**Student Participation in a Simulation to Illustrate the Complexity of Addressing a Simple Problem Through a Clinical Trial**

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Simulation is commonly used in pharmacy curricula to develop student skills in counseling patients and taking medication histories. However, simulating a clinical trial using students as research subjects is uncommon. The exercise described here illustrated the complexity of clinical trials to students by enrolling them as subjects. The simulated clinical trial determined the effect of wire diameter on the resistance of paper clips to breaking from repeated bending. Some aspects of the trial were intentionally flawed to provide for discussion of the limitations of the study as a clinical trial. The students also completed a written evaluation of the exercise. The students were successful in detecting many of the intrinsic study limitations and their observations were used as the basis for discussion of clinical trial design and conduct. The simulation appeared to succeed as an educational technique. Pharmacy faculty should consider incorporating simulations in the curriculum wherever possible to supplement traditional instruction.

**INTRODUCTION**

Randomized, controlled clinical trials remain at or near the top of any scheme of rating clinical evidence, being surpassed only by systematic reviews or meta-analyses of randomized, controlled clinical trials(1,2). Accordingly, it is important for pharmacy students to be able to read and analyze clinical trials, and some instruction on doing so is a component of any contemporary pharmacy curriculum. The difficulty facing the instructor is how to present the evaluation of clinical trials in a manner that both interests the students and serves to illustrate the principles and practice of clinical trials.

Simulation is commonly used in pharmacy curricula. Pharmacy students are frequently called upon to play the role of patient or pharmacist in order to learn how to obtain a medication history or counsel patients on medication use and for learning the techniques of physical assessment. Simulation has been demonstrated to be an effective tool for teaching research techniques(3). However, the use of students as actual research subjects is uncommon. The only previously published example of a simulated clinical trial using students as research subjects was the report of van den Brink et al.(4). They conducted a student-designed, double-blind trial of the effects of regular versus decaffeinated coffee on mean arterial blood pressure in a group of pharmacy students. Since it was unlikely that approval would be granted to us for a clinical trial involving the administration of medication to presumably healthy students just for the purposes of illustration, we developed an alternative approach. Our clinical trial posed little, if any, hazard to the participants but still contained most of the elements of an actual clinical trial. The simulated clinical trial protocol was designed to determine the effect of wire diameter on the resistance of paper clips to breaking from repeated bending.

Paper clips were selected as the study material because despite their ubiquitous nature they are given very little thought by their users. Like the evolution of the clinical trial, the modern paper clip is the product of a long process of experimentation for an effective method to address a simple problem; in this case, keeping related documents together(5,6). The purposes of this exercise were to illustrate to second professional year pharmacy students the complexity facing investigators when addressing a simple problem in the format of a clinical trial and to provide them with insight into the patient experience in clinical trials. Some aspects of the trial were intentionally flawed in order to provide for post-trial discussion of the limitations of the study.

**METHODS**

The study protocol and the combined informed consent and data collection document (Appendix) were approved by the University of New Mexico Health Sciences Center Human Research Review Committee. The students who were asked to participate in the clinical trial simulation were enrolled in the College of Pharmacy's required drug information course during two consecutive academic years. This course was scheduled in the spring semester of the second professional year and was reinforced by a research methods course during the third professional year and a four-week drug information clerkship in the fourth professional year. The research methods course was similar in intent and content to the one described by Draugalis et al.(7). The goal, objectives and course activities for the second-and fourth-year drug information experiences were based on published, consensus-derived guidelines(8). The simulated clinical trial followed several lectures on the design and evaluation of clinical trials. The simulation occurred during a single one-hour class session and the discussion was held during the next class session. All study participants were volunteers and participation was not a requirement for course completion nor did it result in any extra credit or other reward. However, students were expected to recall the lessons learned during the simulation. The following describes the procedure

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used to conduct the simulated clinical trial.

1. The students were asked to sit in every other seat and to leave the back row of the classroom vacant.
2. The title and purpose of the study were read aloud from the consent form by an investigator. The announced ratio nale of the experiment was "Breaking paper clips is thought to be a major source of tension relief for people in many office settings. This study is designed to determine if paper clips made from thick wire are harder to break than paper clips made from thin wire."
3. The students were informed that participation was voluntary, and those who did not want to participate could move to the vacated back row of the classroom.
4. The consent form was then distributed and read in its entirety to the students. During the reading and after it was concluded, the students were asked if they had any questions and were asked if anyone wanted to drop out of the study.
5. The following instructions were given to the students, and they were asked to listen to the instructions before proceeding.
   a. Initial the front page of the consent form in the designated area (lower left) after reading that page.
   b. Print your name in the space provided on the second page.
   c. Sign and date the form with a witness watching you sign.
   d. Have the witness sign and date the form.
   e. Fill in age and gender where indicated.
   f. Leave the rest of the form blank at this time (i.e., clip group and number of complete bends).
6. The students were randomized into two groups by the selection of slips of paper marked with an "A" or "B" from an opaque ceramic container (i.e., large coffee mug). The students were instructed to only observe during this time.
7. The students were given the following instructions prior to passing the opaque ceramic container around the room.
   a. Do not look into the cup.
   b. Hold the cup above eye level.
   c. Select one slip of paper and pass the cup to the next student.
   d. Record the clip group (i.e., "A" or "B") on the consent form.
8. The students then came to the front of the classroom to exchange the slip of paper showing either "A" or "B" for their paper clip. The students were required to display their signed and witnessed consent form and their slip of paper prior to receiving their paper clip. Students whose consent forms had been improperly filled out were to have their consent forms confiscated, would be terminated from the study and would be assigned to the back row of the classroom for the duration of the exercise. Students with slips of paper marked with an "A" were given a standard-size (small) paper clip; those with slips of paper marked with a "B" were given the paper clip of larger wire diameter (large). The students were advised not to bend or otherwise alter the paper clip (e.g., no warm-up bends allowed).
9. The students were continuously and obviously monitored for violations of the instructions including unwitnessed signatures and bending paper clips prior to the completion of the verbal instructions.

The paper clips tested were ACCO® paper clips. Group A received stock number 72380 (wire diameter 0.86 mm) and group B received stock number 72580 (wire diameter 1.22 mm). The diameter measurements are those of the raw wire before it is pounded into an elliptical shape prior to being formed into the familiar Gem paper clip. All small paper clips for group A were supplied from the same box, and all large paper clips for group B were supplied from the same box. During the year between simulation sessions, the paper clips were stored in sealed boxes safely away from accidental handling. According to a manufacturer's representative, paper clips in the same box are made from the same batch of metal and the metal composition is similar for both clip sizes. The manufacturer declined to describe the exact metal composition of its paper clips, claiming trade secrecy.

After the paper clips were distributed, the following instructions were read to the students and demonstrated by one of the investigators using a very large paper clip laying on an overhead projector and projected onto a screen visible throughout the room. The students were instructed to only observe during this time.

1. Read: "Hold the clip in the dominant hand between the thumb and index finger with the cut wire end of the greatest radius turn on top and with the greatest radius turn facing the nondominant hand." The dominant hand was defined as the hand used to write.
2. Demonstrate: The large paper clip on the overhead projector was used to identify "the cut wire end of the greatest radius turn."

Personal communication, Barb Paul, ACCO USA, Inc., 770 South ACCO Plaza, Wheeling IL 60090-6070.
Table I. Characteristics of study groups and results

<table>
<thead>
<tr>
<th>Group (95% CI)</th>
<th>Students</th>
<th>Men/women</th>
<th>Mean age (95% CI)</th>
<th>Mean bends</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (small clips)</td>
<td>58</td>
<td>28/30</td>
<td>28.0 yr (26.5-29.5)</td>
<td>6.8(6.1-7.5)</td>
</tr>
<tr>
<td>B (large clips)</td>
<td>55</td>
<td>18/37</td>
<td>27.2 yr (25.7-28.7)</td>
<td>8.8 (8.0-9.6)</td>
</tr>
</tbody>
</table>

Fig. 2. Number of bends needed to break paper clip.

3. Read: "Grasp the greatest radius turn cut wire end and bend it up and over 180 degrees through the vertical plane of the rest of the paper clip until the bend disappears, leaving that section of the wire straight. The thumb of the non-dominant hand can be used to support the lower aspect of the turn during the final 90 degrees of the bend. The cut wire will then be returned to its original position, restoring the turn in the paper clip. This constitutes a complete bend. Repeat the procedure until the paper clip breaks into two pieces."

4. Demonstrate: The proper bending technique was slowly shown so that there would be no confusion regarding how far to bend the clip or what constituted a complete bend (Figure 1).

5. Read: "Data will be recorded as the number of bends fully completed before the breakage of the paper clip. No fractional bend counts will be recorded. If the paper clip breaks before the wire is returned to its original position, that bend does not count. Are there are any questions or does anyone want to drop out?"

6. Read: "Students are to pay attention to their own work and ignore their neighbors so as not to be influenced by them."

7. Read: "Do not share your data; this is not a competition."

8. Read: "Write on the consent form in the appropriate place the number of complete bends required to break the clip."

9. Read: "Any student injured by the paper clip will immediately notify the investigators." Alcohol swabs and bandages had been brought to the room in case of minor injury.

When all students had completed the procedure, the investigators collected the completed consent/data collection forms. The students could retain their broken paper clips if they wished; however, an appropriate receptacle for safe paper clip disposal was provided.

After the exercise was completed, the students were asked to comment in an open classroom discussion on the conduct of the experiment and to describe potential problems in the protocol. The classroom discussion was used as an opportunity for the course instructor to present some of the statistical interpretation of the data. The students were also asked to complete a simple evaluation of the exercise. The evaluation consisted of 10 statements, nine of which asked the students to respond using a conventional "strongly agree" through "strongly disagree" scale. The 10th question asked if the time devoted to the exercise was "too long," "just right" or "not long enough."

RESULTS AND DISCUSSION

A total of 115 students were present during the two simulated clinical trial class sessions. Two students declined to participate in the simulation: one because he was taking warfarin and the informed consent document mentioned the possibility of skin puncture and the other student declined for unstated reasons. The results of the randomization and the mean number of bends needed to break the paper clips are given in Table I. The distribution of the number of bends needed to break the small and large clips is shown in Figure 2.

As intended, the students detected many possible problems with the clinical trial and their observations were used as the basis for additional discussion on clinical trial design and conduct. The detected problems included:

1. The rationale for the study included the assumption that breaking paper clips is a source of stress relief, but the study did not measure stress or stress relief. The practical application of the study's findings to the relief of stress was, therefore, very limited.

2. The study subjects (pharmacy students) represented a narrow segment of the population and might not resemble stressed office workers. This problem was used as an opportunity to discuss convenience samples and their limitations as well as how subjects are recruited into clinical trials.

3. The procedure for bending the paper clips in the study might not represent how stressed office workers actually bend paper clips. The standardized bending technique may have increased the reliability of the study but at the cost of reducing its generalizability.

4. The study was not blinded; the subjects and the investigators could see the paper clips as they were being bent. This problem provided an opportunity to discuss blinding techniques and situations in which blinding is absolutely necessary and when it may be optional.

5. Despite the detailed instructions on how to bend the paper clips, there could have been variation in how they were actually bent. Some may have bent the clips beyond 180 degrees while others might have failed to reach 180 degrees with their bends. Others may have twisted the clip during bending. This served as the basis for a discussion of the difficulty of compliance with even simple study protocols and the use of techniques to monitor compliance.

6. The data recording process relied on each subject to acce-
Table II. Student evaluation of the exercise

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strongly agree</th>
<th>Agree</th>
<th>Neutral</th>
<th>Disagree</th>
<th>Strongly disagree</th>
<th>No response</th>
</tr>
</thead>
<tbody>
<tr>
<td>The exercise improved my ability to evaluate published clinical trials</td>
<td>3.90</td>
<td>18</td>
<td>64</td>
<td>17</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>The exercise increased my appreciation of the difficulty in selecting</td>
<td>4.10</td>
<td>30</td>
<td>58</td>
<td>13</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>patients for clinical trials</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The exercise increased my appreciation of the importance of compliance</td>
<td>4.19</td>
<td>37</td>
<td>53</td>
<td>12</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>with clinical trial protocols</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The exercise complemented the information given in lecture.</td>
<td>4.14</td>
<td>35</td>
<td>52</td>
<td>14</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>The exercise made me want to learn more about study design.</td>
<td>3.33</td>
<td>11</td>
<td>32</td>
<td>43</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>Simulations like the exercise are an effective way for me to learn about</td>
<td>4.23</td>
<td>42</td>
<td>44</td>
<td>18</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>study design.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I would like more exercises like this one to illustrate concepts</td>
<td>4.13</td>
<td>36</td>
<td>50</td>
<td>15</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>presented in the course.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>The instructions for participating in the exercise were clear.</td>
<td>4.46</td>
<td>59</td>
<td>35</td>
<td>9</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>The exercise was fun.</td>
<td>4.13</td>
<td>40</td>
<td>41</td>
<td>20</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>The amount of time devoted to this exercise was:</td>
<td>too long</td>
<td>14</td>
<td>just right: 82</td>
<td>not long enough: 3</td>
<td>no answer: 5</td>
<td></td>
</tr>
</tbody>
</table>

rately record the number of bends required to break the paper clip. There was no way to verify that the correct number of bends was reported or that the correct counting technique was used. These issues and differences in bending technique were cited by the students as possible reasons for the variance in the reported number of bends required to break the paper clips, especially the outliers (Figure 2). Other identified possible contributors to the distribution of results included variation in the manufacturing of the paper clips and the effect of warming the clip by holding it before bending. A discussion of outliers and their impact on the median, mean and confidence intervals followed these observations. These data were calculated with and without some of the outlying findings to illustrate the influence of outliers.

7. When presented with the results, the students quickly noticed that there was an unequal distribution of men and women in the two groups. Group A (small) had almost equal representation of men and women while in group B (large) women outnumbered men 2 to 1. This pattern existed in both of the classes in which the simulated clinical trial was conducted and led to discussions of how random assignment does not always assure equal distribution of potentially important characteristics in the resulting groups. A statistical analysis did not detect any gender influence on the number of bends needed to break the paper clips.

8. The designers of the study did not perform a power analysis or otherwise try to determine how many subjects would be needed to show meaningful results nor were meaningful results ever defined. This led to a review of sample size selection as well as type 1 and type 2 errors and the impact of sample size on each. It was pointed out that the bio-medical literature provides no paper clip data that could have been used in the construction of a power analysis. The investigators admitted to not having extensively reviewed the business literature.

9. No economic analysis was presented. While it took more bends to break the large paper clips, it could be less expensive to supply workers with a larger number of small paper clips. The costs per bend were calculated and the small paper clips turned out to be more economical if one assumes that the number of bends is the important determinant of stress relief.

As noted, the students were able to detect the major problems including those of study design (e.g., outcome measurement not directly related to the rationale for the experiment), conduct of the study (e.g., lack of blinding, adherence to protocol, data collection methodology), and interpretation of the study results (e.g., differences between treatment group demographic characteristics, generalizability of the findings). Also discussed were several positive attributes of the study (e.g., randomization, clear demonstration of the proper paper clip bending technique). Critical assessment items not identified by the students included unaccounted factors that might have affected the results, statistical significance vs. clinical significance of the results, potential impact of the eligible subjects who did not participate, and appropriateness of the statistical analysis. Since this course was the curriculum's introduction to study design and critique, it is likely that the students were only prepared to identify the major faults of the clinical trial. If this simulation was conducted later, following the research methods course, it is likely that a more sophisticated critique of the study would have occurred.

In general, the exercise was well received by the 104 students who completed and submitted evaluation forms (Table II). The simulation appeared to succeed as an educational technique, and the students expressed a desire for more simulation experiences. However, it didn't reach the instructor's expectations as a method to stimulate student desire to learn about study design. It is possible that the students' limited exposure...
to clinical trials and other published studies at this early point in the curriculum affected their ability to appreciate the applicability of the simulation to the practice environment.

CONCLUSION

Student participation in a simulated clinical trial was a well received way to illustrate the complexity of investigating a simple problem through a clinical trial study design. It also provided the students with an opportunity to gain insight into what it means to be an investigator or a study subject in a clinical trial in a time-efficient and low-risk manner. The students were able to correctly identify many of the limitations of the study protocol and their observations provided an opportunity for the instructor to reinforce and expand upon information previously presented in a lecture format without being unnecessarily repetitive. Pharmacy faculty should consider incorporating simulations in the curriculum wherever possible to supplement traditional instruction.

Acknowledgements. The authors thank Marc Bulterys MD for his translation of reference 4 and Betty Skipper PhD for her assistance with statistical analysis.

References

(2) Center for Evidence-Based Medicine, "Levels of Evidence and Grades of Recommendations," http://cebm.jr2.ox.ac.uk/docs/levels.html (January 2002).

APPENDIX. CONSENT FORM

Title of Study. The Effect of Wire Diameter on the Resistance of Paper Clips to Breaking from Repeated Bending.

Principal Investigator. William G. Troutman, PharmD

Purpose of Study. This study is designed to determine if paper clips made from thick wire are harder to break than paper clips made from thin wire. Breaking paper clips is thought to be a major source of tension relief for people in many office settings and a stronger paper clip might reduce office expenses.

Procedures. By consenting to be in this study, I agree to bend a metal paper clip back and forth in accordance with instructions I will be given. I will accurately record the number of bends required to break my paper clip. I understand that the procedure will be conducted during one regularly scheduled lecture period.

Risks, Stresses, and Benefits. I understand that there are some potential risks and discomforts that may occur as a result of participating in this study. They have been thoroughly explained to me and include:

a. Bending my paper clip might leave little red marks on my fingers. These red marks are not life-threatening and should go away after a few minutes.

b. Bending the paper clip may accidentally result in the puncture of my skin when the two pieces break apart.

c. A piece of my paper clip might fly off and put out my eye.

I am unlikely to receive any benefit from participation in this study nor will I receive any monetary compensation for participation. I will be permitted to keep my paper clip after the conclusion of the study. I might gain an appreciation of the difficulty associated with conducting a simple clinical trial.

Alternatives to Participation. The alternative is to not participate. My identity will be kept confidential, however, the U.S. Occupational Safety and Health Administration may review study records that may include identifying information. Records of this study will be kept until (date).

I may ask questions about this study. I can reach Dr. Troutman at (505) 277-4261 during business hours. Dr. Troutman can be reached through the New Mexico Poison and Drug Information Center at (505) 843-2551 at other times.

My participation is voluntary. I may refuse to take part or stop taking part in this research at any time without penalty or loss of educational benefits to which I am otherwise entitled. The investigators have the right to terminate my participation in the study at any time if they feel that it is not in my best interest or if I do not follow instructions. I understand that if I volunteer for this study I do not have to pay for the paper clip or any of the other equipment used in the study.

I understand that by signing this paper, I am not giving up my legal rights. State of New Mexico laws exist that may help people who think they have been treated carelessly, but which require very prompt notice of any claims. For information, write or call the Risk Management Office of the University of New Mexico Health Sciences Center, Albuquerque, New Mexico, 87131; telephone (505) 277-6638.

Printed Name of Participant

________________________

Signature of Participant

________________________

Date

Witness of Participant

________________________

Date

Age in Years

________________________

Gender: female () male ()

Clip groups: A () B ()

Numbers of bends

________________________