value negative: Go to 223.
- 1 - predictive value negative: Go to 234.

221

Right. This means that 76% of patients with a positive test have the disease. It is easy to confuse the PVP with the sensitivity (the probability of a positive test given the disease). Go to 210.

222

No. The percentage of those with a positive test is markedly affected by changes in prevalence. Return to 210 and select another answer.

223

Wrong. Predictive value negative is the probability of <u>no disease</u> given the test is negative. You want the probability of <u>disease</u> given a negative test. Go back to 220.

224

No. The predictive value positive is the likelihood the patient has the disease if the test is positive. Go back to 215.

225

After doing a history and physical, you decide your patient has only a 10% chance of having pancreatitis (i.e. the prior probability is 0.10). Calculate the likelihood of pancreatitis in this patient if the lipase is positive (posterior probability).

(Hint. Use the partially completed table below. Remember, the sensitivity is 0.8, the specificity is 0.75, and the prevalence is the same as the prior probability)

	Pancreatitis yes	Pancreatitis no	
Positive lipase	80		
Negative lipase	20	675	
	100	900	1000

(Can you see where the 675 came from?)

What is the posterior probability

- 0.03 Go to 204
- 0.26 Go to 214
- 0.34 Go to 218
- I can't see how to get the missing values. Help. Go to 236

226

No. This number (0.79) is the PVN. The probability of disease given a positive test is the PVP. (PVP = TP/(TP+FP)). Go back to 201.

227

No. The test has the same sensitivity and specificity, so technique hasn't changed. Return to 210 and select another answer.

228

In the table below, you can get the true negatives (675) by multiplying the column total (true negatives + false positives) by the specificity (0.75). Specificity is the defined as this ratio: TN/(TN+FP). (or, you could have subtracted 225 from 900).

Obtain the true positives by subtracting the false negatives from the column total (110-20=80). Sum the first row (80+225=305), and sum the second row (20+675=695).

Now that the table is completed, you can calculate the PVN (675/695=0.97). The posterior probability is the complement of the PVN (1-PVN). Or, it can be calculated as the FN/(FN+TN).

	Pancreatitis yes	Pancreatitis no	
Positive lipase		225	
Negative lipase	20		
	100	900	1000

When you are done, return to 230.

229

No. You must have guessed. Go to 238 for a hint. if you are not clear about the calculations. Go back to 205.

230

What would the posterior probability be if the lipase were negative? Remember, when the test is negative, the posterior probability of disease = 1 - predictive value negative.

Use the table below to help calculate. The sensitivity is 0.8, the specificity is 0.75 and the prevalence is 0.1. (Can you see how to get TP and TN?

	Pancreatitis yes	Pancreatitis no	
Positive lipase		225	
Negative lipase	20		
	100	900	1000

What is the posterior probability of disease if the lipase is negative?

- 0.03 Go to 203
- 0.26 Go to 213
- 0.34 Go to 217
- I don't see how to get the missing values. Help! Go to 228

231

No. The specificity is the likelihood the test will be negative if the patient does not have the disease. Go back to 215.

232

Right. Changes in prevalence affect the significance of a positive test. Go on to 215.

233

Answers, first problem.

- sensitivity of the enzyme test = 0.92
- specificity of the enzyme test = 0.90
- predictive value of a positive enzyme test = 0.90
- likelihood of infarction given a positive test = 0.90 (same as PVP)
- likelihood of infarction given a negative test = 0.08
- likelihood of infarction before the test was done = 0.50 (prevalence)

Second Test Problem (harder)

You estimate your patient has a 40% chance of Pudwill disease. The Fubar test has a sensitivity of 80% and specificity of 90% for Pudwill disease. If your patient has a positive fubar test, what is the probability he has Pudwill disease?

If you need a hint, go to 242

Write down your answer, then go to 235.

234

Right. This is the probability of disease given a negative test (false negatives / (false negatives + true negatives)). Good work. Go on to 225.

235

Answer to second test problem:

Given a positive test, the probability of Pudwill disease is 0.84

Explanation: One way to solve this was to construct a table and fill in a hypothetical population (see below). The prevalence was 40% so make the total patients 100, the total with disease 40 (1st column) and the total without disease 60 (2nd column). Since the total with disease is 40 and the sensitivity is 0.8 this makes the true positives 32 (0.8*40) and the false negatives 8 (0.2 * 40) or (40 - 32). Similarly, the total without disease is 60 and the specificity is 0.90. This makes the true negatives 54 (0.9 * 60) and the false positives 6 (.1 * 60). Thus, the predictive value positive is 0.842 (32/38).

	Pudwill Disease		
	Yes	No	
Positive Fubar test	32	6	38
Negative Fubar test	8	54	62
	40	60	100

Go to 239

236

In the table below, you can get the true negatives (675) by multiplying the column total (true negatives + false positives) by the specificity (0.75). Specificity is the defined as this ratio: TN/(TN+FP).

Next, you can determine the false positives (top of middle column) by subtracting the true positives from the column total (900-675=225). Then you can sum the first row (80+225=305), and sum the second row (20+675=695). Now that the table is completed, you can calculate the PVP (80/305=0.26).

	Pancreatitis		
	yes	no	
Positive lipase	80		
Negative lipase	20	675	
	100	900	1000

When you are done, return to 225.

238

The total with no disease is 900, since the prevalence is 10% and therefore the number with disease is 100. Get the true negatives by subtracting the false positives from the column total (900-270=630). Similarly, the true positives are obtained by subtracting 15 from 100. The last two numbers are obtained by summing the rows, (85+270=355), (15+630=645).

The chance of pancreatitis after a positive test = PVP = Posterior probability = TP/(TP+FP). Return to 205 and select an answer.

239

Third Test Problem (hardest),

A patient has come to the emergency room with chest pain. Characteristic ST segment change on the EKG has a sensitivity of 70% and a specificity of 95% for myocardial infarction (MI). Based on this patient's presentation and their examination, the emergency room doctors thought the patient had a 50% chance of having had an infarction. What is the likelihood of infarction if the characteristic ST changes are present on the EKG?

What would the likelihood be (given a positive test) if the doctors had estimated the patient originally had a 20% chance of having had an infarction?

Write down the answer, then go to 243

240

No. This number (0.8) is the sensitivity. The probability of disease given a positive test is the PVP. (PVP = TP/(TP+FP)). Go back to 201.

Summary.

In this unit, we have defined several new terms: The **prior probability of disease** is the probability of disease before you know the results of the test. The **posterior probability of disease** is the probability after you have learned the results of the test. Thus, in clinical tests, the prior probability is the same as the prevalence of disease. The posterior probability of disease given a positive test is the same as the PVP and the posterior probability of disease given a negative test is (1-PVN) or FN/(FN+TN). (The PVN = the posterior probability of no disease given a negative test).

Prior probability = prevalence
Posterior probability = PVP (if the test is positive)
= 1-PVN (if the test is negative)

In this chapter, you also saw that the meaning of a test (i.e. the likelihood of disease after you know the test results) depends on the prevalence. To put it another way, the posterior probability resulting from a given test depends on the prior probability. This is not intuitively obvious to many people. Failure to understand this principle often results in inappropriate use of diagnostic tests.

The following problems will allow you to test whether you have mastered the technique of calculating the likelihood of disease in your patient given the test characteristics, the test result and the prevalence. We'll start with the easiest and work up.

First Test Problem (easy):

In the past year your emergency room registered 1000 patients with a chief complaint of chest pain. Of these 1000 patients, 500 had a myocardial infarction, An enzyme test was positive in 460 of the patients with infarction and 50 of the patients without infarction.

Answer the following questions

- What is the sensitivity of the enzyme test?
- What is the specificity of the enzyme test?
- What is the predictive value of a positive enzyme test?
- If a patient has a positive enzyme test, what is the likelihood that patient had an infarction?
- If a patient has a negative enzyme test, what is the likelihood that patient had an infarction?
- What was the likelihood of infarction before knowing the test results?

Write down your answers then check them at the next problem. Go to 233

242

Hint

To solve this, construct a table and fill in a hypothetical population. The prevalence is 40% so make the total patients 100. This makes the total with disease 40 and the total without disease 60. If the total with disease is 40 and the sensitivity 0.8 then the true positives are 32 (0.8*40) and the false negatives are 8 (0.2 * 40) or (40 - 32). Similarly, the total without disease is 60 and the specificity is 0.90. This makes the true negatives 54 (0.9 * 60) and the false positives are 6 (.1 * 60). You can now calculate the predictive value.

Return to second test problem. Go to 233

243

Answer to third test problem:

Since the doctors thought the prior probability of MI was 50%, we will construct a table with 50% prevalence (equal numbers with infarction and without infarction). I chose to have 100 in each group to make the calculations easier (you could use any number). The 70% sensitivity means the true positives are 70 (70% of 100) and the 95% specificity means that the false postives are 5 (5% of 100). The likelihood of MI with a positive test is the PVP = 70/75 = 0.93)

	MI	noMI	
EKG positive	70	5	75
EKG negative	30	95	125
	100	100	200

In the second part of the question, only the prevalence has changed, so I will construct another table. I left the left column unchanged, but you could use any totals as long as those with disease are 20% of the total.

	MI	noMI	
EKG positive	70	20	90
EKG negative	30	380	410
	100	400	500

The sensitivity and specificity remain the same, but the PVP has declined from 0.93 when the prevalence was 50% to 70/90 = 0.78 now that the prevalence is 20%.

This concludes Unit II, go on to Unit III, frame 300

300

Unit 3

In this unit you will learn how to analyze decisions using a decision tree. This method is most useful for complex clinical decisions where the consequences of several alternatives can be estimated but the calculations are too involved to do in your head. Decision trees are used to determine the cost and benefit of alternative therapies, the value of screening tests, and deciding when empirical therapy is better than testing and treating.

To use decision trees, you should be comfortable with the concept of weighted averages and assigning utilities to different outcomes. We will take up these topics first.

Note on terms: "Probability" of an event and "likelihood" of an event are used interchangably, and we may use either percentages (50%) or decimals (0.5) to express probability.

301

Weighted averages.

We often use weighted averages in our day-to-day lives without being aware that is what we are doing. For example if a family of four buys 2 children's dinners at $6 each and two adult dinners at $10 each, the father can easily calculate the average price of the dinners was $8. This same problem can also be stated using percentages: You buy four meals, 50% cost $6 and 50% cost $10, what is the cost per meal? We will use this form and the related probabilistic form in the problems that follow.

Imagine 100 people in your community have come down with a viral respiratory illness. Forty percent are so ill they have to be hospitalized. Of those hospitalized, half are observed for 1 day and then discharged, the other half develop complications and stay 10 days. What is the average hospital stay for all patients who get the illness?

- 0.22 days. Go to 312
- 2.2 days. Go to 318
- 5.5 days. Go to 323
- I need a hint. Go to 332

302

Not the lowest cost. The treatment requires costly hospitalization even for those without the disease. Try again. Go to 336

303

This is a good answer but not as good as one of the others. Remember, you need to multiply the probability of each cost by the cost and add them up. Try again. Go to 317

304

No. You should choose the action with the highest survival rate. This is the worst of the three choices because it has the lowest survival rate. Try again. Go back to 327

305

No. It doesn't have to go that low. Go back to /331

306

One more problem to be sure you understand this concept:

You are ordering stethoscopes for your class (120 members). One supplier can give you 30 stethoscopes on sale at $30 each. Another has 60 for $40 and a third can supply the remainder at $50. What is the average cost per stethoscope? See if you can solve it using both methods, actual number and percent of total.

- $35.00. Go to 314
- $38.50. Go to 320
- $40.00. Go to 328
- None of the above. Go to 337

307

Right. If you looked only at cost, you would choose to treat no one. However, this is also the option with the highest mortality and is thus not an acceptible option. This shows how important it is to not make a decision without examining all important utilities. Here the best decision based on cost has the highest death rate.

We can use this information to calculate the cost of the additional lives saved by the low mortality alternative (74% mortality, $2200 cost) over the low cost alternative (68% mortality, $350 cost). For 100 patients, 6 lives would be saved (26 vs. 32 deaths) at an additional cost of $185,000 ($35,000 vs $220,000). This amounts to $185,000/6 or $30,833 per life saved.

(Do you think $30,833 per life saved is high or low compared to other therapies?)

Go to 341

308

No. Try again. Go to 311

309

Close, but not the best answer. Remember, you need to multiply the probability of each cost by the cost and add them up. Try again.

Go to 317

310

Yes. Given that there is a 40% chance of Chlorosis, the highest survival rate results from treating everyone without biopsy (74% survival). You can see, however, that this conclusion would be quite sensitive to small changes in some of conditions; the mortality rate of the biopsy, the mortality rate from the medication and the prevalence of Chlorosis in the population.

Go to 331

311

Next, we will consider problems where we know the probability that each of the possible outcomes will occur. To determine the average outcome, we solve it as a weighted average.

In a lottery, winning contestants spin a wheel to determine their prize: there is a 10% likelihood of winning $10,000, a 20% chance of winning $1000, a 60% chance of winning $100 and a 10% chance of winning nothing. What is the average prize for winning contestants?

- 0 Go to 308
- $840 Go to 324
- $1260 Go to 333
- A hint, please Go to 338

312

No, that is too short. You need to calculate the average for all 100 persons. Try again. Go to 301

313

Yes, there is a range of values where the biopsy is the best option. The survival of that limb of the tree only has to exceed 74%, the survival of the "treat everyone" choice. Go back to 331

314

$35. You're too low. To solve this multiply the number of stethoscopes times the cost and divide by 120. (or multiply the percent of the total times the cost and add the products.) Go to 306

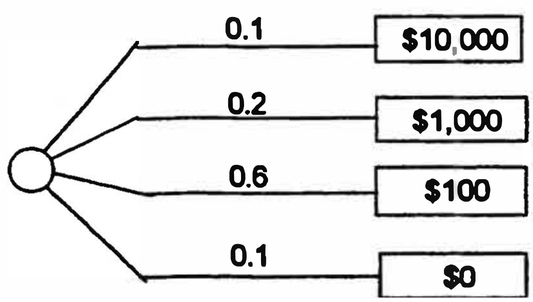
315

To evaluate the decision tree, first multiply each utility (at the end of the branches, at right) by the probability that it will occur. Add these products to get the utility of that chance node. Do this for every chance node. With choice nodes, you cross out the less desirable alternative and bring the better utility forward.

Go back to 336

316

The previous problem can be presented graphically as part of a decision tree.



The circle at left is called a chance node. We used a chance node the outcome is determined by chance alone. The value of this node is the average winnings. It is calculated by multiplying the cash value of the outcome by the probability of that outcome and then summing the four products.

Thus, ($10,000 * 0.1) +($1000 * 0.2) +($100 * 0.6) +(0 * 0.1) = $1260

When decisions are complex, with families of possible outcomes, a decision tree can help keep track of the options.

In solving the next problem, see if you can represent the possible outcomes in a decision tree.

Go to 317

317

The three doctors in the Center City Medical clinic each treat upper respiratory infection (URI) differently. One prescibes a third generation cephalosporin ($60) for half of the patients with URI and nothing for the other half. The second prescribes ampicillin ($6) for all patients with URI. The third prescribes no antibiotics. Assume each physician sees the same number of patients.

What is the average prescription costs for patients with URI who come to the Center City Clinic?

See if you can draw the decision tree for this problem.

- $2 Go to 303
- $10 Go to 309
- $12 Go to 330
- $36 Go to 335

318

(2.2 days). Right. This can be solved either by multiplying the length of stay by the number of people then dividing by 100, i.e.

60 people * 0 days = 0
20 people * 1 day = 20
20 people * 10 days = 200

220 days / 100 people = 2.2 days per person

An equivalent method (and the one we will be using in the problems that follow) is to express the frequency as a percentage, multiply that by the length of stay and add the totals to get the average, i.e.

0.6 * 0 days = 0□
0.2 * 1 day = 0.2
0.2 * 10 days = 2

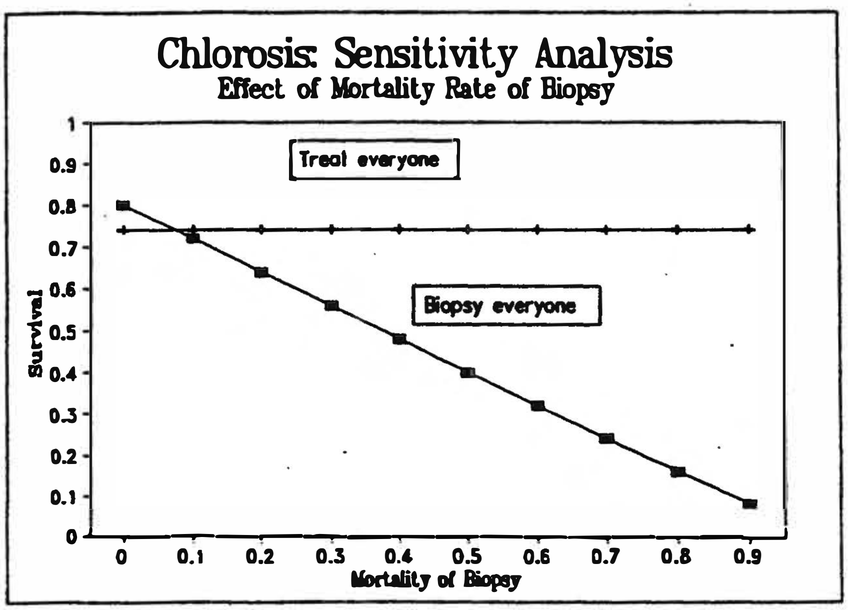
total = 2.2

Go to 306

319

Right. To dominate, the option must exceed 74% survival. This one has (0.93 * 80%) + (0.07 * 0) or 74.4% survival. Testing how changes in the assumptions in a decision tree affect the conclusion, as we have just done, is called "sensitivity analysis".

We can construct a plot of overall survival against mortality rate of the biopsy and see that biopsy everyone becomes the dominant strategy when the mortality rate is just over 7%.



As you may have already figured out, we can do a sensitivity analysis like this one for any of the assumptions: for example, the toxicity of the drug or the prevalence of disease among those with a green rash.

Go to 336

320

$38.50. You're too low. To solve this multiply the number of stethoscopes times the cost and divide by 120. (or multiply the percent of the total times the cost and add the products.) Go to 306

321

Not the lowest cost. The biopsy and hospitalization are expensive even for those that don't survive. Try again. Go to 336

322

Thus far we have seen that a weighted average can be calculated by multiplying each outcome by the probability it will occur and adding the products. This process is often called "averaging out." We have also seen how the probabilities and outcomes can be diagrammed as a decision tree. So far, we have only shown branches of the tree that represent chance occurances. We now introduce "choice nodes". The outcomes leading from a choice node are not averaged out. You simply choose the best outcome and ignore the others.

Sam has the option of choosing between two lotteries. In lottery #1 he has a 30% chance of winning $100, a 30% chance of winning $50 and a 40% chance of winning nothing. In lottery #2 he has a 50% chance of winning $60 and a 50% chance of winning $10. On the average, which one returns the most money? (See if you can draw a decision tree to represent the problem.)

- Lottery #1 Go to 339
- Lottery #2 Go to 334
- Hint, please Go to 329

323

5.5 days. No, that is the average length of stay of those who were hospitalized. We wanted the average of all 100 persons. Go back to 301

324

No. Try again. Go to 311

325

The survival rate to beat is 74%. This option only reaches (0.91 * 80%) + (0.09 * 0) or 72.8%. Try again. Go to 331

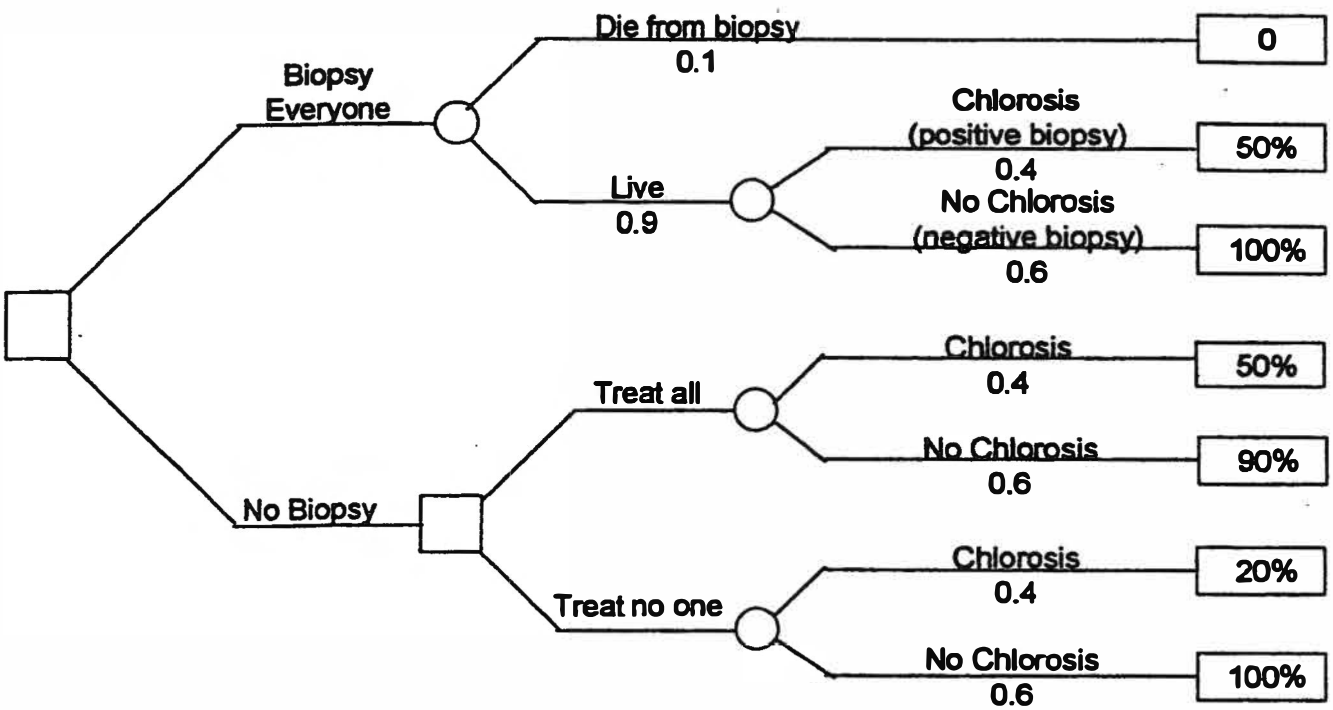
326

Chlorosis is a hypothetical but very serious illness that leads to death in 80% of patients if untreated. Biopsy of the brain stem is 100% diagnostic (no false positives or negatives) but the biopsy has a 10% mortality rate. If treated with Cyclomycin 50% of patients survive. Cyclomycin is highly toxic, however, and causes fatal hepatic damage in 10% of those who take it. Thus, the choice that must be made is whether to biopsy everyone with the attendant 10% fatality rate of the biopsy or to treat everyone and expose them to the 10% fatality rate of the medication. This choice is represented in the decision tree below for patients who develop a green rash. (About 40% of Patients who develop a green rash have chlorosis). The number in the circle near each node is the weighted average for that node.

Try your hand at constructing the chlorosis decision tree before you go on. Remember, the choices are whether to biopsy or not and, if not, whether to treat everyone or no one.

When you are ready, go on to 327

Here is a summary of the problem. Untreated, chlorosis leads to death in 80% of patients. Biopsy has a 10% mortality rate. If treated, 50% of patients survive, but Cyclomycin is fatal in 10% of those who take it. The chioces are whether to biopsy everyone and treat only those with the disease, treat everyone or treat no one. The decision tree below diagrams this for patients with a 40% chance of having chlorosis (patients with a green rash).



Which strategy produces the lowest mortality?

- Biopsy eveyone, treat only positives. Go to 340
- No biopsy, treat everyone. Go to 310
- No biopsy, treat no one. Go to 304

328

Right. You can solve this either of two ways:

1. Multiply the number of stethoscopes by the cost and divide by 120.

30 stethoscopes at \$30 = \$900
60 stethoscopes at \$40 = \$2400
30 stethoscopes at \$50 = \$1500

Cost per stethoscope = \$4800 / 120 = \$40

2. Or, you can multiply the cost by the percentage at that price and add the products to get the price per stethoscope:

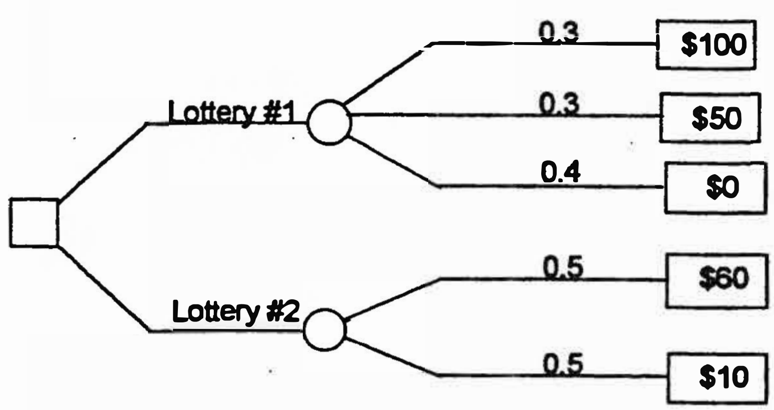
0.25 * \$30 = \$7.50
0.50 * \$40 = \$20.00
0.25 * \$50 = \$12.50

Cost per stethoscope = \$7.50 + \$20 + \$12.50 = \$40

Go to 311

329

Here's the decision tree:

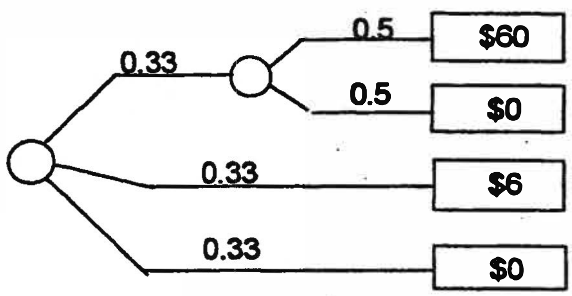


The square box at the left represents a choice node; (chance nodes are circles). To find out which is the best choice, average out the outcomes around each of the chance nodes and see which is worth more.

Go back to 322

330

Correct. This problem was a little more complicated because one of the outcomes was itself a chance node (only half of the patients got a prescription), so you had to evaluate that node before solving for all three doctors. You can see the solution in the decision tree below.



When there are two chance nodes, you evaluate the one furthest to the right first then write the weighted average by that node and use it to calculate the leftmost node.

Thus; the value of the rightmost node is (.5 * $60) +(.5 * 0) = $30 and the the prescription cost is (.33 * $30) +(.33 * $6) +(.33 * 0) =$12

Go to 322

331

You might reach a different conclusion in the chlorosis problem if some of the assumptions were different. For example, in the tree below, how low would the biopsy mortality rate have to fall to make the biopsy option have the highest survival?

- 9% Go to 325
- 7% Go to 319
- 1% Go to 305
- it never has the highest survival. Go to 313

332

To solve this problem, multiply the length of stay (either 0, 1 or 20 days) by the number of people staying that long (60, 20 and 20) and then divide by the number of people. Go back to 301

333

Right. You get the answer for the average winner by multiplying the likelihood (0.1, 0.2, 0.6, 0.1) by the winnings ($10,000, $1,000, $100, 0)

Go to 316

334

Wrong. Go back to 322

335

Not the best answer. Remember, you need to multiply the probability of each cost by the cost and add them up. Try again. Go to 317

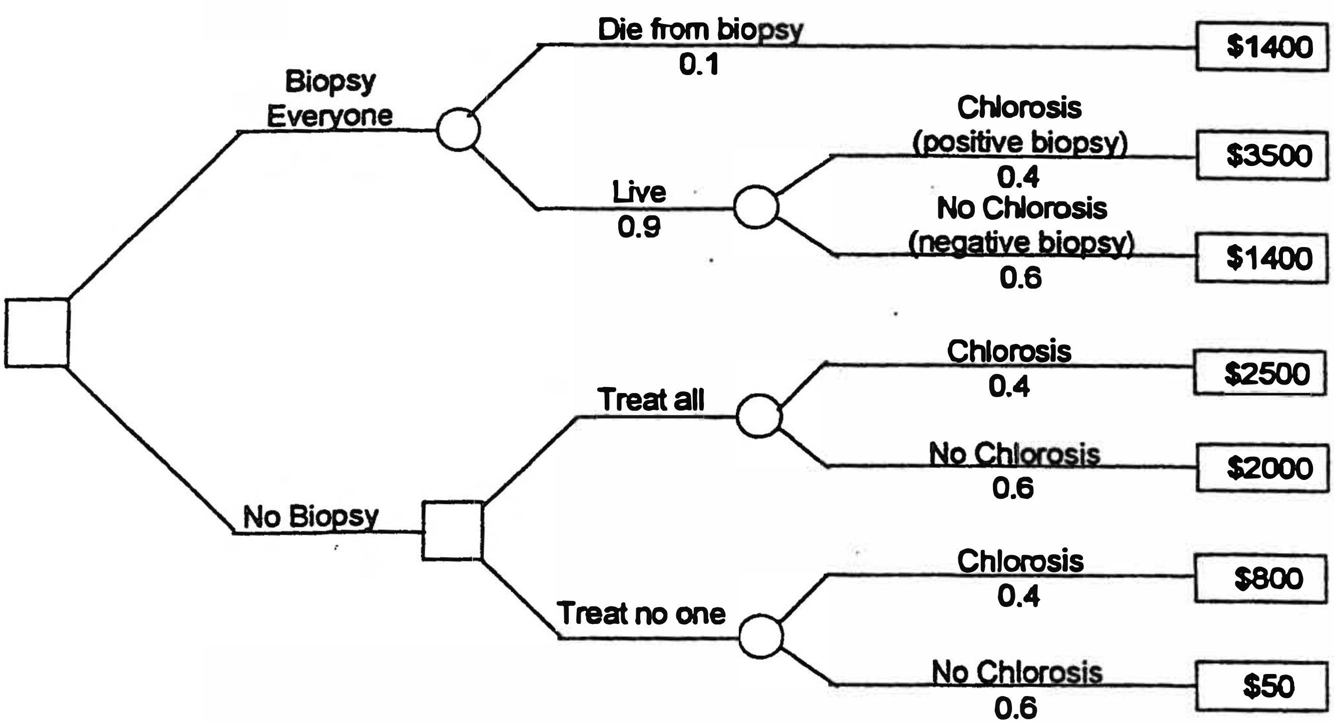
336

Decision trees are often used to analyze medical options. Choosing the right utility, however, can be tricky. For example, a choice that has the lowest cost might produce the highest mortality: if you had not examined the effect of the choice on mortality rate you might have made the wrong decision. ("Utility" is the value of the outcome)

We will use the chlorosis example again, but this time analyze the cost of each outcome. Our assumptions are that chlorosis is fatal for 80% of patients. Biopsy has a 10% mortality rate. If treated, 50% of patients survive, but Cyclomycin is fatal in 10% of those who take it. Following are the estimated costs (hospital stay, medication etc.) for each of the outcomes (Cyclomycin is given intravenously and requires hospital admission).

- Patients with chlorosis treated with Cyclomycin $2500
- Patients without chlorosis treated with Cyclomycin $2000
- Biopsy positive, treated with Cyclomycin $3500
- Biopsy negative, no treatment $1400
- Patients with chlorosis, no treatment $800
- Patients without chlorosis, no treatment $50

Using cost as the utility, what is the best (lowest cost) alternative? See if you can evaluate the decision tree on your own. If you need help or want to check your work, select option d, below and return.



(Frame continues on the next page)

- Biopsy everyone. Go to 321
- Treat all. Go to 302
- Treat no one. Go to 307
- I need help evaluating the decision tree. Go to 315

337

None of the above. No, try again. To solve this multiply the number of stethoscopes times the cost and divide by 120. (or multiply the percent of the total times the cost and add the products.) Go to 306

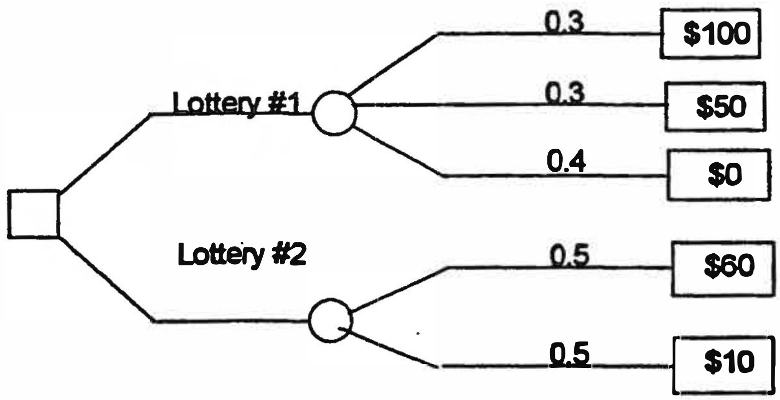
338

You get the answer for the average winner by multiplying the likelihood by the winnings and then adding the products: that is, average winnings = (0.1 * $10,000) + (0.2 * $1000) + ($0.6 * $100) + (0.1 * 0).
Go back to 311

339

Right. The decision tree looks like this:

The square box at the left represents a choice node; (chance nodes are circles). Lottery #1 is worth, on average, (0.3 * $100) + (0.3 * $50) + (0.4 * 0) = $45. Lottery #2 is worth (0.5 * $60) + (0.5 * $10) = $35. The values of outcomes (shown in boxes) are called "utilities".



We have crossed off the line going from the choice node to lottery #2 because it returns less money. Thus, the value of the choice node becomes $45 (not the average of the alternatives). Note that even though it returns less money on average, some individuals might prefer lottery #2 because of their attitude toward risk; (lottery #2 always returns at least $10)

Go to 326

340

No. You should choose the action with the highest survival rate. Remember that you do not average out across choice nodes, you choose the best option and cross out the other.

Go to 327

341

This concludes the first part of Unit 3. In this unit, we practiced calculating weighted averages. We used this technique to evaluate chance nodes in a decision tree. We then added choice nodes and constructed several trees about hypothetical medical decisions. It is easy to see that conclusions about the best therapy may depend on what kind of outcome (utility) is valued. In this example, the lowest cost outcome also had the highest mortality. As you might guess, this is often the case in medical decisions. You must watch out for conclusions about management based on economic considerations without careful analysis of the other consequences of the decision.

Robert S. Wigton, M.D.

TEST CHARACTERISTICS

	DISEASE PRESENT (D+)	DISEASE ABSENT (D−)
POSITIVE TEST (T+)	TP	FP
NEGATIVE TEST (T−)	FN	TN

DEFINITIONS:

Sensitivity = True Positive Rate $= \frac{TP}{TP + FN} = p(T+|D+)$

Specificity = True Negative Rate $= \frac{TN}{TN + FP} = p(T-|D-)$

1 − Sensitivity = False Negative Rate $= \frac{FN}{TP + FN} = p(T-|D+)$

1 − Specificity = False Positive Rate $= \frac{FP}{TN + FP} = p(T+|D-)$

Predictive Value of a Positive Test $= \frac{TP}{TP + FP} = p(D+|T+)$

Predictive Value of a Negative Test $= \frac{TN}{TN + FN} = p(D-|T-)$

Likelihood Ratio of a Positive Test $= \frac{\text{Sensitivity}}{1 - \text{Specificity}} = \frac{p(T+|D+)}{p(T+|D-)}$

Likelihood Ratio of a Negative Test $= \frac{1 - \text{Sensitivity}}{\text{Specificity}} = \frac{p(T-|D+)}{p(T-|D-)}$

Prevalence $= \frac{\text{Those With Disease}}{\text{Population}} = \frac{TP + FN}{TP + FN + TN + FP}$

Terms you need to know to understand how a test works.

Sensitivity.

Asks: What fraction of those with the disease have a positive test?

The sensitivity is what you are most often told about a test: "The serum enzymes go up in 95% of patients with myocardial infarction". It is the easiest to find out, but not as useful in diagnosis as the PVP (below). Sensitivity should be high in tests used for screening since you want to minimize false negatives.
Calculation of sensitivity does not involve prevalence.

Specificity.

Asks: What fraction of those without the disease have a negative test?

Specificity should be high for a definitive test. Specificity is the complement of the false positive rate (1-false positive rate).
Calculation of specificity does not involve prevalence.

Predictive Value of a Positive Test (PVP).

Asks: What fraction of those with a positive test have the disease?

PVP is the most important clinical index.
It tells how powerful a test is in *ruling in* disease. It is often confused with sensitivity.
The PVP can be calculated if your know the prevalence of the disease and the sensitivity and specificity of t the test.
PVP varies greatly with changes in prevalence of the disease.
It answers the clinical question: "What is the meaning of a positive test in this patient?"

Predictive Value of a Negative Test (PVN).

Asks: What fraction of those with a negative test do not have the disease?

Underused. It tells you how powerful a test is in *ruling out* disease. It is often confused with specificity.
PVN, too, varies greatly with changes in prevalence of disease.
It answers the clinical question: "What is the meaning of a negative test in this patient?"

False Positive Rate.

Asks: What fraction of those without disease have a positive test?

Note that the denominator is all those without the disease not all those with a positive test. The false positive rate is used in calculating the likelihood ratio. Often confused with specificity, it is the complement of specificity (1-specificity).

Prevalence.

Asks: What fraction of all patients have the disease?

Prevalence is easily confused with incidence. Prevalence is the number of total cases of the disease divided by all patients, while incidence is the number of new cases that appear during a time period.

Incidence.

Asks: What fraction of all patients develop the disease (new cases) in a time period?

It is often confused with prevalence.

Likelihood Ratio (LR).

Asks: How do the test results affect the odds of having the disease?

The likelihood ratio is the sensitivity divided by the false positive rate.

Thus, it is the ratio of the fraction of those with the disease who have a positive test to the fraction of those without the disease who have a positive test.

It tells you how much a test increases (if positive) or decreases (if negative) the odds that a patient has the disease.

Probability.

Asks: How often does the event occur?

Probability is the frequency of an event divided by all trials

When you toss a coin, the probability of heads is the number of events (heads) divided by all tosses. Probability = 0.5.

For example, the probability of a disease = the number with the disease divided by the total number (prevalence).

To convert from odds: Probability = odds/1 + odds.

Odds.

Asks: What is the ratio of events to non-events?

Odds = the frequency of an event divided by all trials in which the event doesn't occur.

The odds of tossing heads is the number of events (heads) divided by the number of tosses not resulting in heads (tails). Odds = 1.0.

The odds of having a disease = the number of patients with the disease divided by the number of patients who don't have the disease.

To convert to odds: Odds = Probability/1-probability.

Prior Probability.

Asks: What is the probability of having the disease before you know the test results?

For a clinical test, prior probability = prevalence.

Posterior Probability.

Asks: What is the probability of having the disease after you know the test results?

If the test is positive, then posterior probability = PVP.

If the test is negative, then posterior probability = ~~PVN~~. 1 − PVN

Comment sheet for "Analyzing Diagnostic Tests"

Give to Ron Bechtolt in class or send by campus mail to
Robert Wigton M.D.

ZIP 5524

For the following questions, check or fill in the best answer.

1. Did you finish the whole text? ___yes ___no
2. If you finished it, how long did it take? ______
3. Did it move ___too slowly, ___just right, or ___too fast?
4. Was it ___too hard, ___just right or ___too easy?
5. Did it teach you the topics ___very well, ___well or ___so-so?
6. Should it cover more: e.g. cost-benefit, medical guidelines? ___yes ___no
7. Would you be interested in an elective course in this area? ___yes ___no

Overall comments on the text:

Specific comments about errors, typos, confusing areas; suggestions for improving next year's version.