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Using Statistics to Explore Attitudes Towards Gene-Editing

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Rationale

This unit plan is intended to prepare AP Statistics students in the New Haven Public Schools district for the rigorous free response section of the AP Statistics exam. This section of the exam consists of six open-ended questions that require students to interpret statistical results clearly and accurately in the context of data. Many students enrolled in AP Statistics at the school where I teach struggle to communicate statistical results in a coherent manner and use statistical vocabulary in an appropriate context. This might be because historically, students have not had as much experience writing in mathematics courses as they have had in other core academic courses. Regardless of the reason, students have to overcome obstacles related to writing in order to pass the AP Statistics exam. At this stage in their academic careers, students begin to express concerns about how they will pay for higher education. Students who will be dependent on merit-based financial aid could potentially have their financial burdens eased by performing well on the exam. If a student scores a 3 or higher on the AP Statistics exam, one could potentially receive college course credit, avoid excessive tuition fees, increase one's chances of being admitted to a university, or be eligible for college scholarships.

The free response questions on the AP exam typically prompt students to use statistical results to defend arguments. For instance, on the 2015 AP exam, students were given two boxplots summarizing sample employee salary data from two different accounting firms, Corporation A and Corporation B. Students had to imagine that both corporations offered them a job for $36,000 a year as an entry-level accountant. Students then had to use the information in the boxplots to justify why they would accept a job at either corporation. This problem generated a lot of discourse when presented to my students as a warm-up prior to their AP exam. Students came up with their own unique reasons why Corporation A or Corporation B would be a more enticing option, backing up their claims with measures such as the range, lower quartile, mean, median, or maximum salary of an individual working for each corporation.

This problem resonates with all students, including those who demonstrate lower levels of engagement with topic information through poor attendance in class or a low level of self-efficacy in mathematics. The reason for this resonance is due to the topic's real-world relevance. Deciding whether the financial benefits of one job opportunity outweigh those of another is a task many individuals will inevitably encounter. The problem was also met with satisfaction by the students because it allowed them to perform a task similar to that of a professional statistician. Professional statisticians often use data to inform decisions that impact the lives of others. The final reason the AP practice problem hooked all students into the lesson for that day was because they were able to exercise creativity when formulating their responses. The problem had more than one possible answer, so it alerted students to the idea that data can have multiple interpretations or can even be used to benefit a particular perspective, agenda or party.

Many students dislike mathematics because they believe that their success in the subject is solely contingent upon correct execution of procedures and formulas. Students who have difficulty memorizing algorithms or arithmetic facts tend to perform poorly on mathematics assessments. Teachers exert little to no control over how much studying students do for tests or quizzes when they are at home. However, teachers can provide students with in-class experiences that increase their retention of skills and concepts. Implementing a curriculum unit that encompasses the positive components of the AP Statistics practice problem (real-world relevance and opportunities for student choice) can help teachers achieve this goal. Individuals selectively remember experiences that they find meaningful. With this in mind, a teacher can present statistical concepts in a meaningful way by having students learn about them in the context of issues that have consequences for everyone. This interdisciplinary curriculum unit will allow students to apply statistical concepts to understand attitudes towards the controversial practice of gene-editing using CRISPR-Cas9 technology. By the end of the unit, it is expected that students will demonstrate mastery of the following AP Statistics curriculum objectives:

- Use an appropriate random sampling method to select participants for a survey.
- Design a survey that contains non-biased questions.
- Describe the shape, center, and spread of a univariate data distribution.
- Use a contingency table to calculate conditional probabilities.
- Use a contingency table to determine whether an association exists between two variables of interest.
- Calculate and interpret a confidence interval for a true population proportion in the context of real-world data.
- Conduct a hypothesis test to determine how closely a sample statistic estimates a population parameter.

This curriculum unit is also intended to build community within a school. The lessons contain activities meant to foster connections between students who might not have previously interacted. Moreover, students will have opportunities to share newly-acquired knowledge about gene-editing with their peers.

Content and Background Information

Before attempting the tasks that comprise this curriculum unit, AP Statistics students must develop a solid understanding of CRISPR-Cas9 technology and its versatile applications. The information below will be considered the basis for this understanding.

What is CRISPR?

The discovery of CRISPR took place in 1987 when Japanese molecular biologist Yoshizumi Ishino and his fellow scientists at Osaka University studied a gene belonging to Escherichia coli (commonly known as E. coli), a microorganism that is found in the intestines of mammals. The scientists noticed that the gene exhibited a striking pattern consisting of five short repeating DNA segments followed by short nonrepeating DNA sequences they called spacers. By the late 1990s, similar patterns were discovered in other prokaryotes. In 2002, this pattern was assigned the acronym CRISPR, which stands for Clustered Regularly Interspaced Short Palindromic Repeats, by a team of scientists at Utrecht University in The Netherlands. It was not until 2007 that food scientists researching Streptococcal bacteria highlighted the importance of the CRISPR sequences. These sequences play a crucial role in the immune systems of bacteria.1 Bacteria must defend against viruses by generating enzymes. After these enzymes eliminate the viruses, other proteins store remnants of the virus's genetic code in the spacer DNA. The bacteria uses this genetic code in order to prevent future viruses from invading. In the event of a new viral infection, the bacteria releases Cas9 enzymes, which store the genetic code. The Cas9 enzymes can then detect whether or not the virus' RNA is complementary to the stored genetic code. If the RNA matches the stored genetic code, then the Cas9 enzymes destroy the virus by dissembling the DNA.[2] In 2012, a major breakthrough occurred when scientists found that they could manipulate the Cas9 enzyme by injecting it with preconstructed RNA. When fed this fake RNA, the Cas9 enzyme sought out matching genetic codes and cut them. After conducting experiments with test tube molecules, Jennifer Doudna, Emmanuelle Charpentier, and Martin Jinek, discovered that Cas9 enzyme could be used to splice any DNA sequence at the location of one's choice. A system known as CRISPR-Cas9 has been developed to execute this task.[3]

The CRISPR-Cas9 system is comprised of two molecules, the Cas9 protein and a guide RNA (gRNA). The gRNA is constructed by the scientists in advance and consists of about twenty nitrogenous base pairs. The gRNA is responsible for leading the Cas9 protein to the target location of the DNA. Since the gRNA has bases that complement the nitrogenous bases of the target DNA sequence, it attaches to the target DNA. The Cas9 protein acts like scissors and cuts out the target DNA. The cell containing the DNA then recognizes that the DNA has been spliced and uses its natural mechanisms to repair the cuts or accept a more desirable DNA sequence. CRISPR is preferred to other methods of gene-editing because it produces the Cas9 protein, and it has the ability to edit multiple genes simultaneously. Some alternatives require scientists to design an enzyme to splice the DNA at a target location.[4]

Health Conditions Being Addressed By CRISPR-Cas9 Technology

Researchers are currently using CRISPR-Cas9 to cure a number of diseases that are monogenic, meaning that they stem from a mutation in only one gene. Among these diseases is Huntington's Disease, which causes neurons in the brain to degenerate. The list of conditions that can develop as a result of nerve cell degeneration is incredibly long. Those who suffer from Huntington's disease are at an increased risk for obsessive compulsive disorder, depression, anxiety, and suicide.[5] They experience muscle problems that can interfere with their ability to communicate, swallow, or move their eyes. They also might lack skills that are necessary to thrive in an academic or work environment such as organization, emotional regulation, self-awareness, self-control, memorization, and perceptiveness. Children of a parent diagnosed with Huntington's Disease are at a 50% risk of inheriting the disease.[6]   Xiao-Jiang Li, a scientist at Emory University in Georgia, used CRISPR-Cas9 to eradicate defective huntingtin protein in the mutated genes of mice.[7]

Another disease sweeping the CRISPR-Cas9 scene is sickle cell anemia, which occurs when one has an excess of abnormally-shaped red blood cells (sickle cells, which deviate from the circular shape of normal red blood cells) that restrict the flow of blood and oxygen. On average, red blood cells live for about four months, but sickle cells typically do not live longer than a month. The shortage of red blood cells in one's body can result in fatigue, abdominal or chest pain, jaundice, retinal damage, and a risk of stroke. A lack of functioning red blood cells can impact the immune system's ability to defend the body against viruses. Sickle cell anemia is caused by a mutation in the ß-globin gene, which prevents the body from producing enough hemoglobin. Hemoglobin is the compound that enables blood cells to transfer oxygen from the lungs to other parts of the body.[8] A treatment called CTX001 has successfully eliminated sickle cell anemia in laboratory mice. CTX001 is a therapy that involves the use of CRISPR-Cas9 to modify the ß-globin gene to increase production of hemoglobin.[9] If CTX001 proves to be effective in humans, then this could provide a solution to the treatment shortage for sickle cell anemia. CRISPR-Cas9 is increasingly viewed as a potential therapy for sickle cell patients because, right now, the only ways for a patient to battle sickle anemia are to receive a blood transfusion or bone marrow transplant.[10] However, transplants are not widely or readily available.

The number of people presently awaiting an organ transplant in the United States exceeds 113,000. According to the Health Resources and Services Administration, twenty individuals in need of a transplant die every day.[11] For the past few years, xenotransplantation, the process of giving animal organs to humans, has been contemplated as a solution to the human donor shortage problem. Specifically, scientists have been studying the possibility of transplanting pig organs into humans because pigs reproduce in large numbers.[12] Unfortunately, the human body is extremely resistant to pig organs, and as a result, might be susceptible to the porcine endogenous retrovirus (PERV). Geneticists at a company called eGenesis were able to deactivate the PERV in a sample of pig embryos. These embryos were subsequently implanted into female pigs, whose offspring did not inherit the virus.[13]

Use of CRISPR to Improve Crops

CRISPR is currently being used to improve the quality of agricultural produce. Bacterial spot disease is a condition affecting the marketability of tomatoes. Tomatoes infected with bacterial spot disease have unattractive brown spots surrounded by yellow or white rings on their fruits and stems.[14] Scientists are using CRISPR to produce tomatoes that are resistant to bacterial spot disease and contain larger amounts of Vitamin C.[15] In Brazil and Ireland, scientists are utilizing CRISPR to produce a variety of tomato infused with the capsaicin gene, which gives peppers their spicy taste. A naturally spicy tomato could replace the need for chili peppers in salsa, since chili peppers are not as abundant.[16]

Another disease that is interfering with the ability of companies to sell their produce is citrus greening disease, which is caused by a flying insect called the Asian citrus psyllid. In fact, in 2017, Florida suffered from a 75% decline in its production of oranges as a result of the disease.[17] Although citrus greening disease does not harm humans or animals in any way, it causes trees to grow fruits that are malformed, tart, green, and smaller in size than fruits of unaffected trees. The disease also shortens the lifespans of most fruit trees and causes them to display fewer leaves.[18] The United States Department of Agriculture has allocated almost 500 million dollars towards eliminating the disease so that the citrus industry of Florida can thrive again.[19] Recovering the orange crop has been challenging, particularly because citrus trees take three to five years before they bear fruit. CRISPR has provided a solution to the problem of citrus greening. In 2014, scientists from the University of Florida Institute of Food and Agricultural Sciences Citrus Research and Education Center announced that they were able to use CRISPR-Cas9 to modify the citrus genome and make it resistant to citrus greening.[20]

Tropic Biosciences, a United Kingdom-based organization, has utilized CRISPR to successfully produce naturally decaffeinated coffee beans. The most effective method of decaffeinating coffee beans necessitates moistening the beans in water before transferring them to a stainless steel extractor. Liquid carbon dioxide is then dispersed over the bean at a high pressure to dissolve the caffeine molecules. The carbon dioxide is essential for preserving the flavor notes in the beans. The carbon dioxide is then transferred to another vessel called an absorption chamber, where it is converted to a gas. In turn, the caffeine is solidified and collected and the beans are roasted.[21] CRISPR-Cas9 might eliminate the need for this expensive and time-consuming process and increase the production of decaffeinated coffee worldwide. At present, only twelve percent of the world's coffee is decaffeinated.[22]

The cacao tree, an evergreen cultivated in tropical rainforests, is the source of pod-shaped fruits containing cocoa beans. Unfortunately, fungi thrive in tropical environments, too, and climate change is contributing to their presence. At least a fifth of cocoa pods worldwide are deemed unusable before they are harvested for chocolate production because they have been infected by fungal diseases. The majority of the affected cacao trees are in West Africa, which accounts for 68% of the world's cocoa production. The most common condition infecting the cacao tree is black pod rot, which is caused by the fungus Phytophthora and results in brown spots on the tree's fruit. This fungus tends to appear during the rainy season, when excess moisture impacts the soil acidity necessary for the cacao tree to survive. Controlling the spread of black pod infection currently involves spraying the trees with copper-based fungicides, but these chemicals might no longer be necessary.[23] It has been discovered that the gene TcNPR3 plays a key role in helping the tree defend against Phytophthora.[24] Researchers at Pennsylvania State University have theorized that deleting this gene using CRISPR-Cas9 will allow the cacao tree to resist pod rot. They are in the process of growing trees to investigate the accuracy of their hypothesis.

Individuals who suffer from celiac disease do not respond well to gluten, a protein found in wheat and barley. An estimated 2.5 million Americans with the autoimmune disease have not been formally diagnosed and risk damaging the lining of their small intestine if they consume foods rich in gluten. Those diagnosed with celiac disease are four times as likely as their counterparts to suffer from bowel cancer and are more vulnerable to coronary artery disease. If patients do not follow a gluten-free diet, they put themselves at risk for conditions such as osteoporosis, Type I diabetes, infertility, vitamin deficiencies, lactose intolerance, epilepsy, and multiple sclerosis.[25] Food scientists are utilizing CRISPR-Cas9 to produce varieties of wheat that contain smaller amounts of gluten. Researchers in the Netherlands and in the United Kingdom are going as far as to use CRISPR-Cas9 to get rid of epitopes from gluten proteins that are responsible for immunoreactivity.[26]

Use of CRISPR-Cas9 to Generate Biofuels

According to the Department of Energy, fossil fuels including oil, natural gas, and coal accounted for 80% of energy consumption in the United States in 2017.[27] Coal mining can pollute rivers and lakes with acidic water containing large amounts of arsenic, copper, and lead.[28] Oil spills can contaminate water in oceans, destroying animal and plant species. Acidic water can deplete the ocean's supply of calcium carbonate, a substance that crustaceans and other marine creatures depend on to grow their shells.[29] Fossil fuel emissions contribute immensely to global warming because they release gases like carbon dioxide that trap heat in Earth's atmosphere when burned. The environmental problems caused by fossil fuels have incited a pressing need for renewable energy sources such as biofuels. During photosynthesis, algae such as kelp and cyanobacteria have the ability to convert carbon dioxide and sunlight to energy and store the energy as oil.[30] The number of algae strains exceeds 100,000, which makes it an enticing alternative to fossil fuels.[31] The use of algae as a renewable energy source has been slowed by the limited production of lipids in several strains. A team of researchers from the company Synthetic Genomics have employed CRISPR-Cas9 to develop a strain of algae “that produces twice as much lipid as its wild parent.”[32]

In addition to generating biofuels, CRISPR-Cas9 might make traditional plastic use a thing of the past. Traditional plastic is a polymer synthesized from fossil fuels. Its durable, odorless, bendable, lightweight, recyclable nature makes it convenient for a number of purposes including storing food and building car parts. Of the 448 million tons of plastic produced annually, two-fifths are used as packaging material meant to be trashed soon after procurement.[33] The United Nations reports that “79 percent of waste generated from plastic accumulates in landfills or in the environment, while only 9 percent is recycled and 12 percent is incinerated.”[34] When plastic use increases, the environmental repercussions can be severe. First off, before plastics are manufactured, chemicals are added to their efficiency. Among these chemicals are phosphates and asbestos fibers, which make the plastics heat and flame-resistant; colorants made of iron oxide, titanium dioxide, or cadmium; and lead compounds intended to stabilize polymers. These chemicals can seep out of the plastic and enter water and the human body if it appears in food sources.[35] Secondly, plastic is non-biodegradable, so it does not decay naturally. Instead, it just disintegrates into microplastics that are harming oceans and their ecosystems. In 2018, microplastics were detected in 93 percent of bottled water samples from several nations including the United States. Each year, 100,000 marine animals die from plastic consumption, as their stomach bacteria cannot break up the material into smaller units during digestion.[36]

Several individuals and organizations have been working to resolve the problems fueled by plastic. Dutch inventor and founder of The Ocean Cleanup Boyen Slat fundraised over 30 million dollars to establish an ocean clean-up system for removing plastic debris from the Pacific Ocean, which he is testing in San Francisco. The Coca-Cola company is aiding in the effort to reduce plastic waste worldwide by switching to recyclable, compostable packaging by 2030.[37] Scientists are dependent upon production of monomers called omega-hydroxy fatty acids for bioplastics. A team of researchers from the Polytechnic Institute of New York University, led by Dr. Richard Gross, have found a way to produce omega-hydroxy fatty acids using Candida tropicalis yeast. This yeast has the ability to yield large supplies of omega-hydroxy fatty acids by transforming fatty acids of plant oils. Once these fatty acids are combined into a single molecule, the result is a biodegradable plastic that is useful for packing materials. Gross is hopeful that once this polymer is broken down, it can even function as a biofuel for military vehicles.[38] With the knowledge that yeast can maximize output of omega-hydroxy fatty acids, lab scientists might be able to use CRISPR-Cas9 to isolate the gene responsible for production of these monomers.

Cons of CRISPR-Cas9 Technology

Although CRISPR-Cas9 has several applications that could revolutionize the food and medical industries, it is a relatively new technology, so we really do not know much about how it will affect future generations. Individuals who do not support the use of CRISPR-Cas9 for gene-editing are concerned about “off-target effects” that might result when the Cas9 enzyme snips the wrong part of the genome. Since similar nitrogenous base sequences can be found within one’s DNA, it is possible for the Cas9 enzyme to travel to the incorrect site. Even if the enzyme correctly identifies the target site, the long-term consequences of editing the genome are unknown. Chinese researcher He Jiankui made the news in 2018 for using CRISPR-Cas9 technology to remove the CCR5 gene from the embryos of twin girls and implant the modified embryos into their mother. He removed the gene to fulfill the wishes of their father, who did not want his daughters to suffer the way he did from HIV.[39] Jiankui’s work was regarded as highly unethical by critics for a number of reasons. In order to circumvent policies banning HIV-infected individuals from using assisted reproductive technologies, he substituted normal blood samples for infected blood samples. Moreover, he “forged ethics review documents during recruitment of participants."[40] He did not consider other functions of the CCR5 gene that are perhaps essential to one's well-being. Although the CCR5 gene encodes a protein that is not resistant to HIV, it might play a role in protecting individuals against other infections including the West Nile Virus.[41] Therefore, if one or both of the twins contracts the West Nile Virus due to complications from his experiment, he can be held liable and imprisoned for a maximum of ten years.[42]

Not only might CRISPR-Cas9 allow scientists edit a human's genome to reduce the risk of developing a fatal illness, but it might give parents the option of choosing which physical features they want their children to possess. If individuals utilize CRISPR-Cas9 technology for superficial reasons such as editing the genes of an embryo to give a newborn a certain eye color, hair color, or skin color, then this might fuel another eugenics movement. Eugenics is the breeding of individuals with desirable characteristics and was promoted by Adolf Hitler during World War 2 in order to create a superior Aryan race. By implementing a marriage loan program that allowed Aryan couples to avoid paying a quarter of the loan amount for each child they had together, the Nazis convinced Aryan couples to have more children. While this benefitted Aryan couples, many groups of people were negatively impacted by the eugenics movement. Individuals who were not of the Aryan race, blind, hearing-impaired, epileptic, manic-depressive, or schizophrenic were subject to sterilization laws. The Law for the Prevention of Hereditarily Diseased Offspring, enacted in 1934, led to sterilization of 300,000 to 400,000 individuals via vasectomy or ovarian tubal ligation. In 1939, Hitler introduced a law enabling doctors to kill patients who were psychologically ill and did not respond to treatment. He argued that asylum patients were an economic burden to society, so the Nazis used carbon monoxide gas chambers and lethal injections to kill them.[43] Hitler's quest to create his ideal race continued as Jews were placed into concentration camps. Josef Mengele, a doctor at Auschwitz, supervised experiments during which harmful chemicals were used to try to change the eye colors of camp prisoners to blue.[44] If genetic editing of human embryos using CRISPR-Cas9 becomes more prevalent, then parents who decide to use the technology might select physical traits for their children in accordance with the social groups that are the most advantaged. For example, research has shown that height and income are positively correlated. Data from one study showed that an individual (male or female) with a height of six feet is "predicted to earn nearly $166,000 more over the course of a 30-year career than someone who clocks in at 5 feet 5 inches."[45] Furthermore, "nearly all Fortune 500 CEOs are over six-foot two-inches tall, even though people over six-foot-two make up only 3.9% of the world's population."[46] Consequently, parents might have their children's genes edited so that they grow up to be tall. If using gene-editing to equip a child with specific physical traits becomes a common practice among parents, this might create an insensitive society that does not embrace or tolerate diversity.

The economic implications of using CRISPR-Cas9 to edit the human genome might also be severe. Even though CRISPR-Cas9 is considered to be less expensive than alternatives, costs to edit genes using the technology are still high. At the Harvard University Stem Cell Institute, it costs $19,100 to alter one nucleotide base pair (referred to a single-point mutation) in a DNA strand.[47] This is roughly thirty percent of the median annual household income in the United States. At the Yale University Genome Editing Center, the same process costs $15,000 plus up to $2,000 for genotyping.[48] Therefore, if individuals want to use the technology, they will have to pay an amount that is at least twenty-five percent of the United States median household income. This means that at present, only the wealthiest individuals can afford to take advantage of CRISPR-Cas9 technology.

Among the groups of people who might receive an unfair advantage as a result of CRISPR-Cas9 are athletes. In 2007, Lee Sweeney, a physiologist at the University of Pennsylvania, was able to extract IGF-1, a gene that strengthens muscles. He injected mice, which he nicknamed "Schwarzenegger mice" with IGF-1 and found that their endurance level far exceeded that of mice in a control group. Mice in the treatment group were quicker runners than mice in the control group and did not experience weight gain even after consuming foods high in fat. Professional athletes seeking a boost in strength and energy contacted Sweeney after learning that he bred the Schwarzenegger mice. Once he became aware that athletes could use his innovation in an attempt to defeat competitors in sporting events (a practice known as gene-doping), Sweeney joined the World Anti-Doping Agency. This establishment prohibited the use of genetic modifications to enhance an individual's athletic performance. In the past, professional athletes have undergone injections of erythropoietin (EPO), a protein that stimulates production of red blood cells, to increase their energy supply. Blood and urine tests can now confirm the presence of excess EPO in an athlete's system. CRISPR-Cas9, on the other hand, might make it possible for athletes to get away with gene-doping since their DNA would naturally contain excess EPO.[49]

A Need for Clear Regulation of CRISPR-Cas9 Technology

It is very difficult to predict the consequences that CRISPR-Cas9 has for society, particularly when there are very few written laws regulating the use of CRISPR-Cas9 technology. Under the Consolidated Appropriations Act, the United States Congress has banned allocation of Food and Drug Administration (FDA) funds towards germline editing, or modifying the genes of an embryo. However, federal funds can be used for editing of somatic cells (cells other than reproductive cells). The reason for this difference is attributed to the fact that edits made to somatic cells cannot be transferred to subsequent generations. Even though the government has placed restrictions on funding, federal law does not explicitly ban gene-editing of an embryo.[50]

Where Do Adults in the United States Stand on the Gene-Editing Front?

The Pew Research Center conducted a poll in 2018 to determine how adults in the United States feel regarding various aspects of gene-editing technology. According to the poll, 72% of adults believe that it is okay to alter a baby's genome to treat a congenital illness, while 27% feel that doing so would be a misuse of medical technology. Only 33% of American adults expressed support for gene-editing when informed that development of gene-editing technology would require scientists to perform tests on human embryos. Respondents in the sample who identified as "highly religious," meaning they participate in religious services at least once a week and pray at least once a day, expressed more skepticism towards gene-editing. When the Pew Research data scientists broke down the data by religious affiliation, they discovered that the group with the largest percentage of respondents (88%) in opposition to embryonic testing consisted of white evangelical Christians. This might be in part to the fact that the Bible affirms that God is the ultimate creator. Therefore, it is possible that these voters believe that changing the genes of an individual would be usurping God's power. The largest group in favor of using embryonic testing to speed up the development of gene-editing technology consists of Atheists (79%).

Generally speaking, American adults remain concerned about the potentially negative consequences of gene-editing technology. A majority (58%) anticipate that the technology will exacerbate the issue of income inequality since it will only be accessible to the most affluent individuals. Moreover, 54% of American adults believe that unethical use of the technology is an inevitability. Only 18% of respondents expressed confidence that gene-editing technology would lead to positive developments. 62% of adults are not convinced that medical researchers have a keen awareness of the positive and negative consequences of altering a baby's genome.[51]

The Pew Research Center's statistics give us a rough idea of how adults are responding to the prospect of gene-editing. Still, how teenagers within various demographics feel about the possibility remains a mystery and is important to investigate, considering CRISPR-Cas9 technology might be more advanced and widespread by the time they enter the workforce. It is my hope that as students complete the activities in this unit plan, they will uncover this mystery. As they learn about the potential benefits and drawbacks of CRISPR-Cas9 technology previously described and explore the variation in attitudes towards gene-editing through peer-to-peer interactions, they will discover that regulating the use of this technology is a cumbersome process. When the world consists of people who have such different life experiences, goals, and perspectives, it can be difficult to come to a consensus on a lot of issues facing humanity. In the real world, problems do not always have concrete or unique solutions. Individuals might have to think outside the box, and students should be given opportunities to perform mathematical tasks that reflect this reality.

Lesson Plans

Lesson 1: Planning Surveys and Using Random Sampling Methods to Select Participants

After being introduced to background information about CRISPR-Cas9, AP Statistics students can brainstorm in small groups the potential advantages and disadvantages of the technology. Each group will then share its ideas with the rest of the class, and the teacher can provide supplemental information about current applications of the technology. After the “share aloud,” students will formulate a series of questions related to gene-editing that they would like to ask their peers. These questions will be used for surveys that they will later execute to learn more about public perceptions of gene-editing technology. Below are examples of questions students might ask their peers after exposing them to the idea that CRISPR-Cas9 technology is used to edit the DNA of humans, animals, or plants.

- Do you believe that the Food and Drug Administration should allocate funds towards germline-editing?
- What is the single most important reason gene-editing should be utilized?
- Is it ethical to use gene-editing to give a child desirable physical characteristics?
- Would you utilize CRISPR-Cas9 technology if it would reduce your child’s risk of a terminal illness?
- Do you believe that widespread use of gene-editing technology would lead to a greater degree of income inequality?
- What is your biggest concern regarding widespread use of CRISPR-Cas9 technology?

It is important for students to understand that administering surveys and recruiting participants are not easy tasks. Asking students a question such as, “If an individual calls you with a request to complete a survey, how do you feel?” will help them consider the struggles faced by telephone pollsters or market researchers. Students will likely offer a variety of responses including “like hanging up,” “aggravated,” “annoyed,” “impatient,” “important,” “excited,” or “it depends on what the survey is about.” Teachers can then segue into a discussion about the potential problems with survey data.

Administering a survey is not only difficult because of the potential for nonresponse, but because the results must be representative of the population. Teachers can emphasize this point by presenting students with the following case study: The *Literary Digest* was a popular magazine in the 1930s. In 1936, Republican governor Alfred Landon ran against Democrat Franklin Delano Roosevelt for President of the United States. In an article in the *Literary Digest*, it was predicted that Landon would receive the majority of votes (57%). However, Roosevelt was the candidate who actually won the election with 62% of the vote. Landon received only 38%, which is quite far from the predicted percentage. The *Literary Digest* had a reputation for predicting election results accurately since 1916, so why was the magazine's prediction incorrect for this particular presidential election?

Again, students will come up with a variety of responses. Students who remember the Law of Large Numbers might guess that the predictions were based on data from very few surveys. Although this is a reasonable educated guess, it is surprisingly incorrect since 2.4 million individuals participated in the poll. Interestingly enough, the Gallup Poll correctly predicted that Roosevelt would win the election by administering surveys to a relatively smaller sample. The results of the magazine's survey can be attributed to the issue of sampling bias. The names of survey respondents were taken from telephone directories, club membership lists, or magazine subscriber lists, which consisted of mostly upper class voters. On top of this, the polls were conducted by telephone. During the Great Depression, when the unemployment rate reached twenty-five percent, owning a phone was not as common among the public as it is today.[52]

How do we get survey data that is representative of the entire population? We must use random sampling to select survey respondents. There are six different sampling methods to which AP Statistics students should be introduced, four of which are random sampling techniques. Simple random sampling involves assigning numbers to individuals and then selecting them at random for inclusion in a survey by drawing numbers (i.e. from a hat, using a random number generator, or using a table of random digits). Stratified random sampling involves splitting a population into smaller groups and selecting individuals randomly from each group. Systematic random sampling involves selecting every nth individual from a list or every nth individual that enters a location. Finally, cluster sampling involves splitting a population into groups, selecting a few groups at random, and surveying every individual in the selected groups. When one uses convenience sampling, one is simply selecting survey participants who are easy to access. Voluntary response sampling is a method that is unreliable because only individuals who are interested in the survey topic might choose to participate, which can skew the results.

Once students familiarize themselves with the various sampling methods, they will use the random sampling method of their choice to select participants for their surveys. They will describe, using detailed written language, how they will utilize this sampling method to select at least 30 survey participants. For instance, a student who chooses systematic random sampling might decide to administer a survey to every 10th person who enters the school cafeteria on a given day. A student who decides to incorporate stratified random sampling might split the school population up by grade level and select 10 students from each grade at random (using numbered lists of students). It is worth noting that it might be difficult for students to use a simple random sampling method to conduct their surveys. It is expected that they will be surveying their schoolmates and might face obstacles such as students who are absent or students who refuse to cooperate. This is why the AP Statistics students will need to write about any foreseeable obstacles in the process of selecting respondents and discuss how they plan to address these challenges.

Lesson 2: Minimizing Response Bias

Once students have chosen their sampling methods, they will be need to finalize the questions for inclusion in their surveys. Their surveys should include a demographic questionnaire, so that students can study how specific populations feel about various aspects of gene-editing technology. The wording of a survey question can significantly impact how the question is answered by the respondent. To illustrate this, teachers can display an example of a biased survey question on the board such as, "According to one political website, 55%

of Americans disapprove of the job Donald Trump is doing as President. Do you approve or disapprove of the job Donald Trump is doing as President?" Then, students should evaluate whether asking this question to respondents will encourage honest answers. At first glance, this question might not seem biased because survey respondents are not explicitly told how to feel about Donald Trump. However, an individual who is politically apathetic might be encouraged to side with the majority of voters. Students must make sure that their survey questions are phrased in a neutral manner to eliminate this response bias. Once they have proofread and designed their surveys, they can distribute the questionnaires to the individuals in their samples.

Lesson 3: Using Contingency Tables to Calculate Conditional Probabilities

Once students have the results of their surveys, they will need to organize them into contingency tables, also referred to as two-way tables, according to some demographic variable. Examples of demographic variables include gender, race, income, and political party. Students will then use their contingency tables to determine whether an association exists between two variables of interest. There exists an association between two variables "if knowing the value of one variable helps us predict the value of the other."[53]   Imagine that a student has asked survey respondents the question, "Do you believe it is ethical to use CRISPR-Cas9 technology to make a baby more intelligent?" Suppose further that the student has separated the responses to the question by gender. Then, the student can use a table, such as the hypothetical one below, to summarize the counts of male and female students who responded in a specific way.

	Male Students	Female Students	Total
Yes	37	17	54
No	13	33	46
Total	50	50	100

Students will be required to use their contingency tables to determine the marginal and conditional distributions of specific variables. For instance, if a student is asked to determine the marginal distribution of opinion, the student will need to divide each row total by the table total and convert the resulting value to a percentage. 54% of individuals (54/100) surveyed believe that it is ethical to use gene-editing technology to make a baby more intelligent, while 46% of respondents (46/100) believe it is unethical. When one determines the conditional distribution of a variable, one must only take into account respondents who fall into a particular category. Suppose one is prompted to determine the conditional distribution of opinion among females, one must compute the percent of females who responded in each way. That is, 34% of female respondents (17/50) believe that using gene-editing technology to increase a baby's intelligence level is ethical, while 66% (33/50) feel it is unethical. However, the table tells us that 74% of males (37/50) consider utilizing gene-editing technology to heighten intelligence to be ethical, while 26% (13/50) do not. Since there is a clear difference in how males and female respondents answered the survey question, we can conclude that an association exists between gender and opinion. Students can use a relative frequency bar chart to illustrate this association.

If students are further along in an AP Statistics course, they can use a more advanced tool called a chi-square test to see whether the two categorical variables are associated. The chi-square testing procedure will be explained in detail in Lesson 5. It is worth pointing out to students that if there exists an association between two variables, this does not imply that one variable causes the other. In this particular example, we cannot conclude that one's response to the survey question is a direct result of one's gender. There are other factors, called confounding variables, that might contribute to an individual's viewpoint.

On the AP Statistics exam, students might encounter a problem that requires them to calculate a conditional probability without a contingency table. Answering such a question involves memorization of a conditional probability formula $P(B|A)\ =\frac{P(A\ and\ B)}{P(A)}$. This formula looks daunting to memorize, but students can use their contingency tables to derive it. The notation P(B|A) is used to denote the probability that an event B occurs given that a different event A has already taken place. Before deriving the conditional probability formula, students need to define events A and B. Suppose we let B denote the event that a respondent believes gene-editing to make a baby more intelligent is ethical, and we let A represent the event that a respondent is male. Then, P(B|A) in this case would be defined as the probability that a respondent has responded “yes” to the survey question given that the respondent is male. We saw earlier that we can easily compute this probability by dividing the total number of males who answered “yes” by the total number of male respondents. P(B|A) could have also been calculated by dividing the probability of being male and responding yes (37/100) by the probability a respondent is male (50/100). In both cases, one will notice that the resulting value is .74, or 74%.

Lesson 4: Calculating Confidence Intervals

Surveying every single high school student in the United States is neither convenient nor feasible. However, students can make predictions about how teenagers feel about gene-editing technology based on sample data. All they need to know is how to calculate a C% confidence interval for a population proportion. Suppose a student finds that 52% of 100 high school peers surveyed believe that widespread use of gene-editing technology would exacerbate the issue of income inequality. Students might be able to calculate and interpret a 95% confidence interval for the true proportion of high schoolers who believe widespread use of gene-editing would exacerbate income inequality. However, three conditions must be verified to ensure that the sampling distribution of the sample proportion, $\hat{p}$, is normal. If even one of these conditions fails, then the formula for a 95% confidence interval cannot be applied.

- The data must come from a random sample. (Each student is required to use a random sampling method to select survey participants, so we will assume this holds true.)
- The sample size, n, must be less than or equal to 10% of the population size. (We can assume that there are more than 1000 individuals in the population.)
- Both $n\hat{p}$ and n(1 - $\hat{p}$) must be at least 10. [($100 \times .52$) and ($100 \times .48$) are both greater than 10.]

Since all three criteria are met, we can proceed to calculate our 95% confidence interval. The formula for conducting a 95% confidence interval for a proportion is $\hat{p}\ \pm\ z\ast\ \sqrt{\frac{\hat{p}(1-\hat{p})}{n}}$. In this formula, z* represents the critical value for the standard normal curve with C% of its area between -z* and z*. From a z-score table, one can see that the central 95% of the normal distribution lies between -1.96 and 1.96. The critical value is always the positive value of these two cut-off points, so z* will be 1.96 for this example. Plugging in .52 for p-hat and 100 for n will yield a confidence interval of (.42208, .61792). This interval tells us that we can be 95% confident that 42.208% to 61.792% of all high schoolers in the United States believe that widespread use of gene-editing will worsen income inequality.

Lesson 5: Conducting Tests of Significance

Significance tests (also called hypothesis tests) are used to determine whether a claim about a population parameter can be refuted. Suppose a statistician claims that there is no significant difference in the proportions of female and male teenagers who support the use of CRISPR-Cas9 for germline editing. However, suppose evidence from a student’s survey (which was conducted using a simple random sample) shows us that 58% of 50 female teenagers are supporters compared with 42% of 50 males. These statistics might give reason to wonder whether the statistician's claim is false. To conduct a hypothesis test, one must first state the null and alternative hypotheses. Our null hypothesis, which is a statement of "no difference," would be that true difference between the proportions of males and females who are supporters is 0. Our alternative hypothesis is a statement that contradicts the null hypothesis in some way. In this case, the alternative hypothesis would be that this difference of proportions is not equal to 0.

The Z-test for a Difference of Proportions

To decide whether there is evidence in support of the alternative hypothesis, we must execute a significance test called a z-test for a difference of proportions. This test requires computing a statistic called a z-score, which can be used to determine a p-value. However, similar to the confidence interval, a z-test for a difference of proportions can only be executed if three conditions are met. The conditions are similar to those that should be satisfied for conducting a confidence interval for a population proportion. The only difference is that in order to conduct a z-test for a difference of proportions, the conditions must apply to both samples. Was the data taken from a random sample? Yes. Are both samples less than or equal to 10% of their respective populations? Yes. There are far more than 500 teenage males and 500 teenage females in the population. Are the counts of successes and failures for each sample greater than or equal to 10? Yes. The number of female teenagers who support germline editing is 29, and the count of male teenagers who support germline editing is 21. These values are reversed when one takes into consideration the counts of male and female teenagers who are against germline editing.

A z-test statistic for a difference of proportions can be calculated using the formula $\frac{(\widehat{p_1}-{\hat{p}}_2)}{\sqrt{\frac{{\hat{p}}_C\left(1-{\hat{p}}_C\right)}{n_1}+\frac{{\hat{p}}_C\left(1-{\hat{p}}_C\right)}{n_2}}}$. $\widehat{p_1}$ represents the proportion of female teenagers in the sample who support the use of CRISPR-Cas9 for germline editing, .58. $\widehat{p_2}$ is the proportion of male teenagers in the sample who are supporters, .42. The $\widehat{p_C}$ in the denominator of the formula can be obtained by dividing the count of successes in both samples combined by the count of individuals in both samples combined. In this example, "success" is defined as supporting utilization of CRISPR-Cas9 for germline editing. $\widehat{p_C}$ is equal to $\frac{29+21}{50+50}\ $ or equivalently .5. Plugging in our values for $\widehat{p_1}$, $\widehat{p_2}$, and $\widehat{p_C}$, we get a z-score of 1.6. This represents the number of standard deviations the difference of the sample proportions is from the claimed difference of zero.

Knowing the z-score enables us to determine the p-value, a probability that will help us judge whether a sample result is statistically significant. A statistically significant result is an observed effect so large that it cannot be attributed to chance. Statisticians consider a result to be statistically significant if the p-value is less than a pre-specified value called an alpha level. An alpha level is the probability of rejecting the null hypothesis when it is true. If the p-value is greater than or equal to the alpha level, then we do not have enough evidence to reject the null hypothesis. If the p-value is less than the alpha level, then we can reject the null hypothesis in favor of the alternative hypothesis and conclude that our sample result is statistically significant.

The p-value can be found using a z-score table. The table gives us the area under the normal curve to the left of our obtained z-score. However, recall that the alternative hypothesis states that there is a difference in the proportions of supporters in both samples. This difference could be positive or negative, making the significance test "two-tailed." As a result, we should subtract the area that corresponds to a z-score of 1.6

from 1 and double it to get the p-value. Following this procedure, we will obtain a p-value of .1096. This p-value is greater than our designated alpha level of .05. This indicates that we should fail-to-reject the null hypothesis that there is no difference in the true proportions of female and male teenagers who support the use CRISPR-Cas9 for germline editing. We use the phrase “fail-to-reject the null hypothesis” instead of “accept the null hypothesis” because the alpha-level of .05 indicates that we are conducting the hypothesis test with only 95% confidence. That is, we can be 95% confident that the sample difference in proportions is not statistically significant.

The Chi-Square Test for Independence

Another type of significance test students can execute, referenced earlier in this document, is a chi-square test for independence. In a chi-square test, the null hypothesis states that there does not exist an association between two variables of interest. The alternative hypothesis states that there is an association between two variables of interest. We can revisit the fictional table of observed counts from Lesson 3 to provide an example that students can reference before conducting their own tests. Recall that this data organizes the responses of students who answered the question, “Do you believe it is ethical to use CRISPR-Cas9 technology to make a baby more intelligent?” by gender.

	Male Students	Female Students	Total
Yes	37	17	54
No	13	33	46
Total	50	50	100

Before running a chi-square test, it is necessary to make a table of expected counts. An expected count can be computed using the following formula: \(\).

	Male Students	Female Students	Total
Yes	27	27	54
No	23	23	46
Total	50	50	100

Before executing a chi-square test for independence, students must check that three conditions hold true. The data has to come from an independent random sample (which should be the case, since students are required to choose survey participants using one of the approved sampling methods). Secondly, their sample size must be less than or equal to ten percent of the population size. Again, this should hold true since students are required to use at least 30 people in their samples, and this is obviously less than or equal to one-tenth of the population size. Finally, all expected counts must be 5 or greater. All three of these criteria are met for our fictional table. Therefore, a chi-square test statistic can be calculated using the formula $\mathrm{\Sigma}\frac{(Observed\ -Expected)^2}{Expected\ }$.

The corresponding p-value can be estimated using a Chi-Square Distribution Critical Values Table, which requires one to know the degrees of freedom (the product of one less than the number of contingency table rows and one less than the number of contingency table columns). The problem with this method is that it can be tedious to calculate the chi-square statistic by hand, and the critical values table only gives us the range of probabilities containing the p-value. Luckily, students can use the TI-84 Plus graphing calculator to quickly compute the chi-square test statistic and retrieve a more precise p-value. The steps are as follows:

- Press [2nd] [MATRIX].
- Scroll right to the EDIT heading and select option 1: [A]
- Make sure you edit a 2 x 2 matrix since there are two categories for gender and two for response. List the observed counts in the order that they appear in the table.
- Press [2nd] [MATRIX] once you are done inputting the counts, scroll right to the EDIT heading, and select option 2: [B].
- Again, make sure you edit a 2 x 2 matrix. This time, enter the values from the expected counts table.
- Press [STAT] and scroll right to the TESTS heading. Select option C and press [ENTER].
- You will be prompted to enter the matrices you used to store the observed and expected counts. To select matrix A for the observed counts table, press [2nd] [MATRIX] [1], and [ENTER]. To select matrix B for the expected counts table, press [2nd] [MATRIX] [2], and [ENTER].
- Scroll down to Calculate and press [ENTER] to get both the chi-square statistic and p-value.

Following these steps, one will notice that the p-value that corresponds to the chi-square statistic of 16.10 is .00006. This extremely small value tells us to reject the null hypothesis. The p-value provides evidence there is an association between gender and opinion regarding the ethicality of using CRISPR-Cas9 to increase a baby's intelligence level.

Execution of Significance Test to Draw Conclusions About Survey Data

The survey project will include a component that has students executing the appropriate significance test of their choice. To successfully complete this task, students must write a typed report that includes responses to the following prompts.

- Which type of significance test did you execute? Why was this the appropriate significance test for your data?
- What is the alpha-level you will be comparing with your p-value?
- Clearly describe the null and alternative hypotheses in the context of their survey data.
- Provide evidence that the conditions for conducting their chosen significance test hold true.
- Calculate the test statistic, showing all work or listing the graphing calculator commands they used.
- Determine the p-value that corresponds to the test-statistic. Interpret the p-value in the context of the data. That is, what should we conclude about the null and alternative hypotheses based on this value?

Once students are finished gathering, organizing, and analyzing their survey data using the aforementioned statistical methods, they will assume the role of a politician. They will write a speech about how they plan to regulate the use of CRISPR-Cas9 technology. When writing their speeches, they must use statistical evidence or survey data to justify implementation of proposed policies. For instance, a student might find that a large number of survey respondents believe gene-editing should be used to help individuals combat life-threatening illnesses, but it should not be used to change an individual's appearance. As a result, the student might choose to institute a law that bans the use of CRISPR-Cas9 for non-medical purposes.

Final Remarks

This AP Statistics curriculum unit is meant to engage students by giving them autonomy in the learning process. It provides teachers with an effective method of assessment because students will have to complete writing tasks that are specific to their unique survey data sets. The lessons embedded in the unit are not meant to be implemented in succession, since they encompass concepts introduced at different points in the school year. I strongly encourage teachers to combine the lesson tasks to create a cumulative final project to be administered during the weeks leading up to the AP Statistics exam. This ensures that students will have practice applying a number of statistical procedures covered during the course and enter the exam room feeling more prepared.

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Additional Reading Materials

The statistical resources below contain thorough, real-world examples of problems that students can reference while completing the unit plan tasks. Teachers can assign homework problems from these textbooks so that students can practice identifying random sampling methods, computing conditional probabilities, and executing statistical inference procedures.

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Implementing District Standards

The Common Core State Standards addressed in this unit are listed below.

CCSS.MATH.CONTENT.HSS.IC.A.1 Understand statistics as a process for making inferences about population parameters based on a random sample from that population.

CCSS.MATH.CONTENT.HSS.IC.B.4 Use data from a sample survey to estimate a population mean or proportion.

In this unit, AP Statistics students will use an appropriate random sampling method to select participants for a survey regarding gene-editing technology. Using confidence intervals, students will estimate the proportion of individuals in the population who feel a specific way about an aspect of the technology. By conducting hypothesis tests such as the z-test for a difference of proportions or chi-square test of independence, students will determine whether their survey sample statistics are significantly different from population parameters.

CCSS.MATH.CONTENT.HSS.ID.B.5 Summarize categorical data for two categories in two-way frequency tables. Interpret relative frequencies in the context of the data (including joint, marginal, and conditional relative frequencies). Recognize possible associations and trends in the data.

CCSS.MATH.CONTENT.HSS.CP.A.4 Construct and interpret two-way frequency tables of data when two categories are associated with each object being classified. Use the two-way table as a sample space to decide if events are independent and to approximate conditional probabilities.

Students will meet the above two standards by organizing their survey data into two-way frequency tables. By creating these contingency tables, students will be able to compute conditional probabilities to determine whether one's opinion regarding an aspect of gene-editing is associated with a specific demographic variable.