<table>
<thead>
<tr>
<th>Question</th>
<th>Type of Study</th>
<th>Internal</th>
<th>External</th>
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| Cost effectiveness| Economic Analysis                                  | • How accurate are the costs measured?                                                                                                   | • How much risk is associated with the cost?  
• How significant is the cost / effect of each strategy?  
• How much different is the cost / effect among subgroup analysis? |                                                                                  |
| Diagnosis         | Independent, Blind Comparison to Gold Standard     | • How does the study reflect the range of patients with this clinical problem?  
• What is the precision\(^1\) of the estimates of disease probability?  
• What likelihood ratios were associated with the range of possible test results? | • Are study patients similar to local patients?  
• What is the likelihood that the disease probabilities have changed since this evidence was published?  
• How reproducible are the study results in the current clinic setting here?  
• How will the test results change your management approach? |                                                                                  |
| Harm / Etiology   | RCT, Cohort, Case-Control, Case Series             | • If a cohort study, did the exposed and control groups start and finish with the same risk of the outcome aside from the exposure of interest?  
• How did the researchers ensure that patients had similar prognostic factors that are known to be associated with the outcome (or, how was a statistical adjustment addressing the imbalance conducted)?  
• If a case-control study, how were the cases and the controls balanced for risk of exposure?  
• What is the strength of the association between exposure and outcome?  
• How precise\(^1\) is the estimate of risk? | • How was follow-up handled and was it sufficiently long?  
• How similar is exposure to your current patient population?  
• What is the magnitude of risk?  
• What are the benefits that known to be associate with exposure? |                                                                                  |
| Prognosis         | Cohort, Case-Control, Case Series                  | • How were the patients classified into prognostically homogenous groups?  
• How was follow-up handled and was it complete?  
• How unbiased and objective was the outcome criteria? | • How similar are the study patients to your current patients?  
• How can you use the results in your management of patients? |                                                                                  |
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<th>Therapy</th>
<th>RCT, Non-Inferiority Trials</th>
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| • Was randomization concealed?  
• Was data analysis blinded?  
• Was loss to follow-up significant?  
• Was prognosis balanced throughout the study?  
• How precise\(^1\) was the treatment effect estimate?  
• How did investigators guard against unwarranted conclusion of noninferiority?  
• How well were patients analyzed in the groups to which they were randomized?  
• How have RCTs of the same drug class shown improvement in the surrogate end point leading to improved patient-centered outcomes? |
| • How similar were the study participants to my patients?  
• What patient or clinician factors may affect adherence?  
• Are treatment effects worth the potential harm?  
• What patient-centered outcomes are not considered?  
• What biologic factors may modify the treatment response? |

<table>
<thead>
<tr>
<th>Qualitative</th>
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| • What qualitative method is cited?  
• How did the researchers account for comprehensiveness and detail? |
| • How does the study offer helpful results?  
• How does the study help us understand clinic practices? |


\(^1\)Precision – please consider the context and the question type. Studies on treatments may find a statistically significant difference (based on \(p\) values), but may have a wide confidence interval (implying a broad range of possible treatment effect). The confidence interval in these cases then is a measure of precision. Other studies of a diagnostic test for example, utilize Sensitivity & Specificity to describe precision (i.e. minimizing false negatives and false positives) – please see the Properties of a Screening Test.

Other critical analysis considerations:

- **Editorial Commentary** – are there any accompanying statements by authorities on the study? Often, you can find critical discussion on a topic if you check the Comments section of PubMed. For example, see the Comments below the abstract for the ORBITA Trial.
- **Funding Sources i.e. Conflict of Interests (COIs)** – at the end of studies, there is often a COI disclosure section. Do you have concerns?
- **Surrogate Markers** – is the measurement used by the researchers the final outcome of interest, or a surrogate for convenience/availability? For example, some studies of statin medications have used LDL reduction as the primary outcome measure instead of the actual clinical outcome of interest (i.e. reduction in MI or death).