

# Part 1 Lecture 2a The Central Limit Theorem







# Pascal Tyrrell, PhD

Associate Professor

Department of Medical Imaging, Faculty of Medicine

Institute of Medical Science, Faculty of Medicine

Department of Statistical Sciences, Faculty of Arts and Science







# QUESTIONS ABOUT A STUDY COMPARING TWO BLOOD PRESSURE DRUGS

Let's suppose your friend is excited about a study in which the mean decrease in blood pressure was greater in a group of patients on a new drug compared to a group on an old drug. Before you also get excited what questions would you ask her about the study?





# THE SEVEN QUESTIONS

- 1. How long was the follow up period ?
- 2. Did the new drug have any serious side effects ?
- 3. How were patients allocated to the groups ?
- 4. How large is the mean DBP difference between groups?
- 5. How many patients were in each group?
- 6. How large is the *Variation* in response among patients?
- 7. Are the two groups comparable ?

NOTE: DBP = Decrease in blood pressure.





#### CANADIAN GOVERNMENT POPULATION HEALTH SURVEY OF 6,000 CANADIAN WOMEN

One measurement made was the Body Mass Index (BMI):

# $BMI = WEIGHT(kg) / HEIGHT(m)^{2}$





# POPULATION OF 6,000 FEMALES

\*NOTE THE POSITIVE SKEWNESS

LOG NORMAL DISTRIBUTION MEAN = 23.4 VARIANCE = 15.5 SKEWNESS = 3 ERCE BM13





Paul randomly selected a sample of 5 women from this database and calculated their mean BMI. He then placed these women back into the population and again randomly selected a sample of five women and calculated their mean BMI. He did this 1,000 times and produced the histogram of these 1,000 means. He did this 2 more times with each sample having 10 women and then again with each sample having 25 women.

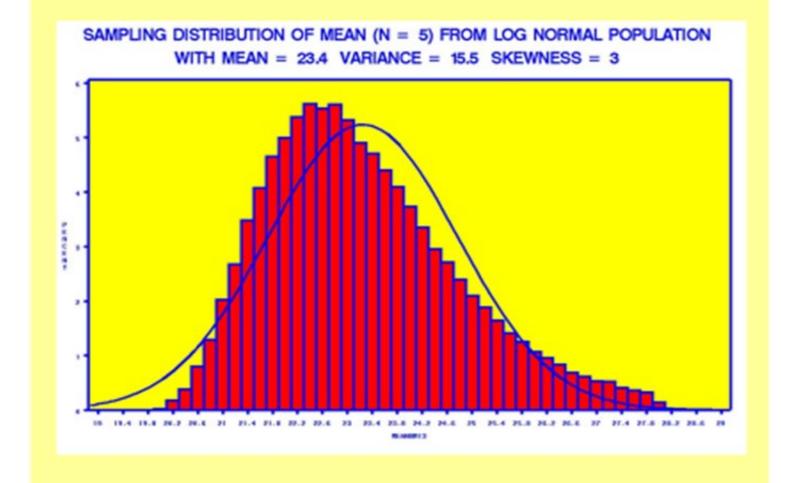




#### DISTRIBUTION OF 1,000 SAMPLE MEANS WITH N = 5

SAMPLE OF 1,000 RANDOMLY SELECTED MEANS OF 5 FEMALES

#### AND OVERLAPPING GAUSSIAN PROBABILITY DISTRIBUTION



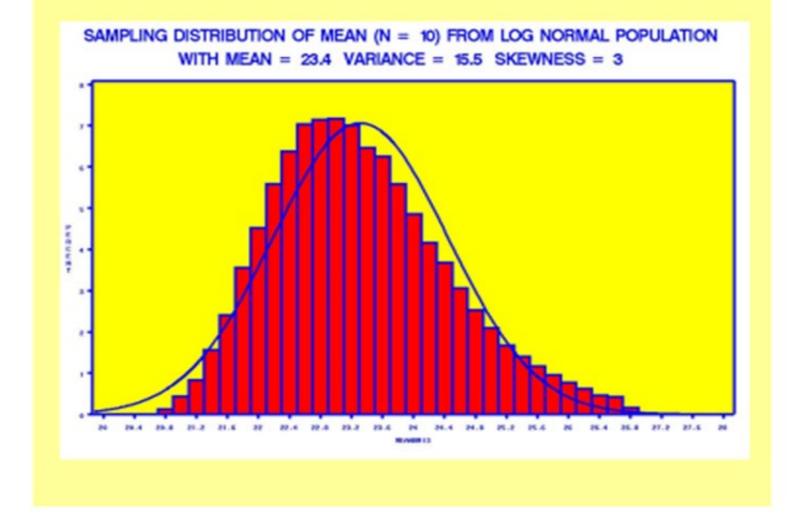




#### DISTRIBUTION OF 1,000 MEANS N = 10

SAMPLE OF 1,000 RANDOMLY SELECTED MEANS OF 10 FEMALES

AND OVERLAPPING GAUSSIAN PROBABILITY DISTRIBUTION



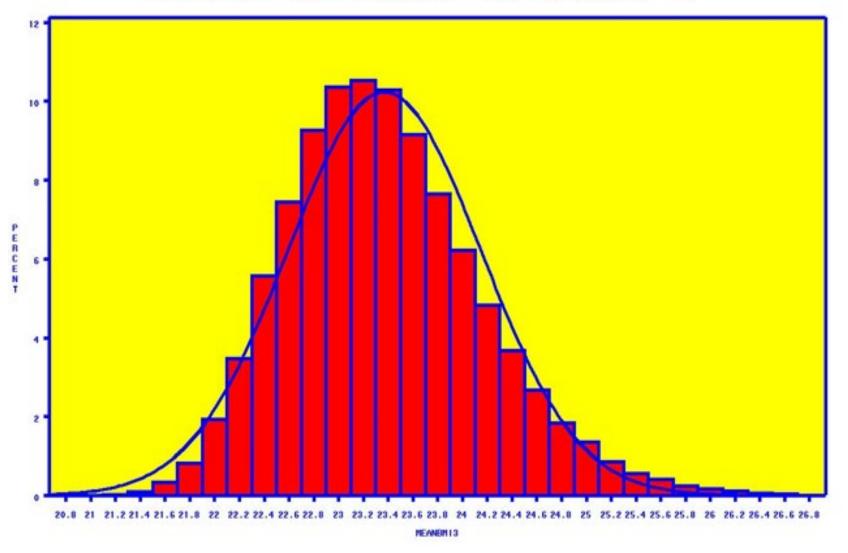




SAMPLING DISTRIBUTION OF MEAN (N = 25) FROM LOG NORMAL POPULATION WITH MEAN = 23.4 VARIANCE = 15.5 SKEWNESS = 3

SAMPLE OF 1,000 RANDOMLY SELECTED MEANS OF 25 FEMALES

#### AND OVERLAPPING GAUSSIAN PROBABILITY DISTRIBUTION







The probability distribution of a sample mean of N observed values randomly selected from a population approaches the Gaussian (Normal) probability distribution as N approaches infinity.

As "N approaches infinity" is mathematician talk. We saw that the distribution of sample means was approximately Gaussian for N as small as 25.





# *Pierre Simon La Place* Carl Friedrich Gauss 1749 - 1827



# 1777 - 1855







#### **GAUSSIAN PROBABILITY DENSITY FUNCTION**

$$f(\overline{BMI}) = \frac{e^{-\frac{(\overline{BMI} - \mu)^2}{2 \times \frac{\sigma^2}{n}}}}{\sqrt{2\pi \times \frac{\sigma^2}{n}}}$$

#### with $\pi = 3.1416$ e = 2.7163

Sample mean  $\overline{BMI}$  is unbiased estimator of theoretical (population)mean  $\mu$ . Many sample means each with many BMI values selected randomly from population has a bell shaped Normal probability distribution with mean  $\mu$ and variance  $\sigma^2$ . The parameter  $\sigma$ , standard deviation of variable BMI, is an important measure of variation. The variance of the mean  $\overline{BMI}$ 

variable is 
$$\frac{\sigma^2}{n}$$
 with standard error  $\sqrt{\frac{\sigma^2}{n}}$ 





Standard Gaussian Probability Density Function

$$If Z = \frac{\left(\overline{BMI_1} - \overline{BMI_2}\right) - (\mu_1 - \mu_2)}{\sqrt{2 \times \frac{\sigma^2}{n}}} \qquad then f(Z) = \frac{e^{-Z^2}}{\sqrt{2\pi}}$$

and Probability (-1.96 < Z < 1.96) = 0.95Mean of the standard Gaussian variable Z is 0. Variance of Z is 1 and Standard deviation of Z is 1.

 $\sqrt{2 \times \frac{\sigma^2}{n}}$  is the standard error of the difference of two **INDEPENDENT** sample means.



