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W241 - Essay 2

Effects of Emergen-C

There are hundreds if not thousands of theories about the human body and its immune system's functionality outside of modern medicine that to this day have not been scientifically proven. At times, it can be overwhelming to decide how to take care of your body, whether it be a new fad diet, good old fashioned exercise, body hacking through the use of supplements, chiropractors, acupuncture, etc. Within this space, our study will focus on helping answer the question of whether taking high dose vitamins have a positive outcome on a person's overall health. Due to loose regulations by the FDA surrounding supplements, high dose vitamin consumption has not had the benefit of being rigorously tested in randomized controlled clinical trials the way allopathic medicines have. For many supplements such as high dose vitamins, it is still not known what their true benefits are aside from some anecdotal evidence. We will work to answer one small part of this larger question.

Emergen-C is an orange colored and flavored powder that contains 1000mg of vitamin C. The study will answer the research question:

> "How does taking high-dose Vitamin C (Emergen-C) effect duration and severity of the common cold and the flu?

The study will randomly sort subjects in a 1:1 ratio into treatment or control groups using R. In an ideal experiment, each subject would receive a placebo in the form of a generic orange powder distributed to them by the researchers, mix it into a cup of water each morning, and consume it without knowing whether they are in the treatment or control group. Those in the treatment would have been administered Emergen-C and those in the control an orange flavored powder just containing a little sugar and flavoring to match the taste of Emergen-C. This would allow the set-up of a blind study and help control for the placebo effect since both the control and treatment groups would think they are consuming Emergen-C each morning. Unfortunately, due to the logistical and financial constraints of this study, we will only be able to ask the treatment group to take Emergen-C while the control group will ingest nothing special and will be asked not to take any Vitamin C supplement. As an additional restriction due to lack of funding, the treatment group will be instructed to only take Emergen-C on days where they feel they may either be getting ill, have symptoms of seasonal illness, or be recovering from the cold or flu. This will help cut down the cost of Emergen-C as it will not need to be ingested each morning by the entire treatment groups.

Blocking may be utilized to reduce noise created by certain variation amongst participants and help increase the statistical power of the results since the experiment participation is expected to be 100 subjects. If our study had the funding and resources to do so, we would have a much larger cohort (order of magnitude of +10,000 subjects) to allow randomization to mitigate natural variation amongst participants. Since we do not possess the resources to do a larger study, we will use blocking to group participants by age and gender. Participants from each subgroup will be randomized into the control and treatment groups, which will help reduce natural variance in the case where women and men or those at different ages react differently to the treatment of Emergen-C or are prone to get sick more or less often. This will additionally address the differing effectiveness of Emergen-C on males vs females and people in varying age groups.

Subjects will be selected through a voluntary sign-up process with the goal of 100 subjects in total. We will attempt to reach out to a diverse set of subjects so that inferences based on the results can be generalized to the population as much as possible. Realistically due to resource constraints, we will mainly utilize the Berkeley Slack groups, our facebook network, and our personal networks. We understand that this will restrict any significant results we find to apply only to the demographics of the participants involved. Additionally, we know that some voluntary bias will occur since we will gather a subsection of our network by asking for voluntary sign up. This may cause bias by selecting only those who have the time to participate or who themselves are interested to find out the answer to our research question. To help boost sign-ups, we will raffle off a few small prizes to those who sign up. I believe this will be the most effective way to motivate participation without coercing those who may have otherwise not participated in this study.

Participants will be kept anonymous to maintain independence. Our goal here is to prevent a participant from discussing the study with any other participant. There are covariates which we will not be able to control for in a study of this size, such as exercise, sleep, blood pressure, and exposure to sickness (working in a hospital, doctors office, or with children). If we had resources to run a larger scale study, these attributes could be controlled for through the use of blocking.

The outcome measure will be the number of days and the severity of illness during our study's timeframe. Each morning, we will ask participants to fill out a short google survey answering a few brief questions. We will ask them if they have taken Emergen-C that day and how sick they feel on a scale of 0-5, with 0 being completely

healthy. We will provide details about what 0-5 are intended to mean to standardize participant feedback. For example, a 1 could be mild effects such as a runny nose or a light cough while a 5 could be a fever (+102), headache, congestion, etc. We want to be sure to ask how sick participants are feeling so that we can quantify the treatment effect and to measure whether Emergen-C reduces the severity of illness regardless of its effect on duration. Gathering data each day will allow us to mitigate the risk of hindsight bias, where participants recall whether or not they were sick and fill out their results delayed at the end of the study, and non-compliance, where participants defect and do not fill the form for some days. We will diligently follow up with subjects if we do not receive their data after each morning. At the end of the study, we will compare the total number of sick days and the average rating (0-5) between the control and treatment groups to calculate the Average Treatment Effect.

The study will last approximately 1 month during the months of October and November. Since this is early in the Fall season, we anticipate that seasonal allergies will minimally affect our participants since these are potential false positives for sick days recorded. Additionally, the beginning of the flu and cold seasons will help increase the potential total number of sick days for our participants, which we hope will increase the magnitude of effect of the treatment.

After data has been collected, we will utilize inferential statistics to capture the statistical significance of the findings. We will compare both the total number of days as well as the average severity of illness (rated by users daily, 0-5) between the treatment and control groups. We will use a p-value of .05 to determine if our findings are statistically significant, and will use our intuition to verify the practical significance.

One of the main constraints of this study will be its total cost. A 10-pack of Emergen-C currently costs approximately $5. Using a rough assumption that each participant in the treatment group uses up to 10 packets over the course of the study, it will cost about $250 to purchase the necessary Emergen-C to distribute to the treatment group participants. If we ask treatment participants to consume it each day as is instructed on the package, this cost will surge to about $600. We will additionally need about $100 to purchase incentive prizes to raffle off to those who participate in this study.

Our study will need to be prepared for non-compliance during its course. In addition to the incentive prizes for sign up, we will also raffle off one prize at the end of the study and add 1 ticket for each participant each day they submit the google form on time. We anticipate that subjects in the treatment group may forget to take Emergen-C during their sick days, or that some may forget to record which days they are sick. Both of

these will skew our results. As previously mentioned, we will follow-up each afternoon with any participants that fail to fill out their google form. The form setup will also allow us to ask a user in the treatment group to take Emergen-C if they are sick and marked that they did not consume it that morning.

The goal of the study is to help provide more definitive proof and one of the many unanswered questions surrounding the effectiveness of supplements in healthcare. If our study is successful and shows that Emergen-C reduces the severity or duration of illness, we may prompt a larger scale study by a pharmaceutical company. Supplements have the potential to join allopathy and help us live longer healthier lives, but until they are studied more rigorously through randomized controlled trials, we will only be able to guess how effective they truly are.