SIGN CRITICAL APPRAISAL
COURSE: EXERCISE 2

This presentation shows one individuals assessment of the RCT used in the second exercise. It links back to sections of the paper in the same way that we did in the video.

If you want to move through the slides more quickly, or go back to a previous slide, you can use the double-arrow buttons at the bottom of the scroll bar on the right of the screen.
Appraising a Randomized Controlled Trial

At the end of the second video you were asked to appraise:

Baxendale S, O’Sullivan J, Heaney D.

**Bright Light Therapy as an add on treatment for medically intractable epilepsy.**

Epilepsy and Behavior 2012;24(3):359–364

This presentation will take you through our suggested answers.
1.1: THE STUDY ADDRESSES AN IMPORTANT AND CLEARLY FOCUSED QUESTION.

Introduction, page 359 (and in the abstract)

This aim of this study was to conduct a randomized controlled trial of BLT as an add on therapy for seizure control in adults with medically intractable focal epilepsy. We hypothesized that:

You should recognise three elements of the PICO format here. The comparison (low intensity light / placebo) is identified in the methods section.
1.2: THE ASSIGNMENT OF SUBJECTS TO TREATMENT GROUPS IS RANDOMIZED

Methods section 2.3, page 360

The participants were randomized to the high-intensity (HI)/low-intensity (LI) treatment arm on receipt of the completed consent form using an automated permuted block randomization with a block size of 10 and an allocation ratio of 1:1 [18]. One of the researchers

Patients were allocated in blocks (of 10 in this case) to one arm of the study or the other. Reference is provided to the software used to generate the randomization sequence.
1.3: AN ADEQUATE CONCEALMENT METHOD IS USED.

Methods section 203, page 360

The investigators have taken steps to conceal allocation from those analysing the data. How easy would it be for them to work out who was getting which treatment despite that? Would they do that?
1.3: AN ADEQUATE CONCEALMENT METHOD IS USED.

Methods section 203, page 360

Size of 10 and an allocation ratio of 1:1 [18]. One of the researchers (J.O'S.) recruited and allocated the participants to each arm of the trial in order of receipt of the signed consent form. Their seizure data was coded thereon. Both senior investigators who conducted the statistical analyses and write up of the results (SB and DH) were blinded to the code throughout the study and at the time of data analyses.

They might!
1.4: SUBJECTS AND INVESTIGATORS ARE KEPT BLIND ABOUT TREATMENT ALLOCATION

Methods section 2.3, page 360.

Both senior investigators who conducted the statistical analyses and write up of the results (SB and DH) were blinded to the code throughout the study and at the time of data analyses. The participants were blinded as to whether they had received a high- or low-intensity light box. The boxes are identical externally, and the difference in luminance is only clear if they are turned on and examined side by side. Since each participant only saw their own light box, they would not know whether it was set as a high- or low-intensity output.
1.5: THE TREATMENT AND CONTROL GROUPS ARE SIMILAR AT THE START OF THE TRIAL

Characteristics of patient groups are listed in Table 1 on page 360.

Although generally comparable, there are some differences in the localization of seizures. Only someone with knowledge of the subject can tell if these differences are significant.

(This should not be an issue when you are reviewing papers in your own subject area).
1.6: THE ONLY DIFFERENCE BETWEEN GROUPS IS THE TREATMENT UNDER INVESTIGATION.

Methods section 2.4 (pages 360-1) describes how the study was conducted. It is clear that there is plenty of scope for variation in how participants dealt with the procedures. The investigators have addressed these issues, but there is still an unknown amount of variation.
1.7: ALL RELEVANT OUTCOMES ARE MEASURED IN A STANDARD, VALID AND RELIABLE WAY.

The primary outcome measure for the trial was seizure frequency.

A clear, objective measure.
1.8: WHAT PERCENTAGE OF THE INDIVIDUALS OR CLUSTERS RECRUITED INTO EACH TREATMENT ARM OF THE STUDY DROPPED OUT BEFORE THE STUDY WAS COMPLETED?

Approximately 23% from each arm, based on data from Figure 2 on page 361.

Although greater than the ‘rule of thumb’ total of 20%, this is probably acceptable – especially given that both arms have similar dropout rates.
ALL THE SUBJECTS ARE ANALYSED IN THE GROUPS TO WHICH THEY WERE RANDOMLY AlLOCATED.

Methods section 2.7, page 361

Intention to treat and per protocol analyses were conducted in the calculation of both absolute and relative effect size for the binary outcome measure (not effective vs. ≥50% reduction in seizures) for the H1 and LI groups.
1.10: WHERE THE STUDY IS CARRIED OUT AT MORE THAN ONE SITE, RESULTS ARE COMPARABLE FOR ALL SITES.

Does not apply.
The planned sample size (n = 100) was estimated on the basis of a power analysis using change in seizure frequency as the main outcome variable. Trials of new antiepileptic drugs normally require at least 4 seizures per month over a three-month period to show an effect. In emulating these stringent protocols, we assumed an average number of 12 seizures in the baseline condition (3 months) with a standard deviation of 5. A total of 100 participants (50 in each condition) would be sufficient to provide over 90% statistical power to detect a reduction in seizures of 25% or more in the treatment condition. The power increases with the % reduction in seizures employed. Allowing for missing data, noncompliance with the protocol and drop outs, 35 participants in each condition would still provide statistical power greater than 80% in this respect.

You may remember that in the video we talked about power calculations. These investigators did one, but were unable to recruit enough participants. They do, however, indicate the extent to which the results are still reliable.
We have now completed work on this exercise.

- How would **you** rate this study overall?

- Would you use it as evidence?

Remember that in both exercises for this course you have been looking at the methodology only. When doing this for real, in a subject you know well, you may find papers where the methodology seems sound but the results are at odds with your clinical experience. Don’t be too easily persuaded – ask more questions about the trials.