**Total 32 points (4+4+2+6+2+2+4+6+2)**

**Submission Guidelines:** Please submit this part in PDF format such that it is named as your roll number. Please make sure that it is clear which question and which part are you answering.

We learnt about RCTs in the lecture, but we didn't get to details of conducting RCTs. The purpose of this question is to extend your understanding of RCTs through self-learning. Along the way, you will also be able to add to your knowledge of the current state of vaccines for the major issue facing the world today: the Covid-19 pandemic!

You will need to read the following guide on clinical trials for this question:

"A simplified guide to randomized control trials" <https://obgyn.onlinelibrary.wiley.com/doi/epdf/10.1111/aogs.13309>

**Q1**: Despite randomization, what sort of investigator bias can creep into RCTs and how can it be prevented?

**Ans 1**. Bias can creep in when the investigators or the participants are aware about who is getting intervention or not. This bias can be prevented by introducing Blinding.

The procedure of blind-

ing the participants (single blind) or both investigators

and participants (double blind) helps to eliminate this

unconscious information bias

**Q2**: What are type I and type II errors in RCTs?

**Ans 2**. The inability to demonstrate a significant difference even when there exists a difference is known as a type II error whereas is the chance that a difference will be found even if there is no difference is known as Type I error

**Q3**: What guiding principle does one need to know in order to calculate the sample size that will be sufficient for an RCT?

**Ans**.

* Knowing the baseline estimate of outcome rate
* Percentage of patients benefiting from the intervention
* How many Type 1 and Type 2 errors are to be willing to be expected before the null hypothesis is rejected

**Q4**: Consider the following clinical trial advertisement for Covid-19 vaccine: <https://www.shifa.com.pk/trial/>

What do the terms double-blind, placebo-controlled, Phase I, II, and III trial refer to here?

**Ans.**

Double-blind: means that the investigators and the patients will be kept in the dark about who is getting the intervention.

Placebo-controlled: an inactive substance, a saline solution in this case, will be administered to the patients.

Phase I, II, III: these different phases refer to the sample size of the RCT

**Q5**: Consider the following Coronavirus vaccine tracker:

<https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html>

1. What does pre-clinical testing mean in a clinical trial mean? Why do we need it?

**Ans:** In Pre-clinical trials, the testing is done on non-human subjects such as animals. This is done to ensure the safety of human subjects. In clinical trials, the testing is done on human subjects.

1. What should an investigator do when observing negative effects in an RCT?

**Ans:** if the trail is to small to detect any effect, it is appropriate to describe the findings as inconclusive

1. Why are certain vaccines more broadly approved than others? For example, Moderna: "Approved in Switzerland" vs. Pfizer-BioNTech: "Approved in several countries"?

**Ans:** the vaccines with good efficacy rates and with minimal side effects are approved more broadly

**Q6**: Consider the following statement:

“Based on [evidence from clinical trials,](https://www.cdc.gov/mmwr/volumes/69/wr/mm6950e2.htm?s_cid=mm6950e2_w) the Pfizer-BioNTech vaccine was 95% effective at preventing laboratory-confirmed COVID-19 illness in people without evidence of previous infection” taken from:

<https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/Pfizer-BioNTech.html>

1. Explain what does “95% effective” mean here by capturing the RCT study set-up as well as how to interpret the RCT results.
2. What are your comments on the demographic data (in the link above) used in the clinical trial?

**Ans 2:** The sample of the RCT is not randomized enough.