QUIZ Sept 5th 2018 (answers below)

1. **What is publication bias?**

2. **What is relative risk reduction?**

3. **What is positive predictive value?**

4. **What are the limitations of subgroup analysis?**

5. **Draw and label the features of a receiver operator characteristic (ROC) curve.**

QUIZ answers Sept 5th 2018

1. **What is publication bias?**

Even if individual studies are perfectly designed and executed, syntheses of studies may provide biased estimates because systematic review authors or guideline developers fail to identify studies. In theory, the unidentified studies may yield systematically larger or smaller estimates of beneficial effects than those identified.

In practice, there is more often a problem with ''negative'' studies, the omission of which leads to an upward bias in estimate of effect. Failure to identify studies is typically a result of studies remaining unpublished or obscurely published. Methodologists have labeled this phenomenon ''publication bias.''

Empirical evidence shows that, in general, studies with statistically significant results are more likely to be published than studies without statistically significant results (''negative studies''). Systematic reviews performed early, when only few initial studies are available, will overestimate effects, while ''negative'' studies face delayed publication. The risk of publication bias may be higher for reviews that are based on small randomised controlled trials.

Recent revelations suggest that withholding of ''negative'' results by industry sponsors is common.

Guyatt et al GRADE guidelines: 5. Rating the quality of evidence – publication bias Journal of Clinical Epidemiology 64 (2011) 1277 - 1282

2. **What is relative risk reduction?**

Relative risk reduction is the difference in outcome event rates between the control and study groups divided by the outcome event in the control group and is expressed as a percentage. It does not give any measure of absolute number of people who might benefit from the intervention.

3. **What is positive predictive value?**

The probability a positive test actually signifies the presence of disease

$$\frac{\text{True positives}}{\text{All positives (true and false)}}$$

Directly proportional to the prevalence of disease:

Low prevalence → ↑ false positives → ↓ positive predictive value

4. What are the limitations of subgroup analysis?

A. *False positives due to multiple comparisons*

If you look hard enough, you will find something.
A great example uses the ISIS-2 trial comparing IV streptokinase, oral aspirin, both or neither Lancet 1988 Aug 13;2(8607):349-60 where subgroup analysis for patients born under the Zodiac signs of Gemini and Libra had 5% higher mortality on aspirin compared to placebo, where as patients born under other Zodiac signs had a 30% lower mortality on aspirin compared to placebo.

B. *False negatives due to inadequate power*

The sensitivity of a subgroup analysis is its statistical power: the probability of finding a true difference between groups if one exists. Most large clinical trials are powered to find a clinically meaningful difference between treatment and control groups around 80 -90 % of the time. Compared with the power for the trial's main effect, most subgroup analyses have much less statistical power to identify subgroup effects. Power might often be closer to 20 – 30% for subgroup effect sizes similar in magnitude to the main treatment effect sizes.

C. *Limited ability to inform individual treatment decisions*

Patients have multiple characteristics that vary simultaneously.

Even a genuine difference between subgroups is not necessarily due to the classification of the subgroups. As an example, a subgroup analysis of bone marrow transplantation for treating leukaemia might show a strong association between the age of a sibling donor and the success of the transplant. However, this probably does not mean that the age of donor is important. In fact, the age of the recipient is probably a key factor and the subgroup finding would simply be due to the strong association between the age of the recipient and the age of their sibling.

The most readable article I found on this is:
Burke et al Three Simple Rules to ensure reasonably credible subgroup analysis BMJ 2015;351:h5651

5. **Draw and label the features of a receiver operator characteristic (ROC) curve.**

A ROC curve is a method of graphically demonstrating the relationship between sensitivity and specificity; you can see the how much specificity is lost as sensitivity is gained, and vice versa.
The desired cut off point for a test can be determined from the graph.
The area under the curve equates to the accuracy of the test.