2009 CME SYMPOSIUM
SUMMING UP

**Topics:**

**HEMATURIA**
- Treat with antibiotics
- Resolution of hematuria
- UTI

**PROTEINURIA**
- How much protein is excreted over a 24-hour period in the normal kidney? Is it due to glomerular disease?
- What different types of protein are normally excreted in the urine?

**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 myelomocytic leukemia, where excessive lysozyme is excreted.
TIPS ON GATHERING YOUR OWN T & R & D DATA

Design a single page A4 'portrait' data collection form

- Set up an Excel Spreadsheet with each field on your paper form that matches the columns on your Excel Data Entry 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

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SPSS - Statistical Package for the Social Sciences
Statistical Package for Students Searching for Significance

SPSS 16.0 for Windows

This copy of SPSS 16.0 for Windows is licensed to:
NT96V2JD1
UNT
9793390
EXCEL IS RECOMMENDED
Version 2003
DATA ENTRY FORM - DIY with VBA
DATA ENTRY FORM - Use an AddIn

dataform3.xla

<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
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<tbody>
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<td>Given Names</td>
<td>Gender</td>
<td>Date of Birth</td>
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<td>789456</td>
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<td>Keeler</td>
<td>Jackie</td>
<td>Female</td>
<td>29/09/2000</td>
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J-Walk Enhanced Data Form

<table>
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<tr>
<th>Data</th>
<th>Criteria</th>
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<td>UR Number</td>
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<td>Keeler</td>
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<tr>
<td>Given Names</td>
<td>Jackie</td>
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<tr>
<td>Gender</td>
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<td>Date of Birth</td>
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<td>Baseline Observations</td>
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<td>Starting Dose</td>
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<td>Maintenance Dose</td>
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<td>Start Wt, kg</td>
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</tr>
<tr>
<td>Start BMI</td>
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</tr>
<tr>
<td>6 months Wt, kg</td>
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<td>6 months BMI</td>
<td>34.722222222222</td>
</tr>
<tr>
<td>Adverse Events</td>
<td>Poor compliance due to recurrent illness</td>
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Record 3 of 3
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 3b** - for Excel 2007

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
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 ($r^2$):** 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.
**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.

**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.

**Minimum Required Sample Size:** 54
<table>
<thead>
<tr>
<th><strong>Alpha Level:</strong> 0.05</th>
<th>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.</th>
</tr>
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<tbody>
<tr>
<td><strong>Number of Predictors:</strong> 1</td>
<td>The total number of predictors in the model, not including the regression constant.</td>
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<tr>
<td><strong>Anticipated Effect Size (f^2):</strong> 0.02</td>
<td>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.</td>
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<td><strong>Desired Statistical Power Level:</strong> 0.8</td>
<td>By convention, this value should be greater than or equal to 0.80.</td>
</tr>
<tr>
<td><strong>Minimum Required Sample Size:</strong> 385</td>
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</table>

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.
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.

Anticipated Effect Size ($r^2$): 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
THE ROC Curve

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

\[
= \frac{\text{# of true negatives}}{(\text{# of true negative} + \text{# of false positives})}
\]

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

\[
= \frac{\text{# of true positives}}{(\text{# of true positives} + \text{# of false negatives})}
\]

HEMATURIA

<table>
<thead>
<tr>
<th>Urine RBCs &gt;3/hpf?</th>
<th>Yes</th>
<th>No</th>
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<tbody>
<tr>
<td>Treat with antibiotics</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Resolution of hematuria</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>UTI</td>
<td>Yes</td>
<td>No</td>
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PROTEINURIA

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

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

Normally, there 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, which is not filtered through the glomerulus, and proteinuria of more than 300 mg per day is considered abnormal. Albumin is the 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
- γ-Globulin
- Fibrinogen
- Clotting factors
- Immunoglobulin
- Lipoprotein

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. Albumin is the only protein which may be readily filtered. Other plasma proteins are generally low molecular weight in nature.

With this in mind, the kidneys:

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 increases tubular reabsorption will allow low molecular weight protein to be excreted in the urine.

Overflow

Overflow proteinuria is the result of concentrating tubular protein.

This occurs when the renal plasma flow increases and the concentration of protein rises, which is then filtered by the glomerulus. The increased amount overwhelms the normal tubular epithelium to catabolize filtered protein, resulting in a 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.
Generate Some Test Data Before You Collect Real Data Use the Data Generator Inside Excel
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<th>Bin</th>
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<td>20</td>
<td>8</td>
</tr>
<tr>
<td>More</td>
<td>9</td>
</tr>
</tbody>
</table>

**Histogram**

Proteinuria. While it is true that proteinuria may may also indicate the presence of serious underline.

Is Excreted Over a 24-Hour Period in Adult?

Protein are normally excreted in the urine over a 24-hour

plasma and the urinary tract. Plasma proteins

as the Tamm-Horsfall protein, which is expressed.

In the present study, the amount of protein excreted in the urine over a 24-hour

by way of the glomerulus. Plasma proteins are

and tubular systems of the kidney. The major contributor to proteinuria is the Tamm-Horsfall protein, which is expressed.

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**ACTUAL STATS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<td><strong>Standard Error</strong></td>
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<td><strong>Mode</strong></td>
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<tr>
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<td><strong>Sample Variance</strong></td>
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<td><strong>Kurtosis</strong></td>
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<tr>
<td><strong>Skewness</strong></td>
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<td><strong>Range</strong></td>
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<td><strong>Maximum</strong></td>
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<td><strong>Count</strong></td>
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DESIGN YOUR STUDY
SIMULATE SOME DATA
ANALYZE – Does the design “work”?  
If Yes then COLLECT REAL DATA
ANALYZE THEM
PUBLISH