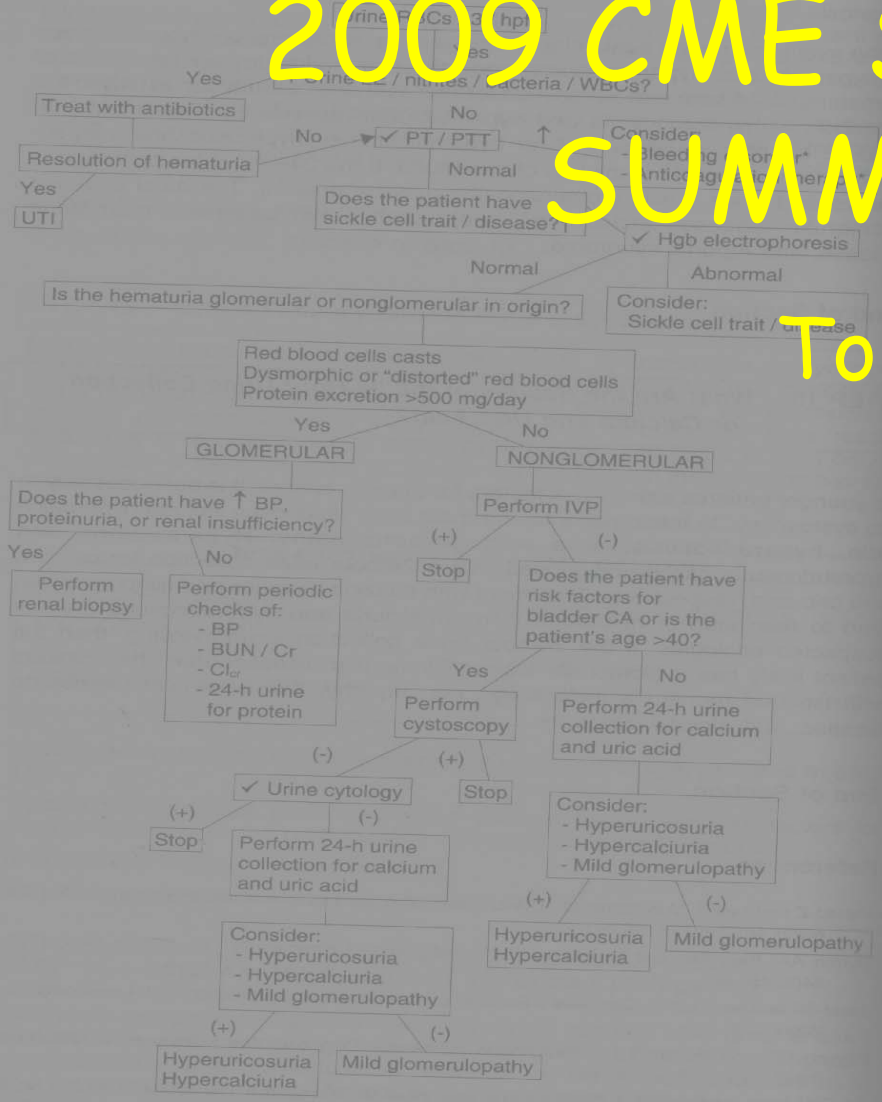
2009 CME SYMPOSIUM SUMMING UP

Topics :

HEMATURIA



*Hematuria that occurs in the patient with an elevated PT / PTT may be the result of anticoagulation therapy or a bleeding disorder. However, an underlying structural etiology cannot be excluded.
†Sickle cell trait/disease may be the sole cause of hematuria; however, this diagnosis must be one of exclusion.

PROTEINURIA

...is important not to ignore proteinuria. While it is true that proteinuria may ...a benign finding, it may also indicate the presence of serious underlying renal and systemic disease.

How Much Protein Is Excreted Over a 24-Hour Period in the Normal Individual?

...normal urine is <150 mg of protein excreted in the urine over a 24-hour period.

What Different Types of Protein Are Normally Excreted in the Urine?

Excreted protein comes from plasma and the urinary tract. Plasma proteins include albumin and a globulin fraction. The major constituent of protein derived from the urinary tract is the Tamm-Horsfall protein, which is secreted by the cells of the ascending limb of the loop of Henle and the distal tubule.

CONSTITUENTS OF NORMAL URINE PROTEIN
ALBUMIN 30%
GLOBULINS 30%
TAMM-HORSFALL PROTEIN 40%

How Is Protein Handled by the Kidneys?

Plasma protein must traverse the glomerular barrier to enter the urine. In general, proteins with a molecular weight >20,000 daltons have considerable difficulty passing through glomerular capillary walls. The glomerular basement membrane is also negatively charged, and therefore impedes the passage of negatively charged plasma proteins such as albumin. Filtered protein may be reabsorbed by tubular cells. Proteins that are absorbed by tubular cells are generally low molecular weight in nature.

With this in mind, proteinuria can be classified as follows.

- Glomerular

  Glomerular proteinuria is the most common type of proteinuria, and may vary from several hundred milligrams to >100 grams of protein per day. It occurs as a result of increased glomerular permeability, which may be due to a variety of processes.

- Tubular

  Any process that damages the proximal tubular epithelium will allow low molecular weight proteins to be excreted in the urine.

- Overflow

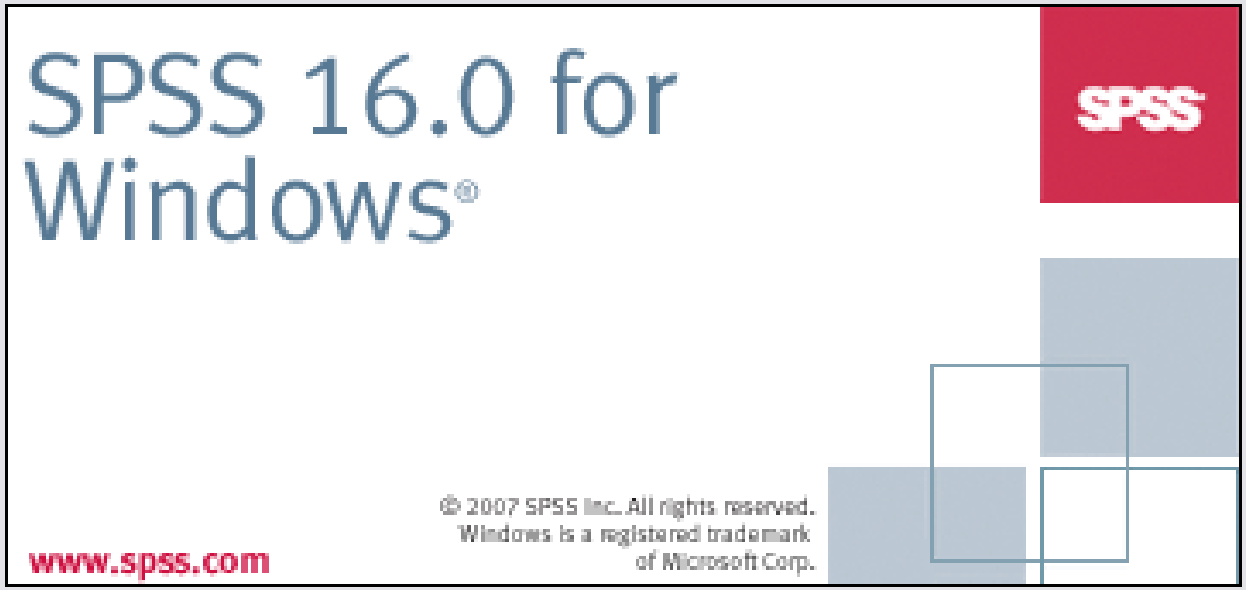
  Overflow proteinuria is the result of overproduction of a particular protein. This overproduction leads to an increase in plasma protein concentration, which is then filtered at the glomerulus. The increased amount overwhelms the ability of the proximal tubular epithelium to catabolize filtered protein, resulting in urinary excretion of excess protein. In clinical practice, this occurs in multiple myeloma, where immunoglobulin light chains are excreted, or in myelomonocytic leukemia, where excessive lysozyme is excreted.

TIPS ON GATHERING YOUR OWN R & D DATA

- Design a single page A4 'portrait' data collection form
- Set up an Excel Spreadsheet with each field on that form as a column
- Set up an 'Excel Data Entry' form that matches your paper form
- Make up some theoretical data
- Analyze the theoretical data with various statistical tests that can detect your hypothesis
- Decide which tests you will use on the real data

SPSS - Statistical Package for the Social Sciences

Statistical Package for Students Searching for Significance



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EXCEL IS RECOMMENDED

Version 2003

Microsoft Excel - Xylose BMI above-below 27-modelling.xls

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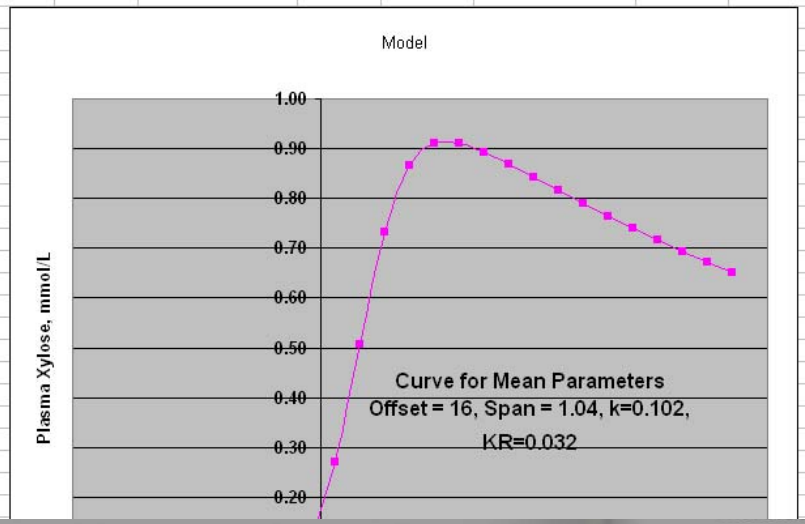
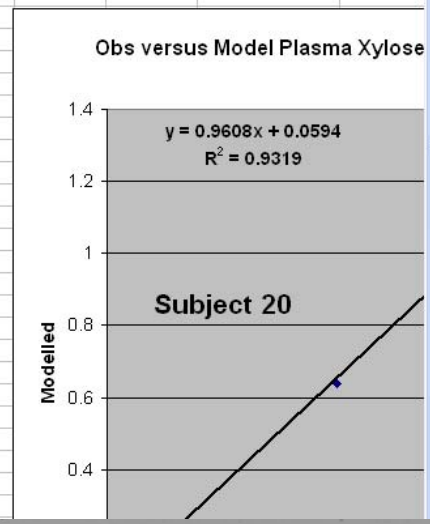
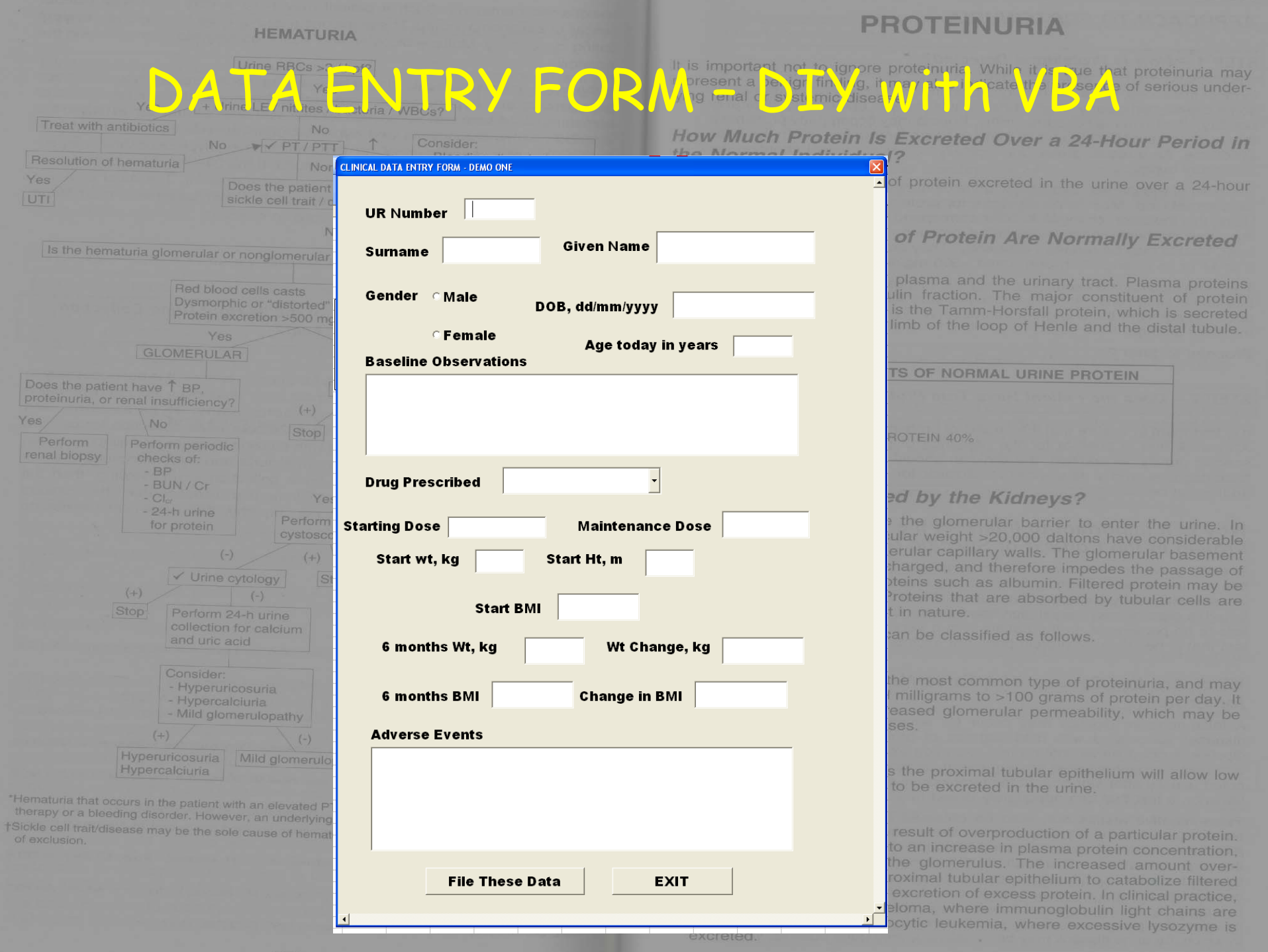
R6

	G	H	I	J	K	L	M	N	O	P	Q	R
1												
2	Time	Subject 2	Subject 4	Subject 6	Subject 10	Subject 11	Subject 12	Subject 14	Subject 15	Subject 20		
3	0	0.0174	0.2078	0.1845	0.1645	0.1775	0.1825	0.3682	0.0901	0.1623		
4	20	0.2384	0.7771	0.5155	0.5790	0.3523	0.5660	0.5943	0.9363	0.6222		
5	40	0.5067	1.2003	0.8123	0.6913	0.6438	0.8022	0.9536	1.2736	1.1015		
6	60	0.5541	0.7794	0.8930	0.7150	0.7064	0.8143	0.8829	1.0641	0.8942		
7	90	0.3883	0.8569	0.6346	0.7776	0.7776	0.8547	0.8849	0.8463	1.1446		
8	120	0.4968	0.7461	0.5902	0.7906	0.7237	0.8183	0.9172	0.6158	1.0540	MEANS	
9	Offset	25	15	24	10	20	13	7	17	17		16
10	Span	0.61	1.45	1.32	0.76	0.80	0.83	0.90	1.55	1.12		1.04
11	k	0.130	0.125	0.070	0.120	0.065	0.100	0.060	0.150	0.100		0.102
12	KR	0.040	0.066	0.090	0.000	0.005	0.000	0.000	0.090	0.000		0.032
13	Slope	1.143	1.056	1.014	0.973	1.040	0.996	0.857	0.981	0.961		1.002
14	Intercept	0.0125	0.0398	0.0106	0.0229	0.0033	0.0012	0.0735	0.0107	0.0594		0.0260
15	R2	0.8857	0.8334	0.9649	0.9819	0.9831	0.9951	0.9307	0.9948	0.9319		0.9446
16	R	0.9411	0.9129	0.9823	0.9909	0.9915	0.9975	0.9647	0.9974	0.9653		0.9715





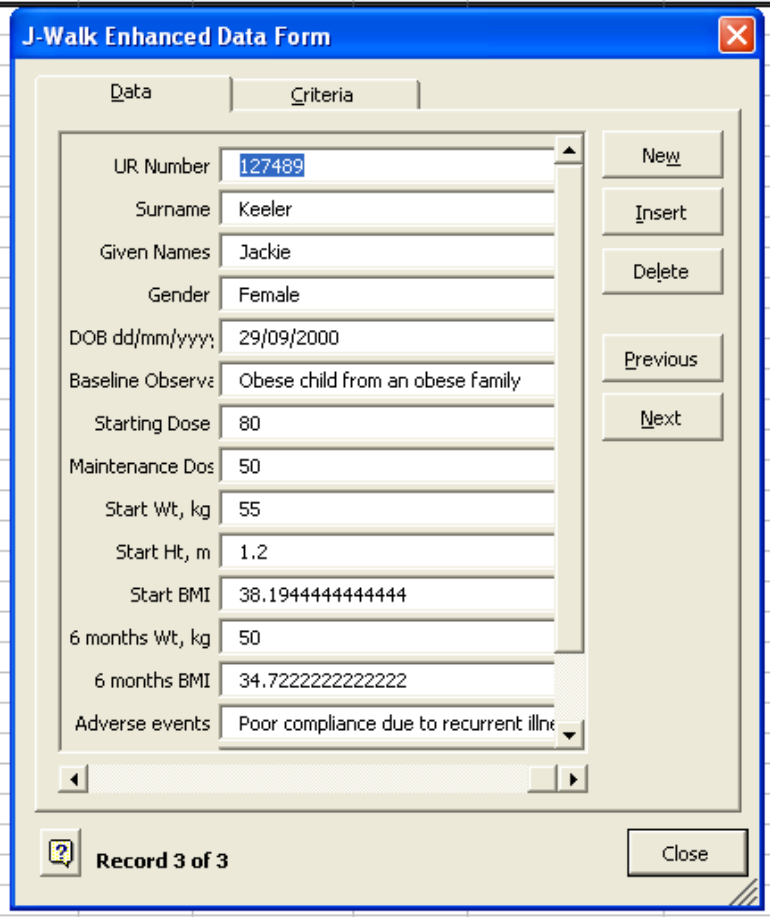
DATA ENTRY FORM - DIY with VBA



DATA ENTRY FORM - Use an AddIn

dataform3.xla

	A	B	C	D	E	F
1	UR Number	Surname	Given Names	Gender	DOB dd/mm/yyyy	Baseline Observations
2	789456	Morris	Kevin	Male	29/08/1995	Overweight asthmatic
3	417896	Hughes	Wendy	Female	5/12/1985	Truncal obesity
4	127489	Keeler	Jackie	Female	29/09/2000	Obese child from an obese family



J-Walk AddIn for Excel

http://spreadsheetpage.com/index.php/dataform/home/

The J-Walk Enhanced Data Form

The J-Walk Enhanced Data Form is a **FREE** Excel add-in that provides a general-purpose data entry dialog box. The Enhanced Data Form adjusts to any database table in any worksheet. It's a significantly enhanced alternative to Excel's built-in Data Form (which is not even part of the user interface in Excel 2007).

Very Important: This add-in comes in two sub-versions, and both are included in the download:

- **Version 3a** - for Excel 97, 2000, 2002, and 2003
- **Version 3b** - for Excel 2007

Not sure that this works

This add-in does *not* work with any version of Excel for Macintosh.

HOW MANY PATIENTS DO I NEED?

The aim in all clinical research is to be '95% confident' about our conclusions. To achieve this it turns out that the Minimum Group Size is 40.

Why ?

Because

"2 in 40 = 5%"

and

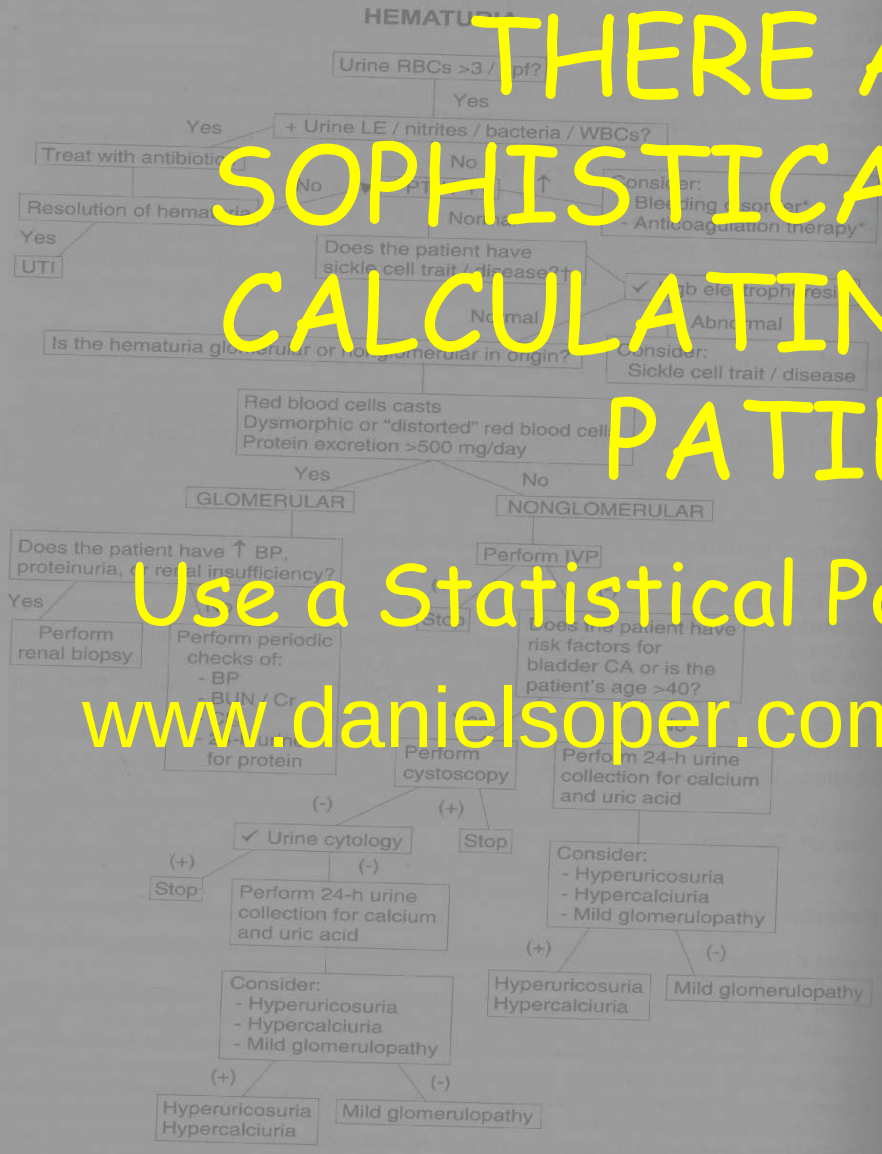
"38 in 40 = 95%"

So with 40 patients you have a reasonable chance of obtaining a reference interval that you can have a "95% confidence" about.

THERE ARE MORE SOPHISTICATED WAYS OF CALCULATING HOW MANY PATIENTS …

Use a Statistical Power Calculator eg :

www.danielsoper.com/statcalc/calc01.aspx



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A-priori Sample Size Calculator for Multiple Regression

This calculator will tell you the minimum required sample size for your study, given the alpha level, the number of predictors, the anticipated effect size, and the desired statistical power level.

For more information about this calculator, including method, formulae, and references, please click here.

Please supply the necessary parameters, and then click the 'Calculate' button.

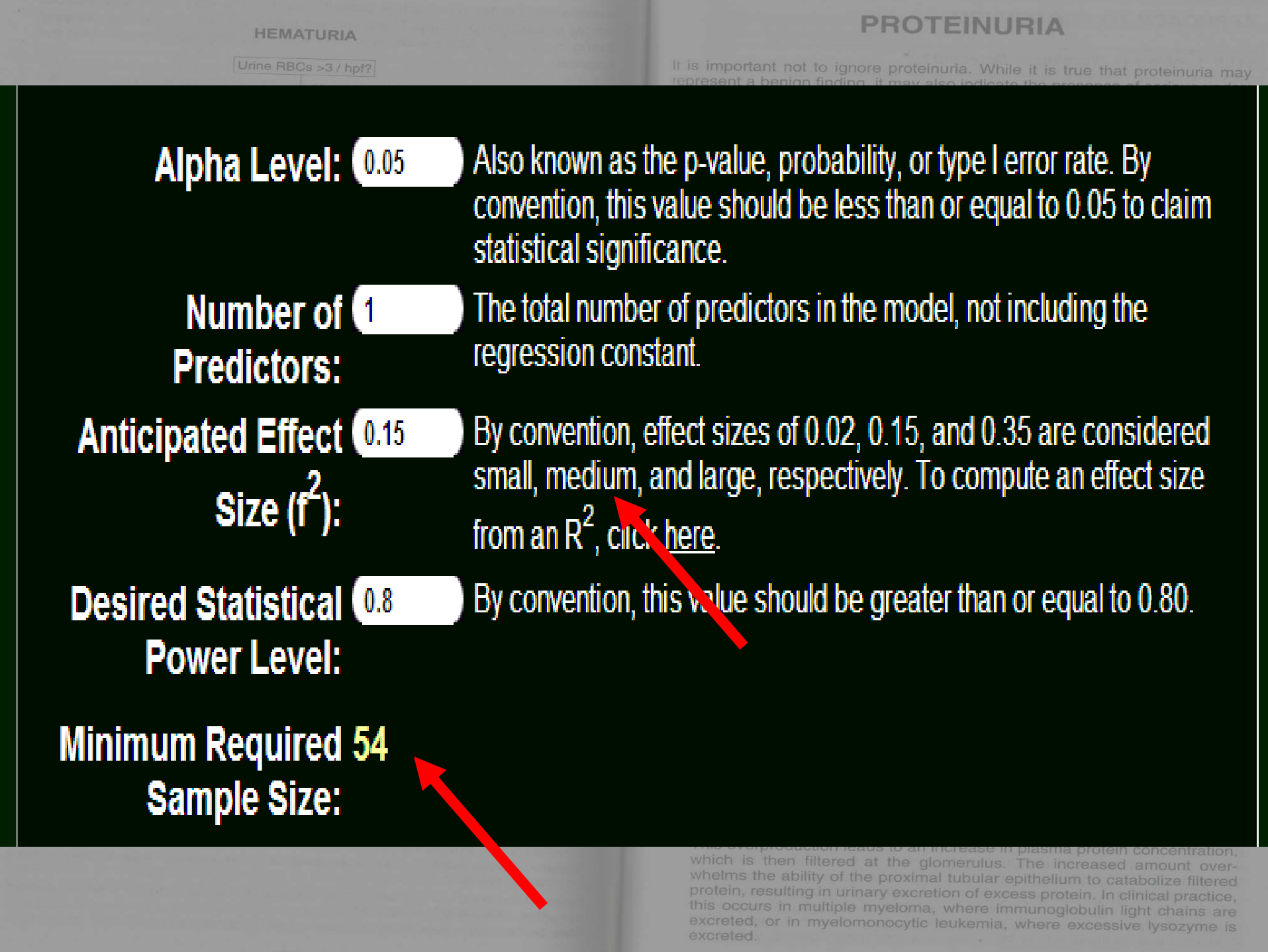
Alpha Level: 0.05 — Also known as the p-value, probability, or type I error rate. By convention, this value should be less than or equal to 0.05 to claim statistical significance.

Number of Predictors: 3 — The total number of predictors in the model, not including the regression constant.

Anticipated Effect Size (f^2): 0.15 — By convention, effect sizes of 0.02, 0.15, and 0.35 are considered small, medium, and large, respectively. To compute an effect size from an R^2, click here.

Desired Statistical Power Level: 0.8 — By convention, this value should be greater than or equal to 0.80.

Calculate


HEMATURIA
Urine RBCs >3 / hpf?
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excreted.
Alpha Level: 0.05
Also known as the p-value, probability, or type I error rate. By convention, this value should be less than or equal to 0.05 to claim statistical significance.
Number of Predictors: 1
The total number of predictors in the model, not including the regression constant.
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Minimum Required Sample Size: 54

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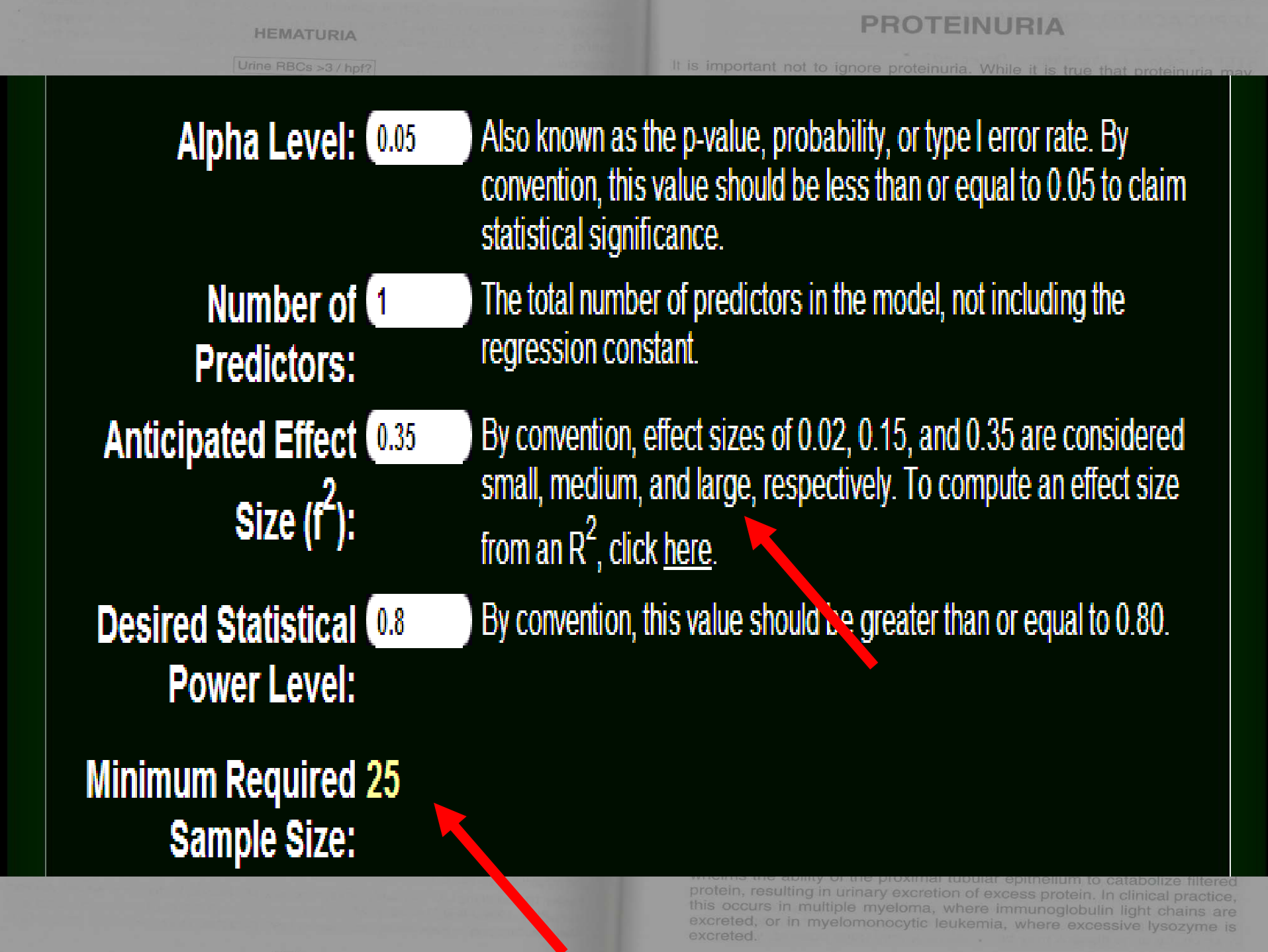
Desired Statistical Power Level:	0.8	By convention, this value should be greater than or equal to 0.80.

Minimum Required Sample Size: 385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Number of Predictors: 1
The total number of predictors in the model, not including the regression constant.
Anticipated Effect Size (f^2): 0.35
By convention, effect sizes of 0.02, 0.15, and 0.35 are considered small, medium, and large, respectively. To compute an effect size from an R^2, click here.
Desired Statistical Power Level: 0.8
By convention, this value should be greater than or equal to 0.80.
Minimum Required Sample Size: 25
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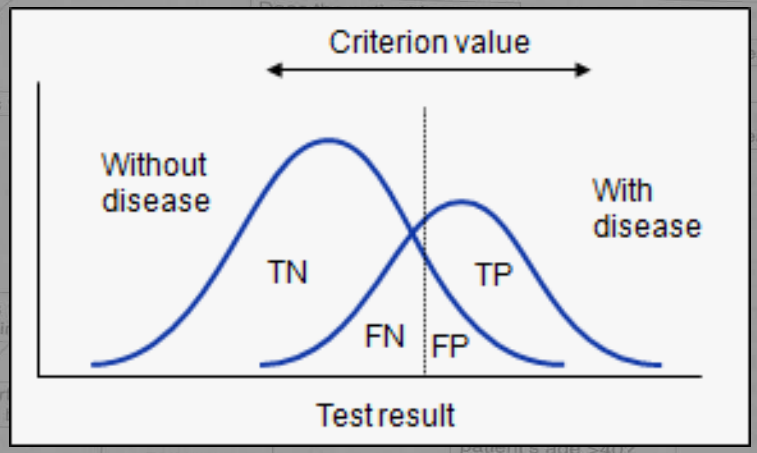
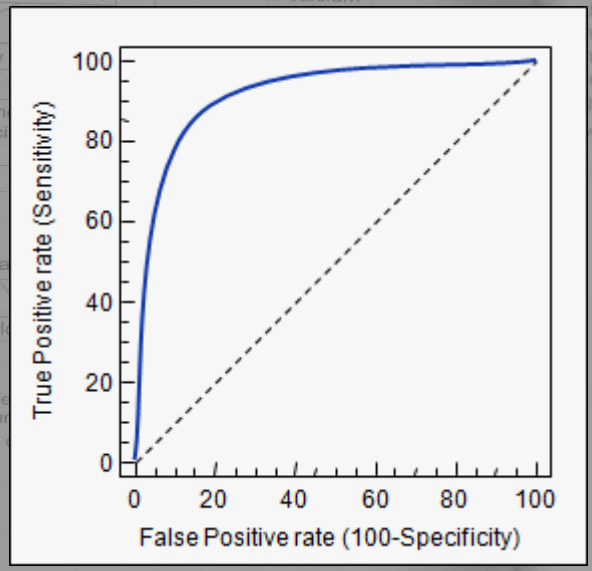
THE ROC Curve





Specificity : the probability that a laboratory test will be negative in the absence of a disease

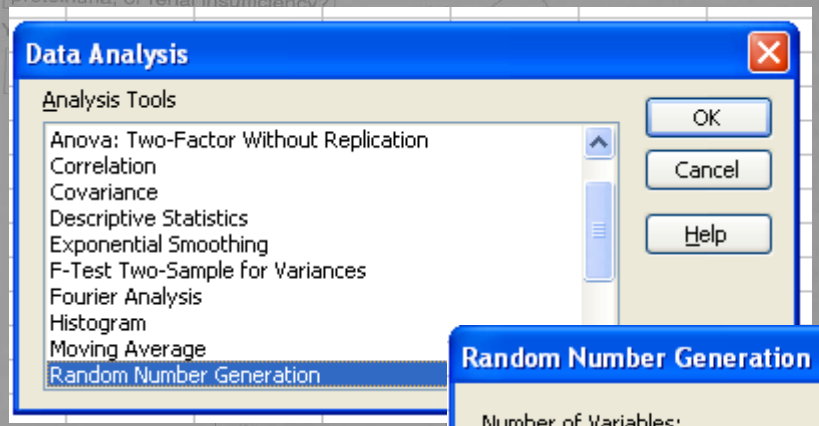
= # of true negatives divided by (# of true negative + # of false positives)

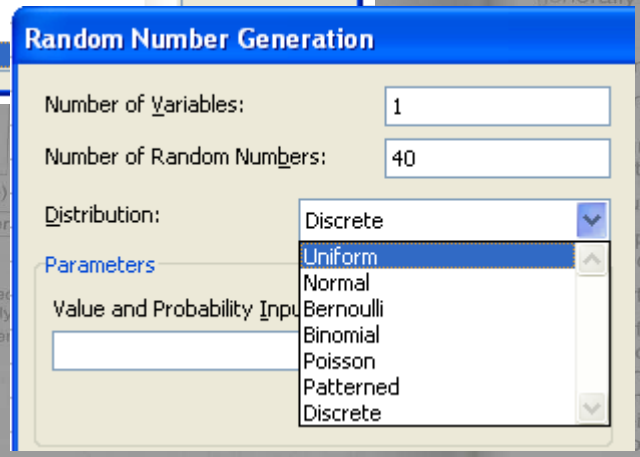
Sensitivity : the probability that a laboratory test is positive in the presence of disease

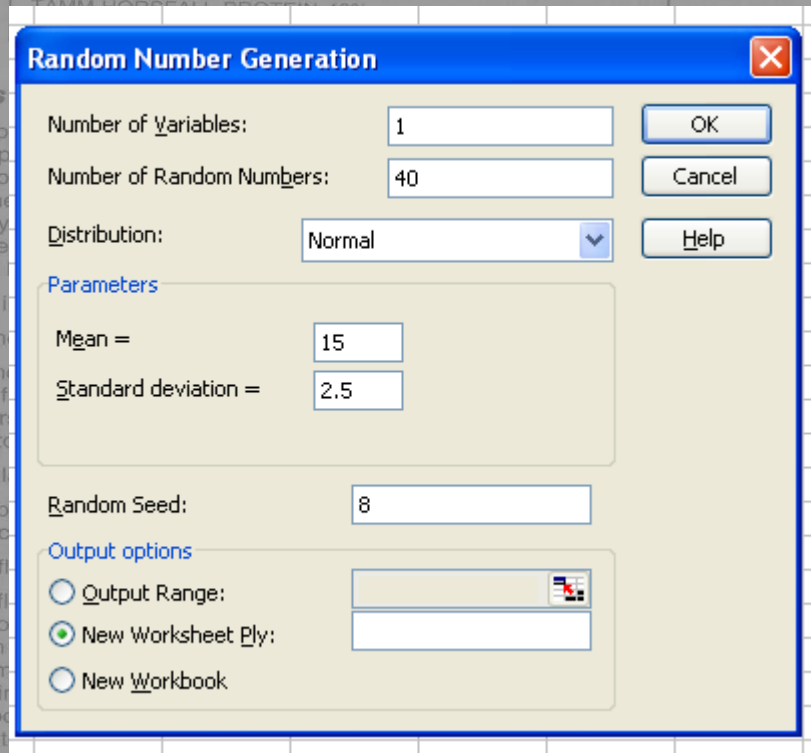
= # of true positives divided by (# of true positives and # of false negatives)

Generate Some Test Data Before You Collect Real Data

Use the Data Generator Inside Excel







	A	B	C	D	E	F	G	H	I	J
1	7.8									
2	9.1		Bins							
3	9.6		6							
4	10.8		8							
5	10.8		10							
6	11.5		12							
7	11.7		14							
8	12.2		16							
9	12.3		18							
10	12.7		20							
11	12.8									
12	13.1									
13	13.2									
14	13.5									
15	13.7									
16	13.8									
17	13.9									
18	13.9									
19	14.0									
20	14.5									
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32	17.0									
33	17.2									
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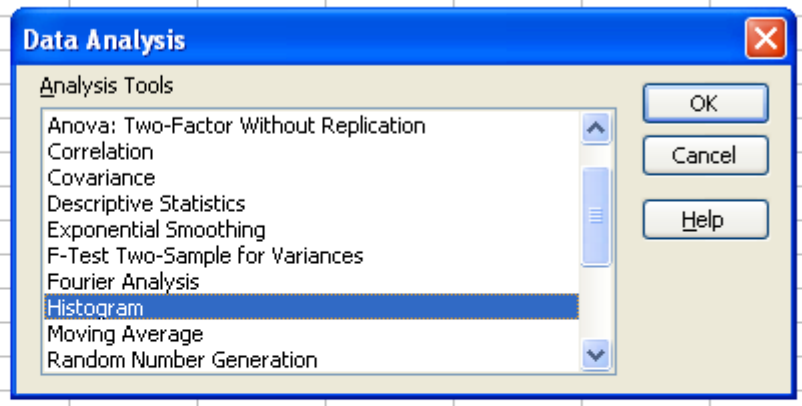
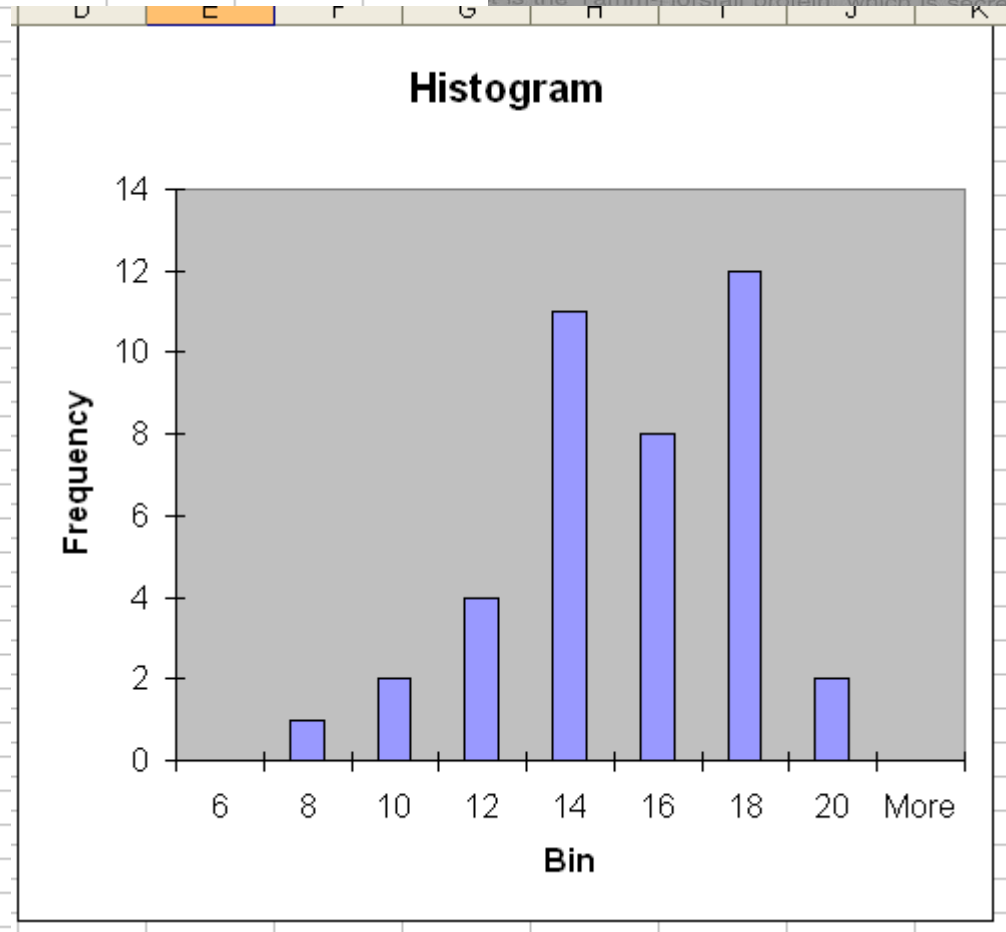
39	19.1									
40	19.4									
41										





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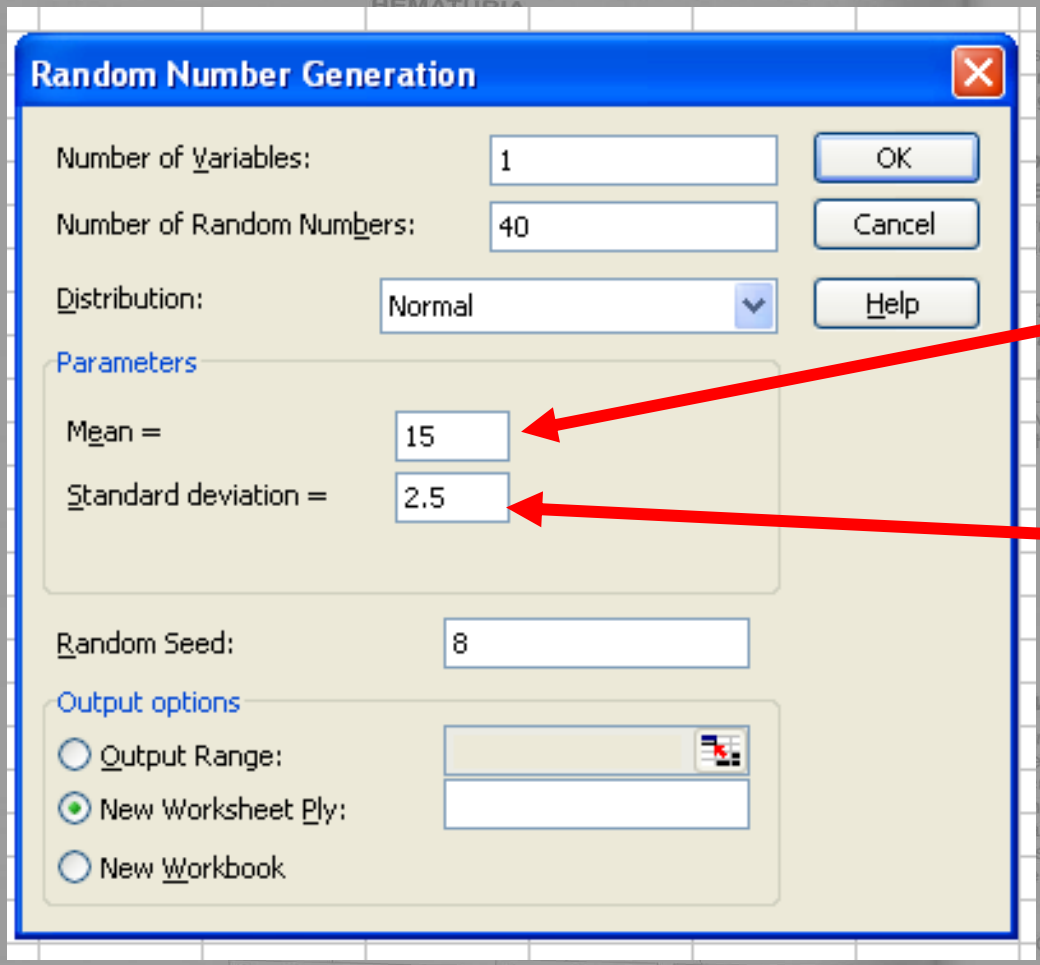

ACTUAL STATS

Mean	14.43
Standard Error	0.43
Median	14.54
Mode	
Standard Deviation	2.75
Sample Variance	7.54
Kurtosis	-0.28
Skewness	-0.34
Range	11.65
Minimum	7.79
Maximum	19.43
Sum	577.27
Count	40.00

PROTEINURIA

Consider:
- Hyperuricosuria
- Hypercalciuria
- Mild glomerulopathy

Hyperuricosuria Hypercalciuria

Mild glomerulopathy

(+)

(-)

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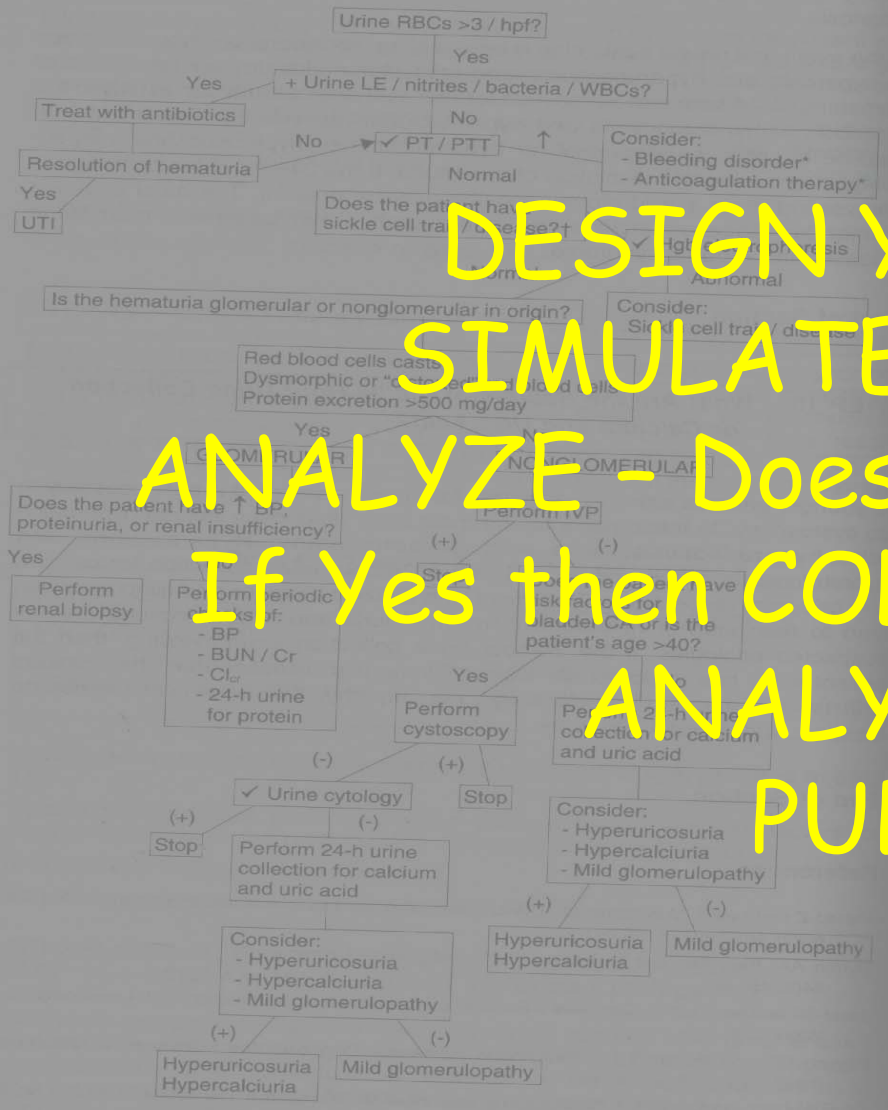

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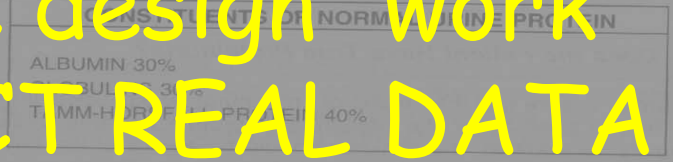

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DESIGN YOUR STUDY
SIMULATE SOME DATA
ANALYZE - Does the design "work" ?
If Yes then COLLECT REAL DATA
ANALYZE THEM
PUBLISH