**Students will be given all questions in advance, and asked to answer two of these questions on the day. They will be provided with the dataset for the two questions, and will have access to SPSS on the day, and should use this to answer the questions. Each type of analysis that is taught in the module must be revised in order to ensure that the student knows which test to run in the exam (correlation/regression [q2], t-test [q3], one-way ANOVA [q4] and mixed ANOVA [q1]).**

Question 1 [will be used in exam]

A pharmacologist wanted to test the most appropriate therapeutic dose for a new drug in the triptan class (Portotriptan), for reducing cluster headaches. She selected a sample of 100 volunteers that suffered from cluster headaches. As a control, in this study, she only chose female participants, and controlled for their weight (70KG±10kg) and age (30 years±5 years). All participants were given either a placebo (0mg), or one of four hypothesized therapeutic doses (25mg, 50mg, 75mg, 100mg). Data collection involved two consultations. In the first, participants were asked how many cluster headaches they had in the past 6 months. They were then given the drug (or placebo) and re-assessed 6-months later at follow up.

Q: Does the drug have therapeutic efficacy at the concentrations tested here? Give evidence from your analysis.

Answer: A **mixed-ANOVA** [15 marks for selecting correct test] shows that there is a significant concentration x time interaction (**F(4,95) = 11.94, p < 0.001, partial eta2 = .34)** [15 marks for reporting interaction effect correctly, including effect size]. Post-hoc **Bonferroni-corrected t-tests** [5 marks for selecting post-hoc tests, dock 5 marks for no Bonferroni correction] show that there is no difference between baseline and follow up for the placebo group (p = 0.16), but there are significant reductions at all concentrations of the drug (all p’s < 0.003) [5 marks for correct ‘p’ values]. This suggests that the drug has therapeutic efficacy at all the concentrations tested [10 marks for answering question].

Question 2 [will be used in the exam]

Ipilimumab is a fully human monoclonal antibody that blocks cytotoxic T-lymphocyte antigen-4 and has demonstrated an improvement in overall survival in two phase III trials of patients with advanced melanoma. In a randomized, double-blind, phase II biomarker study, 40 treatment-naïve patients with unresectable stage III/IV melanoma (all male, all aged 65±10 years) were induced with 10 mg/kg ipilimumab every 3 weeks for 4 doses, and at Week 24, patients received maintenance doses every 12 weeks. Candidate biomarkers (e.g., immunoglobulins) were evaluated in tumor biopsies collected pretreatment and 72 hours after the second ipilimumab dose. The data presented includes the sample characteristics, as well as the immunoglobulin count (high = high count) and the change in tumor score (positive = growth, negative = shrinkage) following the second biopsy.

Q. To what extent does the biomarker score predict the change in tumor score? Give evidence from your analysis.

Answer: A **linear regression** [20 marks for selecting correct test] shows that biomarker count significantly predicts tumor cell growth (**y = -13.14+.015*x*, R2 = 0.17**) [20 marks for reporting interaction effect correctly, including effect size]. This suggests that the biomarker is a good marker for tumor growth [10 marks for answering question].

Question 3 [will not be used in exam]

Foetal alcohol syndrome (FAS) results from the developing foetus being exposed to high levels of alcohol *in utero*, and is characterized by behavioural, cognitive and in some cases, craniofacial dysmorphia. The extent of the damage caused is a combination of both concentration to which the foetus is exposed, and to genetics, with the principles of non-Mendelian inheritance, or “exceptions” to Mendelian genetics, thought to be the driving force behind the severity of the prenatal alcohol-exposed individual's symptomology. One such exception is when maternal alleles lead to an altered intrauterine hormonal environment and, therefore, produce variations in the long-term consequences on the development of the alcohol-exposed foetus. Pregnant Sprague Dawley (S) and Brown Norway (B) dams differ in their thyroid function and thyroid hormonal response to alcohol. In order to test the extent to which this would affect the offspring, 20 pregnant S, and 20 pregnant B, rats were exposed to a low/moderate dose of alcohol throughout pregnancy. When the pups were born, they were tested for craniofacial abnormalities by measuring the distance between the eyes, producing a single measurement for the pups from each mother.

Q. To what extent did the maternal hormonal environment affect the pups’ symptom severity?

Question 4 [will not be used in exam]

Acute ethanol (EtOH) consumption exerts a biphasic effect on behaviour and increases serotonin levels in the brain. However, the molecular mechanisms underlying alcohol-mediated behavioural responses are unclear. A team of investigators wanted to examine, pharmacologically, the involvement of the serotonergic pathway on acute EtOH-induced behavioural changes in zebrafish. They exposed zebrafish to 1.0% (v/v) EtOH for 1 h and analyzed the effects on aggression (which increases after 1% EtOH consumption). As a pharmacological approach, they exposed some fish to 20uM ketanserin (5-HT2A antagonist) and 15uM (±)-DOI hydrochloride (5-HT2A agonist), and had a water-exposed control group, to see how these affected EtOH-induced aggression.

Q. Is there any evidence that acute ethanol-induced aggression is moderated by the serotonin pathway?