Medical Statistics (MATH38071) Exercise Sheet 8

(Analysis with Treatment Protocol Deviations)

1. Tabulated below are data from a randomised controlled trial comparing Inpatient and Outpatient treatment for patients with anorexia nervosa.

	Randomization			
	Inpatient		**Out-patient**	
Recovered	**Received Inpatient**	**Received Outpatient**	**Received Inpatient**	**Received Outpatient**
N	60	10	40	25
Y	140	90	60	175
Total	200	100	100	200

(i) Calculate the point estimates of the a) Intention-to-treat, b) Per-Protocol and c) As-Treated estimates of the treatment effect.

Assume that there are three latent classes of patients in a randomised trial (A) patients who will comply with the allocated treatment, (B) patients who will always have inpatient care and (C) patients who will always have outpatient care.

(ii) By considering those patients allocated to inpatient care, estimate the proportion of patients who will always receive outpatient care.

(iii) By considering those patients allocated to outpatient care, estimate the proportion that will always receive inpatient care.

(iv) Hence, estimate the proportion of patients who will always comply with random allocation.

(v) Estimate the Compliance Average Causal Effect (CACE).

(vi) What assumptions are made in obtaining the CACE estimate?

(vii) Comment on the difference between the CACE point estimate and the point estimates of Intention-to-treat, Per-Protocol and As-Treated estimates of the treatment effect calculated in part (i).

2. Considering a randomized controlled trial, suppose that the patient population can be divided into three latent sub-groups of patients as follows:
   - *Compliers*: patients who will comply to the randomly allocated treatment
   - *Always control treatmen*t: patients who will receive the control treatment regardless of random allocation
   - *Always new treatment*: patients who will receive the new treatment regardless of random allocation.

   Assuming that the proportion and characteristics of *compliers*, *always control treatment*, *always new treatment* is the same in both arms and that randomization can only affect the outcome through the receipt of treatment, show that an *as-treated* estimate of the treatment effect may be biased either towards or away from the null hypothesis of no treatment effect.

3. Consider a parallel group randomised controlled superiority trial that compares a new treatment with a standard treatment. Suppose the outcome measure is continuous with its standard deviation σ. Suppose that the causal effect of treatment is τ and that the proportion of patients expected to comply with randomisation is π.
   (i) Write down an expression for the intention-to-treat estimate of the treatment effect.
   (ii) The formula for sample size per group for a superiority trial is $n = \frac{2\sigma^2}{\delta^2}\left(z_{\alpha/2} + z_{\beta}\right)^2$ where δ the intention-to-treat treatment effect is. Suggest a modified formula for sample size based on the causal effect of treatment τ and that the proportion of patients expected to comply with randomisation is π.
   (iii) Assuming that all patients comply with treatment, the sample size per group for a trial has been estimated to be 256. It is thought that 20% of patients recruited to the trial will not comply with random allocation. Determine a revised sample size per group that takes account of this of level non-compliance.