# **Clinical Decision Support Systems in Health Care:** an introduction to YouTube!

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### **Contents**





### <span id="page-1-0"></span>**1. Introduction**

This section of the course is concerned with Clinical Decision support systems in healthcare and contains several resources for you to read:

Coiera 2003 Chapter 25 – Clinical decision support Systems available online a[t: http://www.coiera.com/aimd.htm](http://www.coiera.com/aimd.htm)

Paul Taylor 2006 Chapter 10 - Probability and decision making

Gerd Gigerenzer 2007 Chapter 9 – Less is More in Health Care

Roger Penrose – 1993 Setting the Scene: the Claim and the Issues – Artificial minds

Each offers a particular perspective, for example Coiera 2003, provides a brief historical overview along with details of the main systems in use in health care. He writes very much from a clinical perspective, one of which many of you will be familiar. He also does a very nice job of introducing the idea of a continuum of approaches from the 'strong' Artificial Intelligence (AI) proponents to those with a more measured 'weak' approach to AI who see it as a 'cognitive prosthesis'.

In the UK, on the opposite side of the world, Taylor 2006 provides a description of some basic scientific knowledge that is required to understand the building block of Clinical Decision Support Systems. I will discuss this in detail latter.

Gerd Gigerenzer is a world famous psychologist, who has moved from the academic to the more main stream domain, with his book Gut Feelings (2007). I have taken a chapter from it in which he describes his research concerning the use of simple heuristics – 'rules of thumb' and in particular his fast and frugal decision trees within healthcare, this is very much at odds to the often very complex models developed using the techniques described by Taylor.

Finally I provide you with a classic paper by the Cambridge mathematician Rodger Penrose in which he describes the problems with developing real Artificial Intelligence and its relationship to consciousness, suggesting that Quantum Mechanics may offer a possible solution. Since writing this he has greatly expanded and refined his argument in two books, The Emperor's new Mind (1990) and Shadows of the Mind (1994). I would recommend that if you do want to read them you start with the first one as the second is largely a sequel with a significant proportion of it discussing the various criticisms of his first book.

I consider the Penrose resource as something you need to read through to get a flavour of the problems but do not try to fully grasp the detail within it, you could say it is verging on optional content for the course.

Because you might find the resources along with my commentary rather boring, I have made use of various youTube videos to hopefully both lighten the load and enlighten you.

The commentary is incomplete in that I have only provided details of background material where I feel it will aid understanding of the core material.

### **2. Coiera 2003 Chapter 25 – Clinical decision support Systems**



The above mindmap provides an overview of the chapter.

<span id="page-2-0"></span>You should read either the online or paper version (2<sup>nd</sup> edition) of this chapter after which you need to complete the Multiple Choice Questions (MCQs) I have produced.

### <span id="page-3-0"></span>**3. Paul Taylor 2006 Chapter 10 - Probability and decision making**

The 24 pages that make up this chapter contain a wealth of material and I will expand on several sections to help you gain some background/additional understanding.

## <span id="page-3-1"></span>**3.1 Dealing with incomplete information**

This section provides a general introduction to two very different interpretations of what probability means. The important thing here to realise is that these different interpretations are not reconcilable and there are deep ongoing feuds/ arguments between the various opposing parties. Gigerenzer et al 1989 provides a readable, lively history of the



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## <span id="page-4-0"></span>**3.2 Axioms of probability**

Probability is difficult, counter intuitive and the terms used such as 'and' and 'or' have a very restrictive if not contradictory meanings compared to that in everyday life (Gigerenzer 2007, pages 93 – 102).

I assume that you all have already come across the concept of classical probability and therefore could answer the following questions:

What is the maximum value a probability can take? If an event, say the possibility of it raining tomorrow, has a probability of zero what does it mean? Representing it as a fraction, what is the probability of me picking a green marble from a jar containing 10 red, 4 white 3 black and 17 green marbles? What is the probability of event A or B occurring if they are mutually exclusive (i.e. single throw), such as obtaining either a 1 or 6 with a single throw of a dice.

Taylor is understandably rather light on notation. However I feel that it is important that you are reminded of some basics.

1. Addition rule 'or'

 $P(a \text{ or } b) = P(a \cup b)$  U means union, and in the Venn diagram below it equates to the shaded area. Notice that the total shaded area is both the circles minus the intersection (this prevents us from counting it twice). To denote the intersection, I use the intersection sign  $\bigcap$ . This situation does not occur if the events are mutually exclusive, as there is no overlap. In mathematical terms:

 $P(a \text{ or } b) = P(a + b) - P(a \cap b)$ 

When the events are mutually exclusive  $P(a \text{ or } b) = P(a) + P(b)$  because the intersection is empty.

Notice that incorrectly considering two events as mutually exclusive when they are not would result in an inflated probability.

When considering the tree interpretation of probabilities we are adding the values on the branches vertically.

Also all the ends of the branches vertically must sum to one.



### <span id="page-4-1"></span>**3.2.1 1. Multiplication rule 'and'**

Often the multiplication rule, commonly called the 'and' rule, is used to model some type of ordering. How humans perceive 'and' is an important topic in psychology and Gigerenzer presents some interesting research, including the famous experiments by Tversky & Kahneman 1982, showing how this very restricted logical use of the word in probability differs from the way it is interpreted normally.

Lets focus on the probability approach. So say event B occurs given that event A has occured. To indicate the situation of both event A occurring and event B we use the notation:

 $P(A \text{ and } B) = P(A \cap B)$  where  $\cap$  means intersection. Taylor on page 160 shows this as P(a,b)

 $= P(A|B)$  x P(B) which, if they are independent, that is neither event affects the other, it simplifies to  $= P(A)$  x P(B)

When considering the tree interpretation of probabilities we are multiplying the values on subsequent branches horizontally. Also each subsequent branch is a conditional probability (see below).

Notice that Mutual exclusivity and independence are two different things (see Campbell & Machin p.39), one relates to events at any one point in time whereas the other is concerned with the sequence of events.

#### **Examples and more help**

If you had problems with any of the above questions or information I suggest that you look at one of the many videos on YouTube, tr[y http://www.youtube.com/watch?v=xA7QGTeQjFk](http://www.youtube.com/watch?v=xA7QGTeQjFk) for starters.

You, like I, might find a graphical interpretation of some of the basic concepts of Probability helpful, such as probability trees: [http://www.youtube.com/watch?v=6E\\_NVnboMB8](http://www.youtube.com/watch?v=6E_NVnboMB8) or Venn diagrams see: <http://www.youtube.com/watch?v=FzcLlhQKkcA> and also the interactive java version at: <http://www.stat.berkeley.edu/~stark/Java/Html/Venn.htm>

### <span id="page-5-0"></span>**3.2.2 Conditional Probability**

 $P(A|B) = \frac{P(A \text{ and } B)}{P(B)}$  The probability of event A given that event B has occurred is equal to the probability of both events A and B occurring divided by the probability of event B occurring. The concept of "conditional probability" is important, but also complex and difficult to grasp. However given that, it is very important to be able to recognise situations where events are conditional and therefore will be either independent or dependent. Many statistical techniques rely upon the data being independent, for the results to be valid.

Actually calculating conditional probabilities, especially when they are not independent, is not that easy. For a good introduction see: <http://www.youtube.com/watch?v=4PwnvqGEHoU> or <http://www.youtube.com/watch?v=xw6utjoyMi4> o[r http://www.youtube.com/watch?v=BLcgeLALLnc](http://www.youtube.com/watch?v=BLcgeLALLnc)

The important thing to realise is that a conditional probability provides you with a more faithful result by removing irrelevant data (technically the 'reduced outcome set *P(B)'*). It is also important to realise that a Conditional probability may not be commutative in a particular situation, that is it is not like addition where  $2+4 = 4+2$ . Order frequently matters and usually P(a|b) ≠ P(b|a) unless the events are **independent**. Conditional probabilities occur everywhere, as you can see from the above videos, one place that you may not have been aware of it is the 'p value' that you obtain from significance tests which is also a conditional probability and really should be written as P(value obtained from data | null hypothesis is true), unfortunately many people believe the p value to be just the opposite P(null hypothesis is true | value obtained from data) this is just wishful thinking. If you are interested in obtaining such a value (which is difficult) you are looking at the mathematical concept of Likelihood. Back to more mundane things now.

Consider the bearded men example on page 159 of Taylor. What he is talking about is P(being bearded|male) = Probability of being bearded given that you are a male. To obtain the conditional probability all he has done is removed the female students from the analysis, so instead of having 20 in the denominator we now have 12 to obtain the 4/12 value. This conditional probability is clearly not independent as P(male|bearded), that is being male given that you are bearded in this instance =  $4/4$  = 1 Also notice that a conditional probability will always be greater than a nonconditional one as we are reducing the size with the denominator. The first YouTube example above gives some nice dramatic examples of this. We will now consider a situation where conditional probability is a very clinical matter.

## <span id="page-6-0"></span>**3.3 Sensitivity Specificity etc**

In the tables below I have shown several ways of looking at specificity, along with other measures etc, including what they mean, how they are calculated and their probabilities. The bowel screening example is fro[m http://www.bio](http://www.bio-medicine.org/medicine-definition/Positive_predictive_value/)[medicine.org/medicine-definition/Positive\\_predictive\\_value/](http://www.bio-medicine.org/medicine-definition/Positive_predictive_value/)







All the terms, of which I have listed only a few, can make your head spin! Also the problem is that sensitivity sounds like specificity if you are only half awake, because of this several writers have suggested that more descriptive terms such as True Positive ratio (TP) be used instead of sensitivity and True Negative ratio (TN) for specificity.

Where you find many different measures you can bet that none of them is perfect and this is the case here. Both TP and TN values sound like they refer to population values but often do not as we will see latter. Similarly both the Positive Predictive Value (PPV) and Negative Predictive Value (NPV) have problems, see Sox, 2006 and also the following.

Quoting fro[m http://www.bio-medicine.org/medicine-definition/Positive\\_predictive\\_value/](http://www.bio-medicine.org/medicine-definition/Positive_predictive_value/):

*Predictive values are often used in medical research to evaluate the usefulness of a diagnostic test. Hence the PPV is used to indicate the probability that in case of a positive test, that the patient really has the specified disease. However there* 

*may be more than one cause for a disease and any single potential cause may not always result in the overt disease seen in a patient.*

*An example is the microbiological throat swab used in patients with a sore throat. Usually publications stating PPV of a throat swab are reporting on the probability that this bacteria is present in the throat, rather than that the patient is ill from the bacteria found. If presence of this bacteria always resulted in a sore throat, then the PPV would be very useful. However the bacteria may colonise individuals in a harmless way and never result in infection or disease. Sore throats occurring in these individuals is caused by other agents such as a virus. In this situation the gold standard used in the evaluation study represents only the presence of a bacteria (that might be harmless) but not a causal bacterial sore throat illness. It can be proven that this problem will affect positive predictive value far more than negative predictive value. To evaluate diagnostic tests where the gold standard looks only at potential causes of disease, one may use an extension of the predictive value termed the [Etiologic Predictive Value](http://www.infovoice.se/fou/epv/)*. (end of quote)

A rather nice alternative graphical interpretation of the table, illustrated using the data in Taylor p161 sometimes helps provide clarity:



The above information is very useful as we now know that a patient with a positive FOBT test result has a 0.08 probability of cancer as well as the probability of a patient with a negative FOBT result not having cancer. Notice that it is not 1-0.08!

Unfortunately the above example is rather contrived in several ways, most notably:

**Cut off value** - In the above example the actual test measurement is not really dichotomous but continuous, as you can have faint positives and strong positives etc.

**Typicality of sample (i.e.** *P(D+)*) we rarely know the prevalence of a disease in the specific group we are dealing with, other than when we are screening the entire population as in the above example .

Ways of dealing with these two problems are the topics of the next two sections, that is ROC curves and Bayes Theorem.

## <span id="page-8-0"></span>**3.4 ROC Curves – a very brief introduction**



As a review please read the following three short articles from the BMJ statistical notes series:

[Diagnostic tests 1: sensitivity and specificity](http://www.bmj.com/cgi/content/full/308/6943/1552) Douglas G Altman & J Martin Bland BMJ 1994;308:1552 (11 June)

[Diagnostic tests 2: predictive values](http://www.bmj.com/cgi/content/full/309/6947/102) Douglas G Altman & J Martin Bland BMJ 1994;309:102 (9 July)

[Diagnostic tests 3: receiver operating characteristic plots](http://www.bmj.com/cgi/content/full/309/6948/188) Douglas G Altman & J Martin Bland BMJ 1994;309:188 (16 July)

The Receiver Operating Characteriestic (ROC) Plot described in the last article has the usual names for the axes, however I prefer the alternative American ones



which highlights the simplicity of the plot. We are plotting the True Positive (TP) ratio and False Positive (FP) ratio for all possible values obtained from our samples. An example should make things clearer.

I have taken this example from the Gayfyd site. Consider 24 samples for a test for cancer, ranked from the lowest to the highest value obtained, along with either a subsequent 'golden standard' test or actual pathology. By using the total number of positive and negative actual outcomes (i.e D+ and also D-) we can calculate for each test value the amount it contributes to either the total number of positive of negative actual outcomes. So from the table opposite a single test result that is correctly classified as a positive contributes 1/12 =.0833 Similarly for a single test result that is correctly classified as a negative result the value is 1/11=.0909 Because we have ranked the test results we can add up these values for each test result giving us the proportion for the actual outcomes.

You may remember that proportions are similar to probabilities and in this instance we have the cumulative probability of obtaining a result given either the actual presence or absence of the disease (the last two columns in the table). You may realise that this

sounds familiar and it is,

it is the TP (True positive =sensitivity) and FP (False Positive= 1-specificity) values. So what we have done is find the TP and FP values for each value of our test.

For the above example I have considered a test which provides continuous values, for a example of a test that produces only 5 values see the excellent description of Roc curves and what you can do in the SPSS statistical package with them at <http://www.childrensmercy.org/stats/ask/roc.asp>

So how do the values in the above table relate to the roc plot? By taking one of the graphics from the above site we see that the diagonal line equates to the chance values.



If the actual results we obtained lie on this line they are basically useless. By looking at the roc plot for our results, using the freely available roc Excel spreadsheet (from the Ganfyd site - see below) we can see that they are well away from the diagonal, suggesting that it is a useful test however, we clearly need more quantitative method of accessing our test and



there exist several methods to obtain a useful measure – the links below provide details.

You will notice that the actual values plotted are the TP and FP unique values so many ROC packages require you to have processed the data in some way, for example the screenshot below from openEpi demonstrates this:

[http://www.openepi.com/Menu/Open](http://www.openepi.com/Menu/OpenEpiMenu.htm) [EpiMenu.htm](http://www.openepi.com/Menu/OpenEpiMenu.htm)

McNeil, Keeler & Adelstein 1975 provide a good description of the process of using roc plots to decide an appropriate 'cut off value for a test which also takes into account an economic evaluation. Zweig & Campbell provide a nice diagram showing the central role ROC plots play in test evaluation. ROC plots are becoming more frequently used as method of evaluating services. In an (in)famous paper



[182\)](http://www.spss.com/success/template_view.cfm?Story_ID=182) in the BMJ, Daly, Beale & Chang 2001,

demonstrated using roc plots and logistic regression that early discharge from St Georges ITU in London resulted in unnecessary deaths

[\(http://www.spss.com/success/template\\_view.cfm?Story\\_ID=](http://www.spss.com/success/template_view.cfm?Story_ID=182)

concluding that "Mortality after discharge from intensive care could be reduced by nearly 39% if these patients stayed another two days before discharge". Searching on the key term 'roc' within the BMJ, demonstrates that their use is becoming more popular in the journal.

### **Tutorials:**

Explanation of the values and cumulative frequencies[: http://www.childrensmercy.org/stats/ask/roc.asp](http://www.childrensmercy.org/stats/ask/roc.asp) Excellent tutorial for anaesthetists with very relevant examples 'The magnificent ROC' <http://www.anaesthetist.com/mnm/stats/roc/Findex.htm> Excellent tutorial (psychology based) with java applets[: http://wise.cgu.edu/sdtmod/index.asp](http://wise.cgu.edu/sdtmod/index.asp) Also see: <http://www.mwra.state.ma.us/harbor/enquad/pdf/2005-20.pdf> <http://faculty.vassar.edu/lowry/roc1.html> [http://www.statsdirect.com/help/nonparametric\\_methods/roc\\_plot.htm](http://www.statsdirect.com/help/nonparametric_methods/roc_plot.htm)

### **ROC calculators on the web:**

Doctors on the net site, called ganfyd have a simple web page about Roc but more importantly a link to a **excel spreadsheet** for doing simple roc curves, also provides details of how to create them in SPSS and R.

[http://www.ganfyd.org/index.php?title=Receiver\\_operating\\_characteristic](http://www.ganfyd.org/index.php?title=Receiver_operating_characteristic) <http://www.rad.jhmi.edu/jeng/javarad/roc/JROCFITi.html>

[http://www-radiology.uchicago.edu/krl/KRL\\_ROC/software\\_index6.htm](http://www-radiology.uchicago.edu/krl/KRL_ROC/software_index6.htm) [site also provides a long list of ROC references]

### **Web sites:**

[http://www.lerner.ccf.org/qhs/software/roc\\_analysis.php](http://www.lerner.ccf.org/qhs/software/roc_analysis.php) + don't forget wikipeadia.

The ROC analysis tells us: 1.How good the test is. 2. Where the cut off point should be

## <span id="page-10-0"></span>**3.5 Bayes Theorem**



Bayes theorem provides us with a method of revising our prediction by making use of previous knowledge. Because it is a conditional probability, that is using the old knowledge to inform our decision, the value obtained will usually differ from not having made use of the knowledge, the degree of change could be considered to be equivalent to its usefulness. In terms of clinical decision making Bayes Theorem is often presented as a method of allowing the calculation of the probably of a disease given a positive or negative test result, thus:

```
P(disease) | test) = \frac{P(disease) P(test | disease)}{P(disease) P(test | disease) + P(No disease) P(test | No disease)}
```
This can be  $P(disease|test +)$  or  $P(disease|test -)$  etc

This equation can be expanded to allow multiple tests but I will stick with the above version. Taylor p.160 presents a simpler version, where the values represent prevalence rates from screening I will now provide an alternative example from a more typical clinical setting. McNeil, Keeler and Adelstein, 1975 provide an example concerning a specific test for liver disease and the actual presence of the disease (at biopsy/autopsy), often in the clinical setting this is some type of



'gold standard' test) :



Therefore the test will detect 90% of patients with liver disease and will correctly classify 63% of those without the disease.

From the above calculations we know that the probabilities of the various test outcomes GIVEN THAT patients have or do not have the disease, but clinically for a specific patient we want to know the opposite, the probability of them having the disease given the test result. Remember I said that conditional probabilities are not commutative; this is where Bayes is so useful it **Bayes effectively turns the conditional probabilities around**. Considering the clinical situation, where we want to know the probability of them having the disease GIVEN the test result, we have two possibilities either the test is positive (T+) or negative (T-). To be able to apply Bayes theorem to both these possibilities we need also to know the prevalence of the disease, that is *P(D+).* If we used the method Taylor p161 does for the screening data we would end up with a prevalence rate of 258/344 =75%! So in this instance the authors take an informed 'guestimate' for it to be 30% (therefore *P(D-)=* 1-.30 = 0.70). Also the authors revise the FP based on roc analysis to be .25 using these values we now have:



The 30% prevalence can be considered to be the unadjusted probability of the person having the disease before we carried out the test, or saw them. So after carrying out the test we can say that:

*The probability of the disease in a patient with a positive test is 61% and that of a patient with a negative test is just 5%. So we can be about twice as confident (61:30 = 2) as before when the test comes back positive that the patient has the disease. But if their result came back negative (5:30 = 6) we changed our belief by a factor of 6, from 30% to 5%.*



#### **The effect of prevalence on the Bayes theorem**

Campbell and Machin 1993, provide a table using the example of a negative exercise tolerance test, reproduced below to demonstrate the affect changes in prevalence have upon the usefulness of a test. Defining usefulness to be the degree to which a test changes the belief of the clinician. Therefore from the table it can be seen that where the prevalence is either very high or very low this specific test is of questionable usefulness for the clinician.

### <span id="page-11-0"></span>**3.5.1 Graphical Explanation of Bayes**

One of the YouTube videos does a nice job of explaining Bayes graphically. I will take the example from Taylor p.160, concerning mammography screening for breast cancer.



#### **Exercises and more help**

Both good and bad explanations of Bayes theorem abound on YouTube. Try

<http://www.youtube.com/watch?v=upqL5Uik2O8> which gives you the standard explanation with also an alternative graphical one. There are several examples of its use, including:

<http://www.youtube.com/watch?v=pPTLK5hFGnQ&feature=related> concerning upwardly revising probabilities of stocks

given knowledge of past market performance, there are other interesting examples concerning alarms and leaking pipes, and e-mail filters. Wikipedia is very good on Bayes Theorem with example 2 being the standard disease/test one. [http://en.wikipedia.org/wiki/Bayes'\\_theorem](http://en.wikipedia.org/wiki/Bayes)

The above was a very short introduction to Bayes Theorem, the best book to find out more about it along with its uses and limitations within the clinical setting is Medical Decision Making by Sox, Blatt, Wiggins and Marton, 1888 republished in 2006 by ACP. You can see some of it at googlebooks[, http://books.google.co.uk/books?id=-Gu-Wz9tiSUC](http://books.google.co.uk/books?id=-Gu-Wz9tiSUC) The new 2006 preface provokes mixed emotions, depending where you site with Decision support.

In the 18 years since *Medical Decision Making* first appeared, the field of medical decision making has moved forward technically, has made its way into the medical curriculum, and has become a mainstream tool for the people who shape medical practice. The last is probably the most successful infiltration of the powerful ideas described in this book. Two major influences on the content of medical practice are practice guidelines and insurance coverage decisions. The former determines the standards against which people measure the quality of medical care; the latter largely determines which tests and treatments a physician can prescribe. Bayes' theorem plays a role in deciding which types of patients may benefit from having a diagnostic test. Cost-effectiveness analysis, which uses decision models, now plays an increasingly important role in deciding about insurance coverage. While these advances are important, they are not enough to satisfy me.

The ultimate goal of the authors was, and remains, to have medical students and practicing physicians use the principles of probabilistic reasoning and expected-value medical decision making in day-to-day practice. Presently, relatively few doctors consciously use Bayes' theorem or decision trees on a routine basis. Undoubtedly, it is difficult to recall numbers and to do calculations quickly. This situation may change, however, as decision support systems integrated into electronic medical records take hold. These systems can reduce the doctor's cognitive tasks. To guide the choice of a diagnostic test, the computer displays the key questions for estimating pre-test probability, uses the answers to calculate the patient's pre-test probability, calculates the post-test probability using test sensitivity and specificity figures stored in the computer, and displays the results.

I think we are entering an era of greater precision in medical decision making. This book will help you to be a part of that revolution.

> Harold C. Sox, MD, MACP September 29, 2006

Another popular book is Clinical Biostatistics: An Introduction to Evidence-based Medicine (Paperback) by Graham Dunn and Brian Everitt, Arnold 1995. As mentioned earlier because everyone including clinicians has problems understanding probability concepts, different writers have offered alternative representations, for example Bayes theorem can be expressed as:

Posterior probability = Prior probability X Likelihood Where the Likelihood = TPR/P(D+)

Another measure called the Likelihood ratio is TPR/FPR = Sensitivity/(1-specificity) (Dunn & Everitt 1995 p.17-20)

Puhan, Steurer, Bachmann and Riet 2005 describe a randomised trial where physicians were provided additional likelihood information to see if it affected their decisions failed to show any difference.

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