Open Access Journal of Clinical Trials

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COMMENTARY

The Kindergarten Clinical Trial

This article was published in the following Dove Press journal:
Open Access Journal of Clinical Trials
25 November 2009
Number of times this article has been viewed

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Abstract: The author describes an imaginary clinical trial performed using her daughter's kindergarten class in Arlington, Massachusetts as study subjects. The children are introduced to several age-appropriate concepts related to clinical trials including defining a study question and randomization. Basic concepts in clinical trials are introduced, the Kindergarten Clinical Trial is described, and possible additional activities with kindergarteners and older children are discussed.

Keywords: clinical trial, role-play, elementary school

Introduction

We finally arrived in the public schools this past year with my oldest daughter Serena entering kindergarten. When her teacher asked for parent volunteers to come into the classroom and talk about their work, Serena immediately tried to recruit me. "My mom is a biostatistician!" she told her teacher with pride. Considering many adults have never heard of biostatistics, I wondered, how I could relate our profession to a bunch of 5- and 6-year-old kids? The vast majority of my teaching experience has been with graduate students. I knew much of what I did in the classroom would not transfer to Mrs Langley's kindergarten class. Based on my limited experience with this age group, I knew I had to do something which allowed the kids to move and also talk as much as possible. Of all the courses that I have taught at the Boston University School of Public Health, the Design and Conduct of Clinical Trials seemed to have concepts that were most accessible to individuals of all ages and backgrounds. I decided to simulate a clinical trial, with the kindergarteners serving as study subjects. I'll first describe some basic concepts in clinical trials and which I chose to include in the imaginary trial. I'll then describe the clinical trial and finally, discuss what concepts could have been further explored with this age group, and which concepts may be appropriate for older students.

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Clinical trials basics

Clinical trials are the subject of numerous courses and text books covering a wide range of topics. Here, I introduce some of the basic concepts that would be covered in any introductory text or course. For further information the reader may wish to consult a text on the fundamentals of clinical trials[1] or the Food and Drug Administration (FDA) website.[2]

A clinical trial can be defined as a prospective study comparing the effect or value of intervention(s) against a control in human beings. For a clinical trial to occur, there should be "clinical equipoise", or genuine uncertainty as to the benefits or harm from an intervention among the expert medical community.[1] The most fundamental, but often one of the hardest steps in designing a clinical trial is determining the question to be answered. A study question can be posed by defining the four concepts of PICO, or the population of interest, the intervention to be tested, an appropriate control or comparison group, and the outcome by which the effect of the intervention can be assessed.

A very common clinical trial design is the parallel group, randomized, double blind, placebo-controlled intervention study. A parallel group design is one in which study subjects are allocated to different groups and stay in those groups for the duration of the study. While there are numerous other study designs, this is most popular. Randomization is the allocation of subjects to treatment group using some chance mechanism. This is often done using a computer, but can also be done by simply flipping a coin. Blinding in a clinical trial is a method by which the treatment assignment is kept masked from the study subjects, investigators or other individuals involved in the study to avoid potential bias. A double-blind study generally means that both the study subjects and investigators are unaware of treatment assignments. Blinding is often performed by using a placebo, or inactive substance given to the control group. For example, in a drug intervention study, a placebo may be a pill made to look and taste like the drug, but that contains no active compounds.

Any introduction to clinical trials should also include some discussion of ethics. While ethics in clinical trials can be a stand alone topic for a course or text, a good starting place is the three Belmont principles[3] of respect for persons, beneficence, and justice. Part of the mandate of respect for persons requires that potential study subjects are allowed to make their own decisions. An important concept is that of informed consent in which potential study subjects must voluntarily agree to be in a research study after having received all relevant information about that study and have shown that they understand what will happen and all possible risks involved. The second principle, beneficence basically means to do no harm. The third principle, justice refers to distributive or social justice rather than procedural justice. Here the idea is that people are treated fairly and that there is a fair sharing of the burdens of research among those who will benefit from it.

For our imaginary study I decided to do a parallel group, randomized, controlled study examining a new mystery cold medication. The kindergarten students would serve as study subjects with some randomized to the new medication and the others randomized to a control group that does not receive the medication.

The kindergarten clinical trial

When the day of my visit arrived, I knew I had a hard act to follow. Serena's classmate Robert had his dad come in the week before. Robert's father was a police detective and he had brought in an explosive detecting (and yet cute and cuddly) dog and his police cruiser. How could I compete with that? I was determined to try.

I started by asking the kids if they had ever done an experiment. Hands flew in the air. What type of experiments? It turns out all of them have been involved in prior research and really, really wanted to tell me about it. It turns out that science had not been neglected in their preschool experience. I explained that a clinical trial was an experiment on humans (also called people*).* Next I asked if anyone had ever had a cold. Everyone admitted to this except for one very lucky little boy. I then asked them to pretend that they had a cold. What were their symptoms? Much dramatic sneezing and coughing ensued. Serena helpfully ran for the tissue box. I then asked if any of them had ever taken medicine when they had a cold and most had. We then talked about how you know if medicine works or not. I then explained the clinical trial. We were going to find out if a mysterious cold medication "worked" or not in getting rid of their colds. Some of the kids were going to get the cold medicine and some were not, and we would see who felt better. Next, we discussed how we could decide in a fair way, which kids got the medicine. Serena handed out a quarter to each of the kids (and the two teachers) and I explained that if they flipped the coin and got a head they would get the medicine and if they got a tail they would not. Next we discussed what would happen when we flipped the coins. I asked the class for ideas. One little boy said that he thought that everyone would get "heads". One girl sat thinking and then said that she thought that half the kids would get "heads" and half would get "tails". A future statistician! We then set about flipping the coins. Everyone flipped and then stood in the heads or tails group. The first time there were 13 heads and 11 tails. I asked the kids if they thought they would end up in the same group if we flipped the coins again. Most decided that they would not. On the second flip the probability gods smiled upon us and we had 12 heads and 12 tails. Serena and I handed out

the imaginary medicine to the 12 kids in the "heads" group. But how to decide who got better? After quickly surveying the group, I decided that anyone wearing the color red was going to feel "better". The dramatic sneezing and coughing started to subside. There were seven kids in the medicine group and six kids in the other group that felt "better". I then asked the class how we could tell if the medicine worked. One of the kids immediately said that since more kids in the medicine group felt better, it showed that the medicine worked. Of course, this difference certainly could have been due to chance alone if the medicine really did nothing. Still, I was pleased that the class seemed to have a preliminary understanding of comparing outcomes between the groups.

Discussion

Our "Kindergarten Clinical Trial" had a lot of elements that were age appropriate including imaginary play, game playing (ie, flipping coins), discussing fairness and some discussion of health. It was also a fun way to introduce some real concepts in clinical trials. These include:

1. Defining your study question using PICO. Population: kindergarteners with colds. Intervention: new mystery cold medication. Control: no medication. Outcome: Feeling "better". The general question was then "Does the new mystery cold medication help kindergarteners with colds to feel "better" compared to kindergartens who did not get the new medicine?
2. Concepts of justice (one of the Belmont principles): What is a fair way to allocate kids to the two treatment groups?
3. Concepts of randomization and probability: How many kids will end up in each group if we flip a coin? Would you end up in the same group if you flip the coin again?
4. Concepts of evaluation: How do we know if the medicine worked?

The time allotted to my visit to the kindergarten was approximately 45 minutes, certainly long enough for the attention spans of 5–6-year-old children. However, if we had more time, or multiple sessions I could have covered the concepts that I did introduce in more depth. Specifically, we could have come up with a more clearly defined outcome instead of feeling "better". This outcome would be considered unacceptable in a real trial because it's not clear what "better" actually means. Kindergarteners could have a discussion of what it means to feel better: Is your nose stuffy? Are you still sneezing? Are you tired? They may also have some understanding of a subjective versus objective outcome. For example, asking someone how they are feeling is a completely subjective outcome. Counting the number of times they sneeze is an objective measure. We could have also discussed whether the outcome should be compared to how they felt at the beginning of the study (ie, baseline) or whether we could just consider how they felt at the end of the study. Kindergarteners may also have some understanding of a categorical outcome such as whether they feel "better", yes or no, versus a measurable response such as the number of sneezes during the past hour. One possible outcome for this age group may be an assessment where children are shown drawings of faces which range from very sad to very happy, and are asked how they are feeling.

We could have discussed why we needed a control group at all in our study. This would involve asking the children whether they were likely to get better even without taking any medication. Did any of the children in the control group get "better"? Why did they get "better"? What if the kids in the medicine group got "better"? How could we know if this was because of the medicine or because the kids were getting "better" anyway?

Concepts of randomization and probability also could have been further explored. In simple randomization (flipping a coin is an example of this) how much of an imbalance could have been observed in the number of children in the two groups? The first time the children flipped the coins we saw a minor imbalance (13 versus 11), but a much larger imbalance could have occurred. We could have flipped the coins many times and drawn a histogram (graph) of the number of heads that occurred. This type of graph had already been introduced as part of the kindergarten curriculum. We also could have discussed whether we might want to know if the medicine worked differently for girls and boys. How could we make sure that both girls and boys were randomized to the medicine group? To introduce the concept of "stratified randomization" I could have divided the children into groups by gender, and discussed how we could make sure, in a fair way, that there were both boys and girls in the medicine group.

Concepts of evaluation also could have been elaborated. What if the same number of people felt better? What if one more child in the medicine group felt better, as we observed? Could this have happened even if the medicine didn't work at all? With slightly older children we could have calculated the percentage in each group that felt better. How far apart do the percentages need to be for us to believe that the medicine really does work? I also could have introduced the concepts of null and alternative hypotheses, ie, there is no difference between groups versus there is a difference

between groups. For much older children basic statistical methods could be introduced. Note that in this example where we had two groups with a categorical yes or no outcome a chi-squared test or Fisher's exact test may be the appropriate method of analysis. For more details the reader may wish to consult an introductory biostatistics text.[4,5]

Older kids could be introduced to a wide variety of topics that would have been difficult for a kindergarten-age group. These topics include more information on defining and measuring outcomes, the choice of an appropriate control group, blinding and placebos, alternative study designs, the process of informed consent, basic methods in biostatistics and concepts related to power and sample size. For example, when choosing a control, it is appropriate to randomized to no medicine if there are other medicines currently available? This is both a scientific and ethical question related to the second Belmont principle, beneficence. Older children could also discuss why informed consent is important and perhaps do a mock informed consent process.

As my daughter gets older, I'd like to repeat this clinical trial. I was quite impressed by this group of 5- and 6-year-old children. I can't even imagine what they will be ready to learn by the time they are in high school.

How my visit compared to a police dog and cruiser, I'm not sure, but I think the kids had a lot of fun and even managed to learn something. What was the highlight for me? Hearing over 20 kindergarten voices shout out "clinical trial!" when I asked them what you call an experiment on humans. What was the highlight for them? Probably getting to keep the quarters!

Acknowledgments

The author has no conflict of interest or financial disclosures to report.

References

1. Friedman LM, Furberg C, Demets DL. *Fundamentals of Clinical Trials*. New York, NY: Springer-Verlag; 1998.
2. US Department of Health and Human Services, Food and Drug Administration. Available from: http://www.fda.gov/. Accessed September 1, 2009.
3. US Department of Health, Education and Welfare. *The Belmont Report: Ethical Guidelines for the Protection of Human Subjects*. Washington, DC: Department of Health, Education and Welfare; 1979.
4. Pagano M, Gauveau K. *Principles of Biostatistics*. Boston, MA: Duxbury Press; 2000.
5. Rosner B. *Fundamentals of Biostatistics*. Boston, MA: Duxbury Press; 2005.