Large Research Studies

Core Concepts:

- Traditional large research studies involve collecting and analyzing data related to an independent variable and dependent variable for a large number of research subjects.

- Data for a large research study could be acquired from a large scale health project that recruits and collects data from a large number of research subjects.

- Large research studies with large sample sizes provide better evidence for evaluating claims because the control group and the experimental group are more likely to be similar.

- Data for a large research study could be acquired from meta-analysis that combines data from multiple smaller studies.

- Traditional science research studies, such as controlled experiments and clinical trials, may be time-consuming, expensive, and difficult to do for long-term research or for complex diseases.

Class Time Required:

2 – 3 forty-minute class periods

Teacher Provides:

For each student

- 1 copy of student handout entitled **Large Research Studies.** (Note: You can also divide this into two separate handouts for Part 1 and Part 2.)

- 1 copy of **Box and Whiskers Plot Grid** (page v)

- Access to calculators

For each pair of students

- 1 copy of **Reference Sheet: Statistical Summary and a Box and Whiskers Plots** (page iv). Laminate if this will be used for multiple classes.

- Set of 7 **Research Study Description Cards** (pages vii-viii). Laminate if these will be reused for multiple classes.

- 1 copy of **Checklist for a Well-Designed Research Study** (page ix). Laminate if this will be used for multiple classes.

- Optional: 1 copy of **Understanding Osteoporosis** poster (page vi) to provide background information on osteoporosis. Laminate if this will be used for multiple classes.

Teacher Resources:

- **What is Osteoporosis and What Causes It?**
  https://www.nof.org/patients/what-is-osteoporosis/

- **Calcium: What's Best for Your Bones and Health?**
  https://www.hsph.harvard.edu/nutritionsource/calcium-full-story/

- **Bone Density Exam/Testing**
  https://www.nof.org/patients/diagnosis-information/bone-density-examtesting/

- Additional activities related to osteoporosis and big data are available online from University of Rochester's Life Sciences Learning Center.
  www.urmc.rochester.edu/life-sciences-learning-center/lessons.aspx

Suggested Class Procedure:

1. **Prior knowledge of <u>osteoporosis</u> and <u>bone density</u> is suggested for this activity.** This can be obtained by:

   - Completing the **A Case of Osteoporosis** activity included in the Big Data lessons

   - Providing the **Understanding Osteoporosis** poster

   - Encouraging students to use Internet to learn more about osteoporosis

2. Assign students to work with a partner.

3. Distribute a copy of **Large Research Studies** to each student.

4. Read the **Introduction** aloud to the class.

5. Students work together to complete Part 1: A Large-Scale Health Study

6. When students get to page 4, distribute:

   - **Box and Whiskers Plot Grid** to each student

   - **Reference Sheet: Statistical Summary and a Box and Whiskers Plots** to each pair of students

7. Take time to have students share and discuss their answers to the questions in Part 1.

8. Class discussion: Ask students to suggest reasons why there are relatively few large health studies that have provided data on human health issues such as bone density and osteoporosis, heart disease, and diabetes. *Note: Large health studies are expensive and it is difficult to find people to participant fully in these studies because they require long-term participation.*

9. For Part 2: A Meta-Analysis Study, distribute a set of 7 research study description cards and a **Checklist for a Well-Designed Research Study** to each pair of students.

10. Each team selects 4 research studies that should <u>NOT</u> be included when data is combined for meta-analysis. Allow time for students to use their "common sense" to select studies to eliminate and explain why the studies should be eliminated.

11. Ask students to discuss and reach consensus on which 4 research studies should be excluded.

12. Students work with their partners to complete Part 2.

13. Class discussion of their answers to the questions on pages 6 and 7.

14. Optional wrap-up discussion: Which is better, a large scale health study or a meta-analysis?

Reference Sheet: Statistical Summary and Box and Whiskers Plots
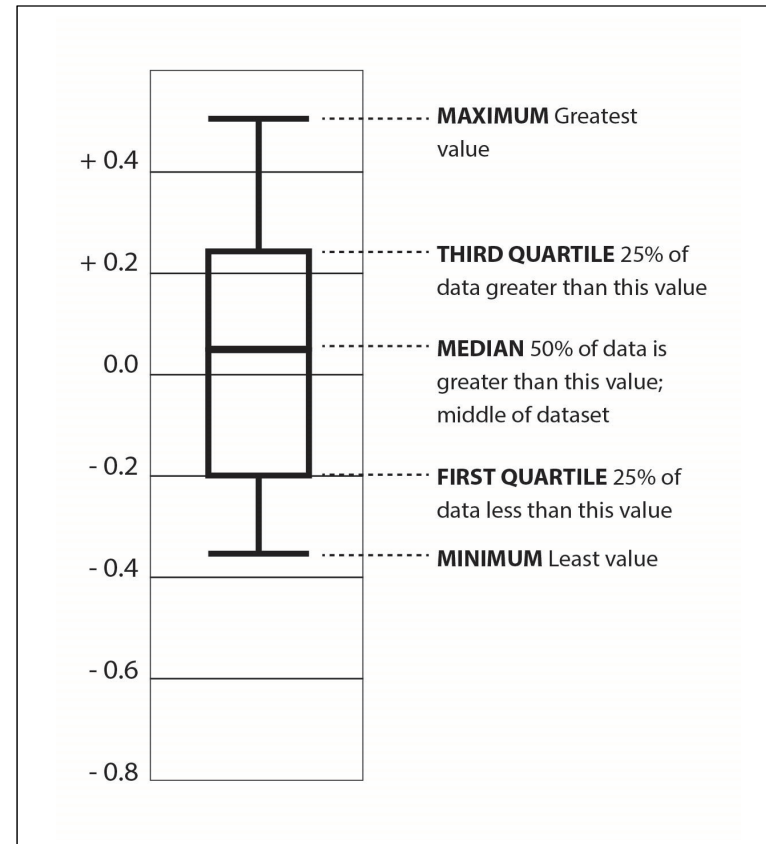
Minimum and Maximum

- The minimum is the lowest value.

- The maximum is the highest value.

- The minimum and maximum are at the ends of the "whiskers".

Median (or Second Quartile)

- The median (or second quartile) is the value that separates the data into two equal parts. Half of the values are above the median and half of the values are below the median.

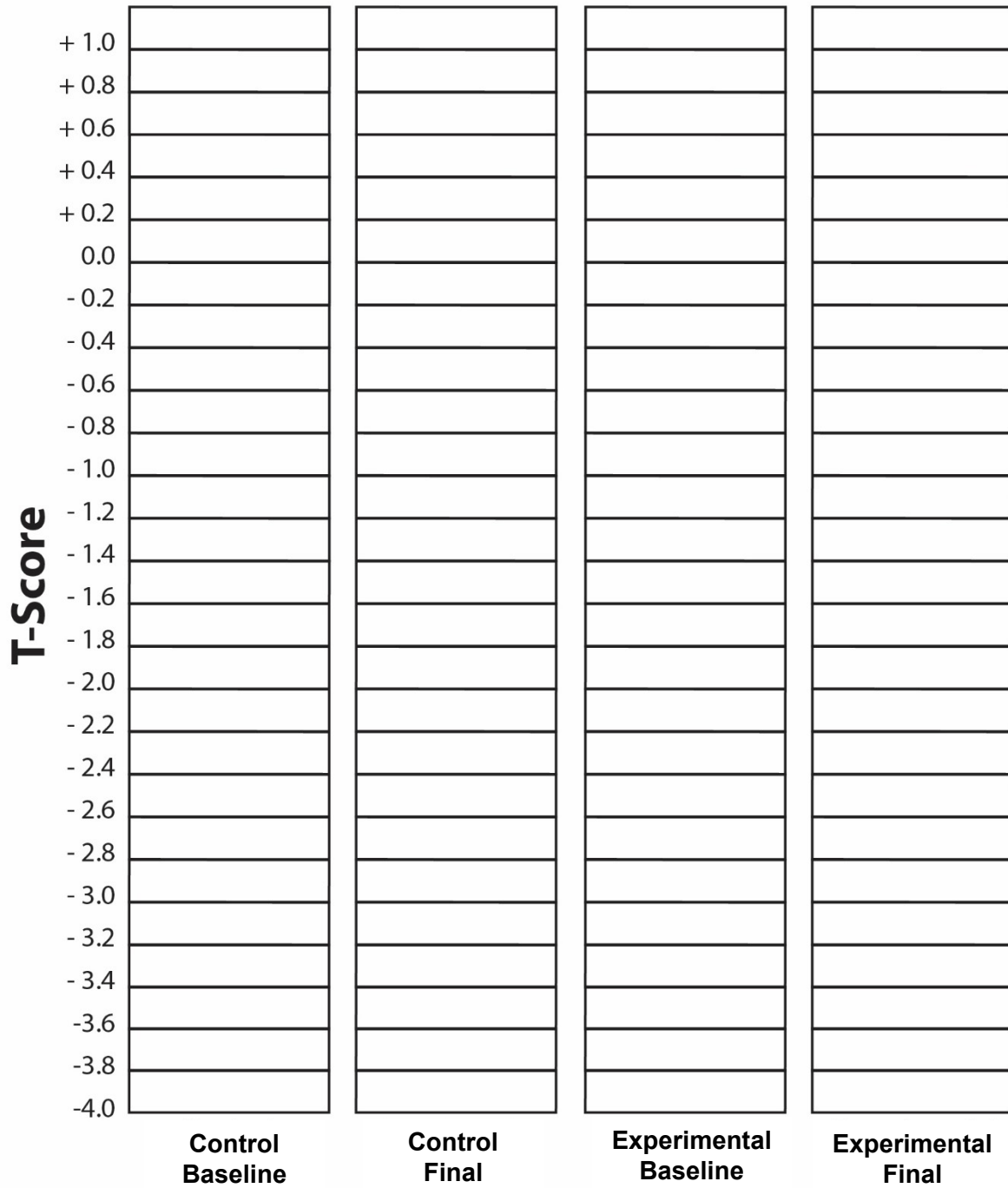- The median is represented with a line in the box.

First and Third Quartiles

- The first quartile is the value that separates the lower half of the data into two equal parts. One quarter of the data is below the first quartile and three quarters of the data is above the first quartile.

- The third quartile is the value that separates higher half of the data into two equal parts. Three quarters of the data is below the third quartile and one quarter of the data is above the third quartile.

- The first and third quartiles are at the ends of the box.

+ 0.4

+ 0.2

0.0

- 0.2

- 0.4

- 0.6

- 0.8

MAXIMUM Greatest value

THIRD QUARTILE 25% of data greater than this value

MEDIAN 50% of data is greater than this value; middle of dataset

FIRST QUARTILE 25% of data less than this value

MINIMUM Least value

Box and Whiskers Plot Grid

The Effects of Calcium Supplements on T-Scores

T-Score	Control Baseline	Control Final	Experimental Baseline	Experimental Final
+ 1.0				
+ 0.8				
+ 0.6				
+ 0.4				
+ 0.2				
0.0				
- 0.2				
- 0.4				
- 0.6				
- 0.8				
- 1.0				
- 1.2				
- 1.4				
- 1.6				
- 1.8				
- 2.0				
- 2.2				
- 2.4				
- 2.6				
- 2.8				
- 3.0				
- 3.2				
- 3.4				
-3.6				
-3.8				
-4.0				

UNDERSTANDING OSTEOPOROSIS

What is Osteoporosis?
Osteoporosis is a bone disease that makes bones weaker and more brittle because they are less dense. Osteoporosis increases the risk of bone fractures.

What Causes Osteoporosis?
Bone tissue is constantly being formed and broken down. Osteoporosis occurs when bone loss is greater than bone building.

Healthy Bone
Strong Bone
More Dense

Osteoporosis
Brittle Bone
Less Dense

Symptoms
- Brittle Bones
- Back Pain
- Height Loss
- Bad Posture

Risk Factors

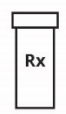Calcium and vitamin D deficiency

Smoking

Family history

Getting older

Alcohol

Inactive lifestyle

Thin and/or small frame

Corticosteroids and anti-seizure medications

Women, especially post-menopausal

Medical conditions that weaken calcium absorption

Low testosterone levels (men)
Low estrogen levels (women)

Diagnosis
Bone Density Test
- Recommended for people 50 and over
- Simple Test
- Takes 10-15 minutes

Treatment
Follow your doctor's recommendations.

Take calcium and vitamin D supplements.

Eat dairy and dark leafy and green vegetables.

Take prescribed medications.

Prevention

Take calcium and vitamin D supplements.

Eat dairy products and dark leafy and green vegetables daily.

Limit alcohol intake.

Stop smoking.

Walk or jog regularly.

1 in 2 women and **1 in 5 men** over 50 will fracture a bone due to osteoporosis. **25%** of those who fracture a hip die within six months of the injury.

In women over 45, osteoporosis accounts for more days spent in the hospital than many other diseases, including diabetes, heart attack and breast cancer.

Over **40 MILLION** people in the United States either already have osteoporosis or are at high risk for developing osteoporosis due to low bone density.

DUE TO PREVIOUS LACK OF FOCUS ON BONE HEALTH, THE NUMBER OF HIP FRACTURES IN THE UNITED STATES COULD BE **TRIPLED BY 2020.**

Research Study Description Cards *Cut along solid lines to separate into 7 cards.*

Dr. Laura Anderson asked 50 sixty-year-old women to participate in a research study by taking the free calcium supplement pills that she would provide for five years. After five years, bone density tests were done for 42 of the women who were still involved in the study. Dr. Anderson then calculated the percentage of these women who had T-Scores that were higher than the mean (average) T-Scores for 65-year-old women.

Dr. James Franklin identified 50 women whose T-Scores from their bone density tests indicated that they had osteopenia (low bone density). The 50 women were randomly assigned to two groups. Twenty-five of the women were asked to take one red calcium capsule each morning. Twenty-five of the women were asked to take one red placebo capsule each morning. The women did not know what the red capsules they took contained. Bone density tests for the 40 women were repeated three years later. Final T-Score data was then collected and used to calculate the percentage (%) change in T-scores.

Dr. Donald Covert from Scholar University replicated (repeated) the research done by Dr. Franklin. However, Dr. Covert's research involved a larger sample size (500 participants instead of 50 participants) and a longer time period (10 years instead of 3 years).

Dr. Jamal Milo collected baseline T-Scores for 50 women who had bone density testing done at his radiology clinic. He told 25 of the women that they were in the experimental group and they should take calcium pills. He told the other 25 women that they were in the control group and they should not take calcium pills. Bone density tests for the 50 women were conducted five years later. Data was analyzed by calculating the median percentage (%) change in T-scores.

Nature's Best is a company that produces "Nature's Best Calcium" capsules. They conducted an experiment with 20 women. The 10 oldest women were told that they were in the experimental group and they should take two "Nature's Best Calcium" capsules each day for one year. The 10 youngest women were told that they were in the control group and they should <u>not</u> take any calcium. Bone density tests to determine T-scores for the women were done at the beginning of the experiment and at the end of the experiment one year later. Data analysis was done by calculating the average percentage (%) change in T-scores for the two groups.

Dr. Sal Santora surveyed 100 women who have osteoporosis and 100 women who do not have osteoporosis. He asked the women in each of these two groups whether they took calcium supplements on a daily basis. He calculated the percentage (%) of women in each group who took daily calcium supplements.

Dr. Frank Voelker used the electronic medical records of a large hospital to identify 654 women who had bone density tests done 3-5 years ago and again within the last year. Computer software was used to identify:
- An experimental group of 115 women who had told their doctor that they took daily calcium supplements.
- A control group of 195 women who said they never took calcium supplements.

Data for both groups was analyzed by calculating the median percentage (%) change in T-Scores from previous bone density tests with bone density tests done within the last year.

Checklist for a Well-Designed Research Study

- **Single independent (manipulated) variable** – A research study should only test the effect of one independent (manipulated) variable at a time.

- **Constants or controlled variables** – Researchers should describe plans to keep other variables constant or the same.

- **Dependent (outcome) variable** – Researchers should describe what data will be collected for the dependent variable.

- **Controlled** – A controlled research study includes a control group serves as a basis of comparison. The control group and the experimental group should be the same except for the independent variable.

- **Large sample size** – In general, increasing the number of samples or subjects for an experiment reduces the effects of chance events or uncontrolled variables.

- **Replicable** – The procedures and materials for the research study should be clearly described so that others can repeat the experiment.

- **Random assignment** – To avoid bias, subjects should be randomly assigned to the control group and the experimental group.

- **Blind** – To avoid bias, research subjects should not be told whether they are in the control group or the experimental group.

- **No Conflict of Interest** – To avoid bias, the research study should <u>not</u> be done by a company or an individual who might profit from certain results.

> **Bias**
>
> - A lack of objectivity, or an inclination to favor one thing, result or person over another.
>
> - A one-sided point of view about something, which tends to influence decisions, observations, or opinions about other things.

Teacher key for Box and Whiskers Plot Grid:

Box and Whiskers Plot Grid

The Effects of Calcium Supplements on T-Scores
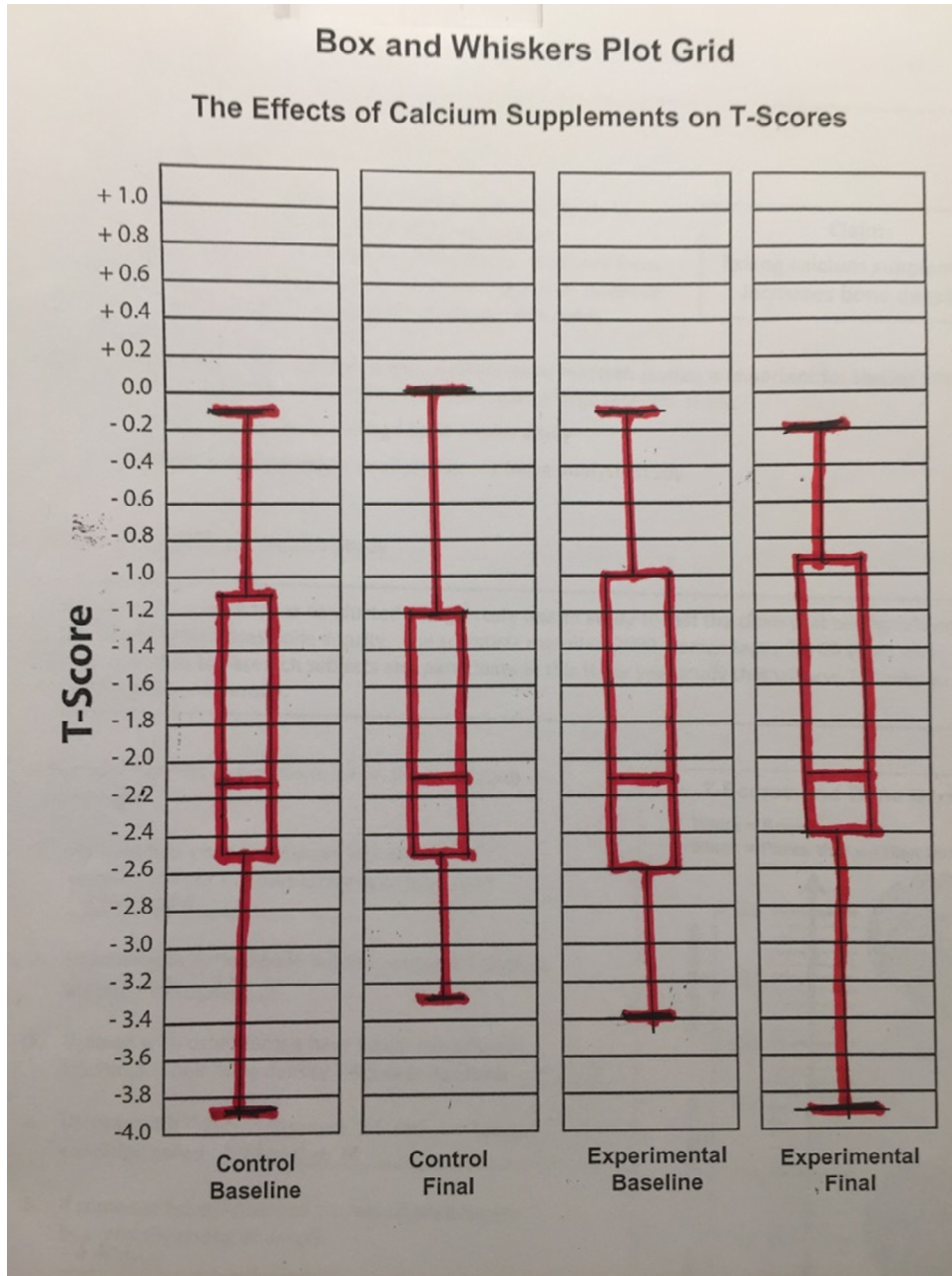
Large Research Studies

Introduction:

As people age, their bones become less dense and more likely to fracture (break). Some people claim that taking calcium supplements is a good way to increase bone density. The evidence for this claim is conflicting. Some small research studies support the claim. Other small research studies do <u>not</u> support this claim.

<div style="border:1px solid black; padding:10px;">

Claim:

Taking calcium supplements increases bone density.

</div>

When testing claims, large research studies that include a large sample size (many people) are more likely to reliable than small research studies. There are two different ways to collect and analyze data for a large research study.
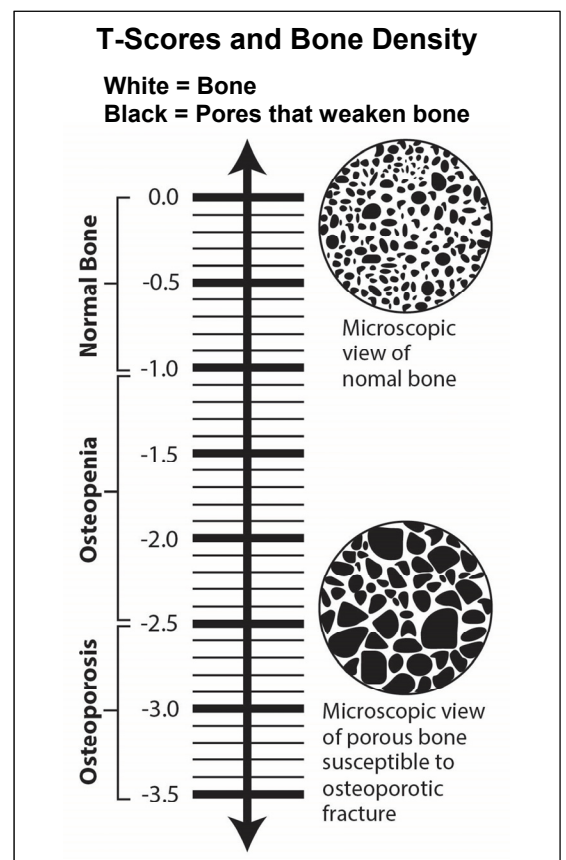
- Conduct one big study – a **large-scale health study**

- Combine data from many small studies – a **meta-analysis study**

Part 1: A Large-Scale Health Study

> A team of six scientists has conducted a **large-scale health study** to test the claim that taking calcium supplements increases bone density. The scientists recruited 2000 women (ages 50–60 years old) who agreed to be research subjects and participate in this three year study. Women in the study will have their bone density tested. The results of the bone density tests will be expressed as T-Scores.

Base your answers to questions 1-5 on the illustration on the right.

1. As a woman's bones becomes less dense and weaker, will her T-Scores increase or decrease? _*decrease*__

2. Women with normal bone density will have T-Scores greater than _*- 1.0*_.

3. Women with osteoporosis have a high risk of bone fractures. Their bone density T-Score is less than _*- 2.5* _.

4. Women with T-Scores between -2.5 and -1.0 have a condition called _*osteopenia* _.

5. If someone has a T-Score of – 0.1, would their bones be unusually strong or weak? __*strong*__

T-Scores and Bone Density

White = Bone
Black = Pores that weaken bone

Microscopic view of nomal bone

Microscopic view of porous bone susceptible to osteoporotic fracture

Expectations for participants enrolled in the three year study include:

- Have a baseline bone density test of the hip bone to determine their T-Score at the beginning of the health study.

- Take two capsules per day for three years.
    - Participants in the experimental group will take capsules that contain calcium.
    - Participants in the control group will take **placebo** capsules (capsules with no calcium).

Note: The participants will not be told whether they are in the experimental group or the control group, and they will not know if the capsules are placebos or calcium supplements.

- Have a final bone density test of the hip bone to determine their T-Score after three years.

- All participants will be told their T-Scores (results of bone of their bone density tests) at the end of the health study.

6. What is the independent variable in this research study?

   Calcium supplements

7. What is the dependent variable in this research study?

   T-Scores or Bone Density

8. It would be easier to do a research study with a sample size of 200 research subjects instead of 2000 research subjects. Explain why it is better to do research studies that involve a large sample size.

   Increasing the number of samples or subjects for an experiment reduces the effects of chance events or uncontrolled variables.

9. Make a list of at least <u>four</u> difficulties that the team of scientists may encounter when they try to recruit research subjects and collect data for this large health study project.
   Student answers will vary but may include:
   - *People want to be in the experimental group*
   - *Making women aware of need for participants in the large health study.*
   - *Recruiting women who are willing to become involved.*
   - *Maintaining accurate records for data*
   - *Maintaining accurate records for contacting women who may move out of the area*
   - *People may not want to be in the control group OR experimental group*
   - *Worried about the final outcome for their participation*
   - *Transportation to bone density tests*
   - *Distrust of doctors or scientists*
   - *Concern that participant self-reporting on taking capsules in not accurate*
   - *Length of study—subjects prefer short-term studies*
   - *Other logical explanations*

The budget for the large-scale three year health study includes:

- $100,000 per year for each scientist's salary for three years

- $500 for each participant who completes <u>all</u> research study expectations

- $300 for each bone density test

- $50 per participant for a one year supply of capsules (calcium or placebo)

10. Approximately how much should be budgeted for this large-scale <u>three year</u> health study? You should budget for six scientists and all 2000 women completing the study. Show your work.

$100,000 X 6 X 3 = $1,800,000 for scientist salaries
2000 X $500 = $1,000,000 for participants who complete expectations
2000 X $300 X 2 = $1,200,000 for bone density tests
2000 X $50 X 3 = $300,000 for capsules
Total = $4,300,000 for total health study

11. Who should pay for large-scale health studies to determine if calcium supplements are effective in preventing osteoporosis - the government (taxpayers) or companies that produce the supplements? Explain your answer.

Student answers will vary.
Companies—they will profit from supplement sales.
Taxpayers—avoid conflict of interest/bias because companies may try to bias the results to promote sales

12. Only 705 out of 1000 women in the experimental group and 698 out of 1000 women in the control group completed the research study expectations. List at least <u>two</u> possible explanations for why many of the participants did not complete the study?
Student answers will vary but may include:
- *They forgot to take capsules*
- *Did not have second bone density tests,*
- *Moved*
- *Died*
- *Too busy to continue with study*
- *Unpleasant side effects from capsules*
- *Complications from other health issues*
- *Other logical explanation*

At the end of the large-scale health study, mathematicians analyzed the data and prepared statistical summaries to compare the T-Scores for the control group and the experimental groups. This data analysis is presented in the table below.

Baseline T-Scores		Final T-Scores	
Control Group	**Experimental Group**	**Control Group**	**Experimental Group**
Median = - 2.1	Median = - 2.1	Median = - 2.1	Median = - 2.1
First Quartile = - 2.5	First Quartile = - 2.6	First Quartile = - 2.5	First Quartile = - 2.4
Third Quartile = - 1.1	Third Quartile = - 1.0	Third Quartile = - 1.2	Third Quartile = - 0.9
Minimum = - 3.9	Minimum = - 3.4	Minimum = - 3.3	Minimum = - 3.9
Maximum = - 0.1	Maximum = - 0.1	Maximum = 0	Maximum = - 0.2

13. On the separate handout entitled **Box and Whiskers Plot Grid**, make box and whiskers plots to help you visualize the distribution of the T-Score data in the table above.

   - Refer to the information on the **Reference Sheet: Statistical Summary and a Box and Whiskers Plots** for information on how to plot the T-Score data and what this data means.

   - Make your plots on the separate handout entitled **Box and Whiskers Plot Grid.** *Be sure to look at the labels to make sure your plots are done in the appropriate grid*

   See teacher key for Box and Whiskers Plot Grid on page X.

14. Are the median <u>baseline</u> (starting) T-scores for the control group and the experimental group similar enough for this to be a fair test of the claim? Be specific.
   The median baseline scores for the control group and experimental group are both - 2.1. The other values are similar.

> The **median** is the middle value for the T-Scores. Half of the T-Scores will be above the median and half will be below the median.

15. Does this large-scale health study support the claim that taking calcium supplements increases bone density? Support your conclusion with specific evidence from the box and whiskers plots.
   <u>No</u> because the median bone density remained the same for subjects who took calcium supplements. The median baseline and final T-Scores were the same for the control and experimental groups.

16. State one advantage of a large-scale health study.
   It provides a lot of data.
   More likely that the control group and experimental group will be similar.
   Reduces the effects of other variables such as age, life style, genes, and medical history.
   More reliable results

17. State one disadvantage of a large-scale health study.

   Large health studies are expensive, require a lot of work or are difficult to conduct.

Part 2: A Meta-Analysis Study

A scientist wants to conduct a **meta-analysis study**. Meta-analysis studies combine data already collected during many small research studies. He wants to test the claim that taking calcium supplements increases bone density as measured by T-Scores.

> **Claim:**
> **Taking calcium supplements increases bone density.**

The scientist has identified 7 small research studies that investigated the effect of calcium supplements on T-Scores that measure bone density. He summarized information on the design of these 7 studies that might provide data for the meta-analysis.

1. For the meta-analysis, it is important that the scientist only use data from controlled research studies that are fair tests for the claim. Read the 7 cards that describe the design for each of the small research studies.

   - Choose the <u>four</u> research studies that you think should <u>not</u> be included in the meta-analysis because they are <u>least</u> likely to be unbiased (fair) tests of the claim.

   - Complete the chart below by writing the names of the authors for the four studies you would exclude (not include). For each study that you excluded, explain why you think the study is not likely to be an unbiased test of the claim.

RESEARCH STUDIES TO BE ELIMINATED (NOT INCLUDED):

Last name of the author of the research study	Reason for excluding the research study
Santora	*Not random assignment* *Data collected did not measure bone density*
Anderson	*No control group*
Milo	*No random assignment* *Not a blind study—he old subjects what group they were in*
Nature's Best	*Potential conflict of interest or bias* *Small sample size*

2. Ask your teacher for a **Checklist for a Well Designed Research Study**. Did the information on this checklist cause you to change which studies you would want to eliminate? If so, use cross-outs and a different color of pen to change the chart above.

Base your answers to questions 3 through 10 on the following information.

The scientist chose three of the research studies for meta-analysis. Data from these studies was analyzed to determine the percentage (%) change between the baseline and final T-Score data. The results of this analysis are shown in the graphs below.
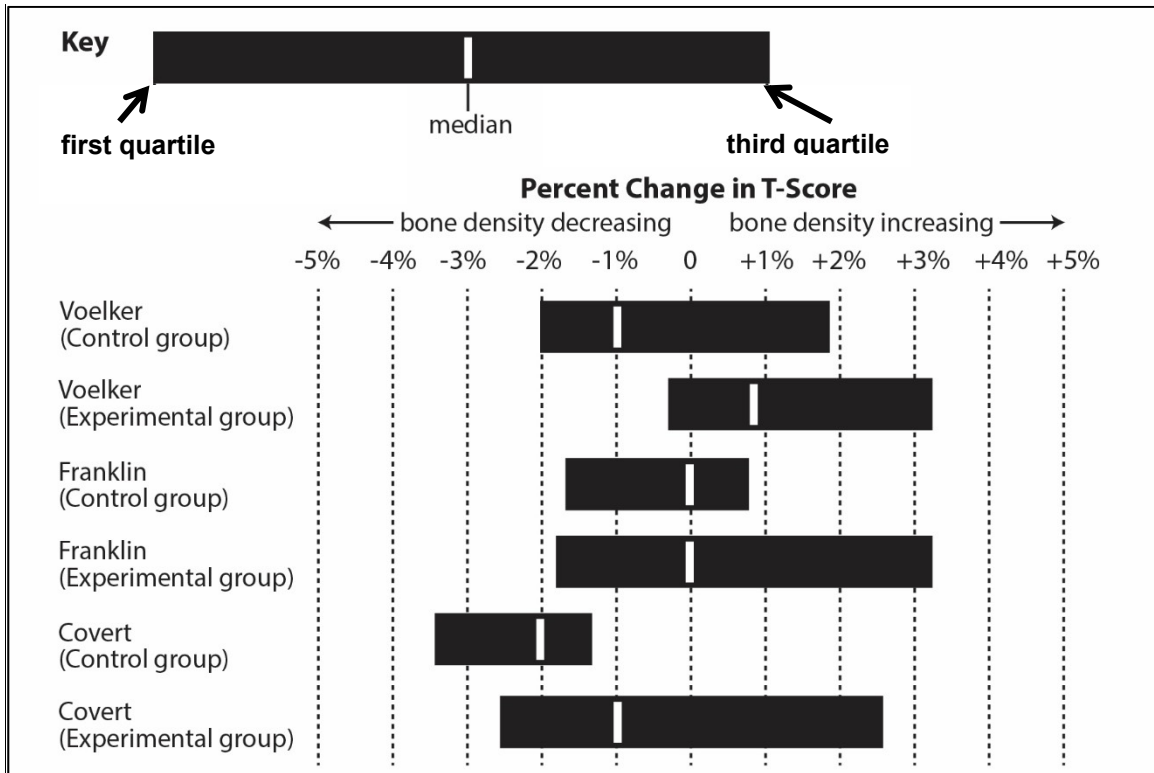
3. What was the unit of measurement for the dependent variable in the graph for this meta-analysis study? Be specific and include the units of measurement.

   Percent change in T-Score

4. Can you tell what the maximum and minimum values for % change in T-Score are for these graphs? Explain why or why not.
   No there are no whiskers on the graph OR the ends of the bars only show the quartiles.

5. Which researcher found that the median % change in T-Scores were the same for both the experimental group and the control group?

   Franklin

6. Which researcher found that the experimental group had median T-Scores that improved?

   Voelker

7. Based <u>only</u> on the research done by Dr. Voelker, what would you conclude about the effect of calcium supplements on bone density (T-Scores)? Support your conclusion with specific evidence from the graph.

   Women who take calcium supplements had a 0.8 % increase in bone density. Women who did not take calcium supplements had a 1% decrease in bone density.

8. Based <u>only</u> on the research done by Dr. Franklin, what would you conclude about the effect of calcium supplements on bone density (T-Scores)? Support your conclusion with specific evidence from the graph.

   Taking calcium supplements does not affect bone density. The T-Scores for both the control group and the experimental group had 0 change.

9. Based <u>only</u> on the research done by Dr. Covert, what would you conclude about the effect of calcium supplements on bone density (T-Scores)? Support your conclusion with specific evidence from the graph.
   Women who take calcium and do <u>not</u> take calcium supplements both have decreased bone density. However, women who take calcium supplements have smaller decrease. Women who take calcium supplements have a 1% decrease in bone density.   Women who did not take calcium supplements had a 2% decrease in bone density.

10. Based on <u>all</u> of the information in the graphs on the previous page, does the meta-analysis provide clear evidence that the use of calcium supplements increase bone density and prevent osteoporosis? Support your answer with specific evidence from the meta-analysis.

    No, the different researchers showed results that were small and inconsistent.

11. State one advantage of a meta-analysis study.

    Combines information from a larger number of research subjects; Lower costs; Less time consuming

12. State one disadvantage of a meta-analysis study.

    Difficult to find well-designed tests focused on the topic of interest.
    The inconsistencies in the different experimental designs could make drawing conclusions difficult.

13. Which type of large research study is <u>better</u> for testing the claim that taking calcium supplements increases bone density - a large-scale health study or a meta-analysis study? Support your answer.

    Student answers will vary depending on how they perceive "better." Encourage students to share and discuss their answer to this question.