PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

CER Questions
Screening and Diagnostic Tests

1. *Evaluation of methods for staging HCV+ patients:*

Methods for staging the amount of liver fibrosis in HCV+ patients are important for any selective treatment strategy. They help to answer the question, "does this patient need treatment?" What is the best way to classify patients as needing treatment? This question could be approached in a randomized trial comparing the two approaches to staging the patient. It could also be approached in a study that measured the sensitivity, specificity, and harms of the two tests and modeled the outcomes of false—positive and false-negative results.

Various multiple component prediction rules for fibrosis have been evaluated against liver biopsy. Most include age, platelet count, liver function tests (AST and ALT) and several other tests. As a measure of fibrosis, they have a positive likelihood ratio (the amount by which the odds of the target condition increase when the test is positive) of 5 to 10 and an area under the ROC curve (a measure of test discrimination where 0.5 means no better than chance prediction) of 0.70 to 0.85 for the conventionally used thresholds for defining an abnormal result. The negative likelihood ratio varies widely within the range 0.2 to 0.8; the test with the lowest result (indicating a lower post-test probability if the test is negative) and narrow confidence interval has a 0.21 negative likelihood ratio.

Proposed question: What are the comparative benefits and risks of FibroScan and other non-invasive tests for liver fibrosis vs. liver biopsy in staging patients with hepatitis C? (two participants nominated this topic).

2. *Comparison of strategies for using Hepatitis C screening tests:*

There are two types of tests. The first tests for antibody against HCV. It has a sensitivity of 97%% and a similar specificity when measured against the reference standard for active infection (PCR) which detects the viral genome in the blood. Typically, positive HCV antibody tests are confirmed with PCR.

We received two *proposed questions* in this category.

- Compare the conventional two-step screening and confirmation protocol (anti-HCB Ab followed by HCV PCR if positive) with a "reflex test" (in which anti-HCB Ab followed by "reflex" HCV PCR if the antibody test is positive).
- Compare the impact of rapid anti-HCV Ab with "conventional" testing on the outcome of informing the screened people of their HCV status.

3. *Comparison of methods for selecting high risk patients for anti-HCV antibody screening:*

Currently, the USPSTF recommends screening everyone in the 1945-65 birth cohort and high risk individuals in other age groups (B recommendation). The several studies that have addressed the problem of identifying high risk individuals were of fair to poor quality. All applied clinical risk factors retrospectively and studied patients at relatively high risk (4-8%); 4 of the 5 studies were cross-sectional. These studies used questionnaires of HCV risk factors to identify high risk patients for antibody screening. When only one criterion was the screening threshold, 90+% of screen+ patients were identified with 60-80% of the people getting antibody screening. When several criteria were required to say that a person was at high risk, the sensitivity dropped to 25-35% but with 5-10% of the people being screened.

According to the USPSTF systematic review of 2013, no one has directly compared strategies to identify non-birth cohort people at high risk. The USPST concluded that well designed prospective studies in the target population were needed. Based on this evidence gap, PCORI staff puts forth this topic for discussion.

Proposed question: What are the harms and benefits of different methods to identify people at high risk of hepatitis C?

4. ***What screening guidelines are likely to identify the largest number of people with HCV?***

   We would probably reframe this question by incorporating it as an outcome in one of the studies that compare different screening strategies (see above).