Biostatistics - Dr. Patrick
BMEN 350; Section 201
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Project 6

A. Read and Reflect

The maintenance of ethics in biostatistics is paramount to the protection of the safety and well-being of the general public. I say this because there have been instances of data fraud and doctoring of scientific results for the purposes of satisfying some ulterior motive in medical device companies and similar engineering companies. The ulterior motive usually being financial gain. Actions such as doctoring scientific results and data fraud have potential to harm the public as falsified performance results of drugs or medical devices can cause harm to the public. Individuals may believe that a purchased drug or device will provide care, when instead the drug or device actually does not have any of the desired effects, or worse, the drug or device has adverse effects. Of course, maintaining ethics in biostatistics goes far beyond just preventing data fraud and doctoring results, ethical standards must be enforced all throughout the research process. In the following paragraphs, I will explore some applications of ethics in biostatistics as it relates to industry and research.

The publication called "Data fraud in clinical trials" by Dr. George and Dr. Buyse clearly outlines common unethical biostatistics practices when putting a drug or medical device through a clinical trial. Dr. George and Dr. Buyse clearly state in their publication that "research misconduct means fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results". As a biomedical engineer, this information is indeed valuable to me. I say this because if I am working in a med-tech start up where resources and funding are limited, I must be vigilant of any instances of falsification, fabrication, or plagiarism. Acts of fabrication, falsification, or plagiarism as they pertain to research may occur in some med-tech startups as resources and funding are limited, and scientifically devious acts may be done in order to raise funds. Being a part of a startup that engages in such unethical behavior can taint the reputation of a biomedical engineer for years. In a general sense, this information is indeed essential for me. I say this because I work in an undergraduate research lab and the principal investigator often enlists me to perform literature studies on anti-head and neck cancer drug studies. I must ensure that I refrain from plagiarizing from these studies when I am reporting their findings for a literature review. I plan on continuing to be vigilant of unethical research practices in internships with startups as well as in my own research projects.

I mentioned above that some med-tech startups may engage in unethical research practices such as fabrication and falsification of data as well as plagiarism in order to increase investments and funding. One such example of this is the case of the med-tech startup Theranos, led by CEO Elizabeth Holmes. Holmes was poised to create a device called the "Edison", and it would serve to dramatically reduce the amount of blood required in

order to administer a blood test. Traditionally, blood tests have been conducted by first drawing blood intravenously. Holmes' device would only require a small pin prick of blood, and this pin prick would then be analyzed for diseases and ailments. This idea was indeed very revolutionary in the early days of Theranos, so much so that the startup was valued at USD 9 Billion by the year 2014. After that however, a series of investigations and exposures displayed that Theranos was barely putting the "Edison" device to use when testing blood samples. Theranos was mostly using the traditional methods to test blood samples. It was also uncovered that Holmes had doctored performance results of the "Edison" device so as to make it appear that the device was capable. According to the "Declaration on Professional Ethics" by the International Statistics Institute Council, Holmes' actions would certainly be in violation of shared professional value number three. Shared professional value number three of the "Declaration on Professional Ethics", supports truthfulness and integrity. By doctoring performance results of the "Edison" blood testing device, Holmes violated this professional value. In addition, according to the "Ethical Guidelines for Statistical Practice" approved by the American Statistical Association, Holmes' actions would be in violation of clause B. This is because clause B of the "Ethical Guidelines for Statistical Practice", supports integrity of data and methods. Holmes' actions as seen above certainly did not uphold clause B.

Last but not least, more and more engineers are finding employment in software intensive industries. The industry of data analytics and data science are examples. Engineers in these fields have to develop cutting-edge software to analyze and interpret large volumes of data. These engineers must ensure that their methods of acquiring, analyzing, and protecting data are ethical. The fifth fundamental canon of the NSPE Code of Ethics for Engineers clearly says to avoid deceptive acts. Therefore, acquiring data through deceptive means, or failing to protect data would violate this fundamental canon. This can be applied to biostatistics in med-tech startups as well. Biostatistics or bioengineers in such startups must adhere to the fundamental canons of the NSPE code of ethics, especially the first one which states that engineers must hold paramount the safety, health, and welfare of the public. There are some med-tech startups that create software to accurately read EKG plots. The biostatisticians and bioengineers behind the programming of such software must indeed hold paramount the safety, health, and welfare of the public when designing such impactful technologies.

In the above few paragraphs, some of the applications of ethics in biostatistics were discussed. I am indeed grateful for the existence of organizations such as the International Statistics Institute Council and the American Statistical Association for their input on the ethical collection of data and ethical conduction of research. I firmly believe that biostatisticians and bioengineers who uphold ethical data collecting and ethical research practices, are protecting the health and wellbeing of the general public.

B. Problem 1

The following criteria were entered into ClinicalTrials.gov. Breast Cancer Stage IV was entered for condition or disease, Herceptin (trastuzumab), Perjeta (pertuzumab) was entered for other terms, and Germany was entered for country. The following study was found based on these criteria. The clinical trial identifier or NCT number is NCT02344472. The estimated enrollment of the study is 270 participants. The estimated study completion date is June 2023 (estimated primary completion date is September 2021). If the female patient has had 4 chemotherapy regimens, the female patient is not eligible to be included in the study. This is because it is clearly stated in the inclusion criteria that the female patient should have "No more than two prior chemotherapies for metastatic disease". A female patient who has undergone 4 chemotherapy regimens has exceeded the maximum number of chemotherapies (two) in order to be considered eligible for this study. A female patient who is 56 years old is certainly eligible to be included in the study as the inclusion criteria states that the age of the participant must be greater than or equal to 18 years. The primary outcome that will be measured is the number is the number of participants with adverse events within the time frame of 3-9 weeks. The principal investigator is Dr. Jens Huober, MD PhD.

C. Problem 2

Upon entering the provided field values into ClinicalTrials.gov, approximately 4300 studies were returned. One study was chosen, its clinical trial identifier was NCT05096845. This study was selected because it was relevant with current events, as many companies are competing to obtain a dominant share in the vaccine market for a vaccine against Covid-19 virus. This study is a phase III interventional study, and it has an active recruitment status. The estimated enrollment of this study is 22,500 participants. The primary outcome measure of this study the efficacy, safety, and immunogenicity of a recombinant SARS-Cov-2 Fusion Protein Vaccine (also called V-01) in adults aged 18 years and older. Another primary outcome measure of this study is the incidence of adverse events of this Fusion Protein vaccine (V-01). The participant recruiting for this study occurs in multiple cities across the Philippines (Lipa City, Iloilo City, Makati City, Manila, and Quezon City). This study is funded by Livzon Pharmaceutical Group. I did see one inclusion criteria that could be perceived as unusual. This was inclusion criteria number 4. This inclusion criteria states that males of reproductive potential and females of child-bearing potential should agree to take effective contraceptive methods for 12 months after signing their consent form to enter the study. I thought this was a bit out of place because I honestly don't see how controlling for sexual protection has anything to do with the primary outcome measures listed above. Perhaps it is present as inclusion criteria because contracting a sexually transmitted disease may worsen the effects of Covid-19 virus and may this reduce the immunogenicity of the SARS-Cov-2 Fusion Protein Vaccine. Therefore, it is in the best interests of the organizers of the study to ensure that the participants do not contract any sexually transmitted

diseases for up to 12 months after they have signed their consent form. There wasn't quite anything published from the phase II trial from the principal investigator or the sponsor (Livzon Pharmaceutical Group).

D. Appendix

Links for resources used:

- Elizabeth Holmes case: https://money.yahoo.com/timeline-events-leading-trial-theranos-154234101.html?guccounter=1&guce_referrer=aHR0cHM6Ly93d3cuZ29vZ2xlLmNvbS8&guce_referrer_sig=AQAAAK7ODJqyQaVo4dq7lTxkQZlB1749gfp7Quf_8SOhLDKgmnXnBkzFy3kyFqKBgddDJowubidUTSX4aaYIqGzk9k0WxnSDQ2NH84Lw6Acd8lR_vxZVqizeEoxNVOajAsaVi4euJx1XbBBiyAzlZF9GYRx4Hyj1ERWkynKJ7CpH2m9k
- Problem 1 link: https://clinicaltrials.gov/ct2/show/NCT02344472?term=Herceptin+%28trastuzumab%29%2C+Perjeta+%28pertuzumab%29&cond=Breast+Cancer+Stage+IV&cntry=DE&draw=2&rank=1
- Problem 2 link: https://clinicaltrials.gov/ct2/show/NCT05096845?term=phase+III&recrs=a&type=Intr&phase=2&draw=2&rank=8