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Appendix 1

Questionnaire

Question 1

Two treatments used for depression were tested against placebo for clinical outcome. The results were as follows.

- Treatment A *v.* placebo for depression had a mean difference in Hamilton Rating Scale for Depression (HRSD) scores of 2 points ($P = 0.001$).
- Treatment B *v.* placebo had a mean HRSD difference of 4 points ($P = 0.05$).

Which treatment (A or B) would you choose in clinical practice?

Question 2

A study of serious side-effects in 1500 patients receiving two treatments (X and Y) compared with placebo had the following results.

Their serious side-effect rates are as follows:

- treatment X 1.2%, treatment Y 0.8%, placebo 0.45%;
- treatment X has 50% more side-effects than drug Y; relative risk 1.5 (95% CI 0.95–1.67).

If treatments X and Y are equally efficacious, how would these results affect your prescribing?

A Treatment Y should be prescribed first line
B Treatment X should be prescribed first line
C Treatments X and Y should be prescribed equally

Question 3

You are a consultant in general adult psychiatry with admitting rights to two wards in a teaching hospital. Your specialist registrar has compiled an audit of admissions to these wards over a 6-month period; *t*-tests are used in the data analysis. The results are as follows.

	James Ward ($n = 75$)	Henry Ward ($n = 62$)	*P*
Length of in-patient stay, weeks: mean (s.d.)	16 (7)	10 (5.5)	0.01
No. of patients needing readmission, *n* (%)	23 (31)	27 (44)	0.05

Your specialist registrar concludes that Henry Ward discharges patients significantly earlier than James Ward but has significantly higher rates of readmission. Do you:

A try to admit more of your patients to James Ward?
B ask your specialist registrar to re-examine the length of stay data?
C ask your specialist registrar to re-audit in 6 months?

Question 4

A randomised controlled trial (RCT) studied the effect of adding a new mood stabiliser to carbamazepine in patients with bipolar affective disorder. A total of 4000 patients were included and the groups arranged as follows:

- treatment group I ($n = 2000$): carbamazepine alone;
- treatment group II ($n = 2000$): carbamazepine + new mood stabiliser.

The study was conducted over 5 years. Relapse rates were found to be similar in both treatment groups. However, those in group II were at a higher risk of severe life-threatening hepatic side-effects (4% group II *v.* 2% group I). When the rates of suicide were examined, the following results were found.

- Group I: (carbamazepine alone) 88 out of 2000 (4.4%) died by suicide
- Group II: (carbamazepine + new mood stabiliser) 70 out of 2000 (3.5%) died by suicide
- The risk ratio (II *v.* I) is 3.5/4.4 = 0.8 (95% CI 0.63–0.86; $P = 0.001$)
- The relative risk reduction of suicide is (4.4 — 3.5)/3.5 = 26%
- The absolute risk reduction of suicide is 4.4 — 3.5 = 1.1%

The study concluded that treatment group II (carbamazepine + new mood stabiliser) gave a 26% reduction in suicide rates at 5 years compared with group I (carbamazepine alone). Based on these results, would you:

A Start prescribing the mood stabiliser combination for your patients?
B Continue to prescribe carbamazepine alone for your patients?
C Prescribe the new mood stabiliser alone for your patients?

Question 5

A new drug (A) for mixed dementia was studied in a country-wide RCT. The main end-point was time to institutionalised care or death: 700 patients were randomised to either treatment as usual (TAU, with lifestyle advice +/— aspirin +/— blood pressure monitoring and management; $n = 350$) or the new medication (A) + TAU ($n = 350$). Medication A has a wide side-effect profile, but the most troublesome side-effect is gastric irritation. Patients unable to tolerate treatment A + TAU revert to TAU only. The following results were obtained at 5 years.

	Patients institutionalised/dead *n*	Patients self-caring/supported at home *n*
TAU	240	200
TAU + A	70	190

Figure 1 shows the results according to treatment received, and Fig. 2 as randomised.

The study concluded that at 5 years TAU + A produced a 28% reduction in death or institutionalised care. Do you:

A start prescribing TAU + A for your patients?
B continue with TAU only for your patients?

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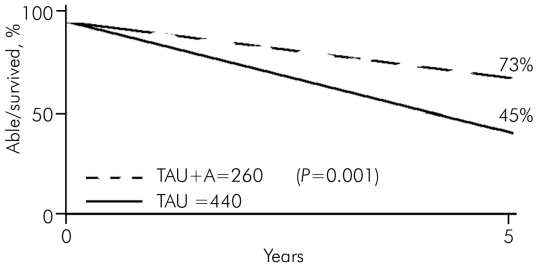

Fig. 1. Treatment received.

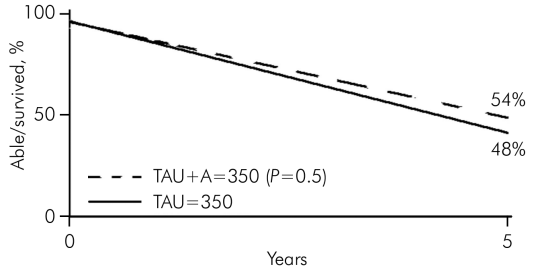

Fig. 2. As randomised.

Appendix 2

Worked answers for questionnaire

Question 1
Answer: B
Both are statistically significant at the 95% confidence interval, but treatment B shows a greater improvement in scores on the HRSD so should be favoured in clinical practice.

Question 2
Answer: C
The 95% confidence interval for the relative risk includes 1 so is not statistically significant. With such small percentages no conclusion can be drawn about the side-effect profile comparison given. As both drugs are equally efficacious, they should be prescribed equally on the basis of this study.

Question 3
Answer: B
Data for length of stay are flawed because *t*-tests cannot be used for non-parametric data such as length of stay in hospital (continuous variable and not normally distributed). A simple check for standard deviation normal distribution is to calculate if 2 standard deviations (includes 95.4% of data) taken away from the mean are still within the possible range for the variable.

- For James Ward $(7 \times 2) - 14 = 16 - 14 = 2$ (possible for mean).
- For Henry Ward $(5.5 \times 2) - 10 = 11 - 10 = -1$ (impossible for mean).

So the sample is not normally distributed and *t*-tests cannot be applied. Non-parametric statistical tests are required.

Question 4
Answer: B
The relative risk reduction of suicide appears convincing (26%), but the actual risk reduction (ARR) of 1.1% is less startling for a rare event like suicide. If there is apparent disparity between these indices it is useful to calculate the number needed to treat (NNT). The NNT is 1/ARR. So in this study NNT = 1/1.1% = 1/0.011 = 91 patients. Therefore, 91 patients are needlessly given the group II combination (carbamazepine + new mood stabiliser) to prevent just one suicide in 5 years. As the hepatic side-effect profile of treatment group II is twice as high as group I, the group II patients are at considerably greater risk of serious liver problems. Therefore the combination is not recommended and the clinician should continue to prescribe carbamazepine alone.

Question 5
Answer: B
This study highlights the importance of 'intention to treat' and how data can be manipulated if it is ignored. Looking at the 'treatment received' data (Fig. 1), the TAU + drug A group appears to do much better than the TAU only group. The graph suggests a positive outcome for drug A in 28% more patients, at the highly significant *P*-level of 0.001. However, as patients unable to tolerate the side-effects of drug A revert to TAU, the differences presented are actually statistical artefacts. The 'treatment received' graph shows the outcome only in those who ultimately receive TAU + A (260 of original 350 participants) and loses all those who had to revert to TAU owing to troublesome side-effects of drug A (90 of original 350 participants, expanding the TAU group to 440). If 'intention to treat' is applied (looking at outcomes of all the original participants as randomised, the effect of offering treatment rather than receiving it), the actual result is very different. The 'as randomised' graph (Fig. 2) looks at all the 350 original TAU + A patients compared with the 350 original TAU only controls. It shows a non-significant *P*-value of 0.5 and no actual benefit of drug A. Drug A is therefore not helpful, and has a wide side-effect profile so could actually be harmful. It should therefore not be prescribed on the basis of this study.