FINAL ASSINGMENT REPORT

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Submission date: 20 September 2021

Question A (Short Essay) [Marks 5* 3 = 15]

Answer followings questions-

A1. Briefly describe lead time and lead time bias and its implication in a screening program

A2. Briefly describe the design of Randomized Clinical Trial.

A3. Briefly describe the phases of drug trial.

A1. Briefly describe lead time and lead time bias and its implication in a screening program

Lead time: The lead time is defined as the interval by which the time of diagnosis is advanced by screening and early detection of disease compared to the usual time of diagnosis.

Lead time bias: Lead-time bias is a type of information bias specific to screening studies occurs when a disease is detected by a screening or surveillance test at an earlier time point than it would have been if it had been diagnosed by its clinical appearance. We can state it another way as the Lead time is the period between the detection of a medical condition by screening and when it ordinarily would have been diagnosed because a patient experienced symptoms and sought medical care.

Example: A man with metastatic lung cancer dies at age 70. His cancer was discovered 1 year ago, when he was 69. Therefore, it appears as if he lived for 1 year with the cancer. However, imagine that instead his cancer was discovered on a screening CT scan when he was 65 years old. If he still dies at the age of 70, it now looks like he survived for 5 years with the diagnosis of cancer (the 5-year survival rate is much better), but in fact there was no real change in his survival.

Implications in screening program:

The amount of lead time for a given disease depends on the biologic rate of progression of the disease and how early the screening test can detect the disease. When lead time is very short, as is true with lung cancer, it is difficult to demonstrate that treatment of medical conditions picked up on screening is more effective than treatment after symptoms appear.

On the other hand, when lead time is long, as is true for cervical cancer (on average, it takes 20 to 30 years for it to progress from carcinoma in situ into a clinically invasive disease), treatment of the medical condition found on screening can be very effective.

A2. Briefly describe the design of Randomized Clinical Trial.

Randomized Clinical Trial: Clinical trial comparing the effects of interventions in an interventional (experimental) group against a control group following random allocation of participants to intervention and control groups. All elements are the same as for a cohort study except that treatment is assigned by randomization rather than by physician and patient choice.

Design of RCT: It is an experimental study where subjects are randomly allocated to groups which either do or do not receive a therapeutic or preventive intervention being evaluated. The groups are compared in terms of their outcome. A RCT can be used in clinical, field and interventions trials.

The patients for this study are selected from many populations with the condition of interest. Using randomization, the patients are then divided into two (or more) groups of comparable prognoses. The following figure shows that the basic structure of a RCT.

One group, called the experimental group which is exposed to an intervention that is believed to be better than current alternatives. The other group, called a control or comparison group, is treated the same in all ways except that its members are not exposed to the experimental intervention.

Patients in the control group may receive a placebo, usual care, or the current best available treatment. The course of disease is then recorded in both groups, and differences in outcome are attributed to the intervention.

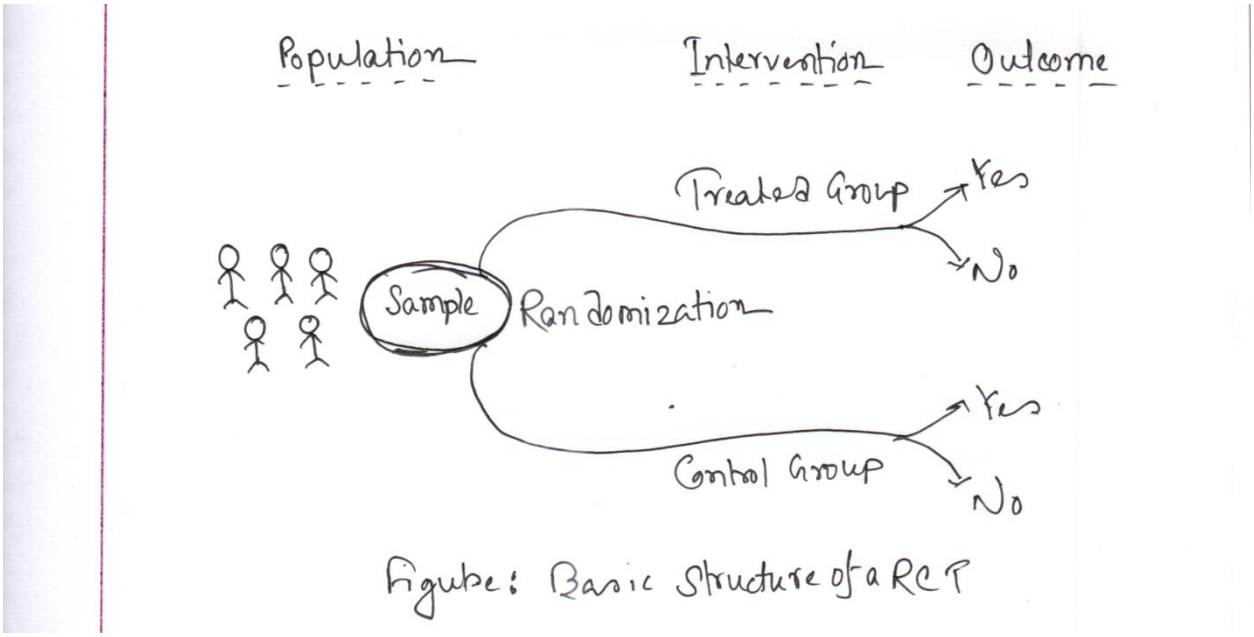

Figure: Basic Structure of a RCT

There are some advantages of randomized control trial such as similar intervention and control group, best design to prove cause and effect, standardization of eligibility criteria, treatment and assessment of outcome, statistical test without many assumptions. On the other hand, it has some disadvantages like expensive, sometimes unethical, unsuitable if lack cooperation and for artificial situation.

Blinding: Blinding to prevent the patient or researcher from knowing what group they are assigned to. In a blind trial, the participants don't know what treatment they are receiving (Which may be a placebo). In a double-blind trial, neither the participant nor the researcher knows which group the participant is in. Trials are often double blinded to avoid selection bias on the part of the researcher.

Ethical approval: An ethical approval must need for this trial. Informed consent is needed every participant. Four moral principles of ethics committee

1. Autonomy (self-determination)

2. Beneficence (providing care)

3. non-maleficence (avoiding harm)

4. Justice

A3. Briefly describe the phases of drug trial.

The phases of clinical trials are multi-stages which conducted experiment with human intervention. For any drugs trial, one group receives an existing treatment for a condition, and the second group receives a new treatment. Researchers then compare which group has better results. One group receives a new treatment, and the second group receives a placebo, an inactive product that looks like the test product.
The following phases are involved in testing new drugs:

Phase-I: Clinical pharmacological studies have been conducted. The investigators spend several months looking at the effects of the medication on about 20 to 80 people who have no underlying health conditions. The toxic and pharmacological effect of drugs have been looked in this phase.

This phase aims to figure out the highest dose humans can take without serious side effects. Investigators monitor participants very closely to see how their bodies react to the medication during this phase.

Phase-II: Phase II of a clinical trial involves several hundred participants who are living with the condition that the new medication is meant to treat. They're usually given the same dose that was found to be safe in the previous phase.
Investigators monitor participants for several months or years to see how effective the medication is and to gather more information about any side effects it might cause.

Phase-III: Phase III of a clinical trial usually involves up to 3,000 participants who have the condition that the new medication is meant to treat. Trials in this phase can last for several years.

The purpose of phase III is to evaluate how the new medication works in comparison to existing medications for the same condition. To move forward with the trial, investigators need to demonstrate that the medication is at least as safe and effective as existing treatment options

Phase-IV: In this phase, Investigators use this phase to get more information about the medication's long-term safety, effectiveness, and any other benefits. It is the post marketing surveillance.

Question B1 [Marks 5]

Read the abstract of an article "Quality of life after PCI vs CABG among patients with diabetes and multivessel coronary artery disease: a randomized clinical trial. By Abdallah et al. (JAMA. 2013 Oct 16;310(15):1581-90. doi: 10.1001/jama.2013.279208) and answer the following questions.

1. What was the type of study? 1
2. Who were the target population? 1
3. What were the intervention factors? 1
4. What were the outcome factors and how were they assessed? 1
5. Is this conclusion valid? Why? 1

Answers:

1. **Type of study:** Prospective randomized clinical trial
2. **Target population:** A total 1900 Patients from 18 countries with DM and angiographically confirmed multivessel CAD were randomized on a 1:1 basis to undergo revascularization by either CABG or DES-PCI. Patients with diabetes and multivessel coronary artery disease

3. **Intervention factors:** Initial revascularization with coronary artery bypass graft (CABG) or drug-eluting stents using percutaneous coronary intervention (DES-PCI). Initial revascularization with coronary artery bypass graft (CABG) or Drug Eluting stents-Percutaneous Coronary Intervention (DES-PCI)
4. **Outcome factors:** Health Status

   Way of assessment: Health status was assessed using the angina frequency (AF), physical limitations (PL), and quality of life (QOL) domains of the Seattle Angina Questionnaire (SAQ) at baseline, 1, 6, and 12 months, and annually thereafter. Quality of life is outcome factor and health status are unknown

5. **Conclusion validity:** No, Invalid and may not be clinically meaningful.

Question B2 [Marks 5]

As a public health official at a district, you are given the task for developing a diabetes screening program. Answer the following questions in relation to your planned screening program

1. Design a screening program by considering the important characteristics of a medical screening program.

Answer: Screening is the process of using tests on a large scale to identify the presence of disease in apparently healthy people. Screening tests do not usually establish a diagnosis but determine presence or absence of an identified risk factor, and thus require individual follow up and treatment.

Though there are different types of screening each with specific aims such as mass screening, multiple screening, targeted screening, and case finding screening. The screening of diabetes test includes urine glucose, random blood glucose (RBG), fasting plasma glucose (FPG), glycated hemoglobin (HbA_{1c}), fructosamine, and a 75-g oral glucose tolerance test (OGTT). I will consider the following elements for implementing a medical screening program for diabetes:

- **Disorders:** It should be well defined.
- **Prevalence:** Prevalence should be known for diabetes screening.
- **Natural history:** It is the long period between first signs and overt disease, medically important disorder for which there is an effective remedy. For diabetes screening, it should be known.
- **Test choice:** For diabetes screening, the test should be simple and safer.
- **Test performance:** The distribution of test values in affected and unaffected individuals known.
- **Financial support:** The screening should be cost-effective.
- **Facilities:** It is one of the important that should be available and provided easily.
- **Acceptability:** For screening programme, procedures following a positive result are generally agreed upon and acceptable to both the screening authorities.
- **Equity:** It is the access to screening services, effective, acceptable, and safe treatment that should be ensured for diabetes screening.

Despite this, I would consider the following approaches:

Questionnaire development: Several questionnaires will be developed to screen for undiagnosed diabetes and will include a range of questions covering both symptoms and recognized risk factors.

Urine glucose: The usefulness of urinary glucose as a screening test for undiagnosed diabetes is limited because of the low sensitivity which ranged from 21% to 64% with specificity > 98% in studies which included performing an OGTT in the entire study population or a random sample of negative screeners (1). Despite its low sensitivity, urine glucose testing may have a place in low resource settings where no other procedure is possible. This is particularly so, of course, when the prevalence of undiagnosed diabetes is likely to be high.

Blood glucose: Venous fasting plasma glucose, fasting capillary blood glucose, random blood glucose could be used for Blood glucose screening.

Glycated haemoglobin: The desire to replace the OGTT with a simpler test has been a major factor behind the evaluation of glycated haemoglobin as a screening test for undiagnosed type 2 diabetes.

Combinations of tests: Screening tests, as mentioned above, may be combined to improve performance. In relation to type 2 diabetes this can be done using the tests serially or simultaneously (e.g. measurement of blood glucose and HbA1c at the same time). Combination testing is more resource intensive, especially if applied sequentially (2).

Question B3 [Marks 5]

Please read the following abstract and answer the questions related to this abstract. The full paper is shared with this question.

1. Which Phase of clinical trial this paper reporting? 1
2. How patients were recruited and randomized? 1
3. What is intention to treat analysis mentioned in this paper? 1
4. Is this an effectiveness or efficacy trial? 1
5. Comment on the conclusion 1

Answers:

1. **Phase of clinical trial:** Phase III trial had been conducted for this research.

2. **Patient's recruitment and randomization**: Patients were included in the modified intention-to-treat analysis, and it was a block randomization.

3. **Intention to treat analysis:** Patients with a confirmed diagnosis of Covid-19

4. **Type of trial:** It is an effectiveness trial

5. **Comments:** The study was performed a multicenter, randomized, open label, controlled trial (Coalition Covid-19 Brazil I) to assess whether hydroxychloroquine, either alone or in combination with azithromycin, would be effective in improving clinical status at 15 days after hospital admission due to mild-to-moderate Covid-19.

References:

1. Englelgau MM, Narayan VKM, Herman WH. Screening for Type 2 diabetes. *Diabetes Care* 2000;23:1563-1580.
2. WHO/NMH/MNC/03.1, Screening for Type 2 Diabetes: Report of a World Health Organization and International Diabetes Federation meeting.