Key Questions with Ratings

For each voting question, the following scale was used to identify the level of confidence - with a score of 1 being low or no confidence and 5 representing high confidence. A score of ≥2.5 is considered intermediate confidence that there is robust clinical literature to support the question.

1	—	*2*	—	*3*	—	*4*	—	*5*
Low Confidence				*Intermediate*				*High Confidence*

1. Is there sufficient data to use molecular testing to identify and risk-stratify patients with BE with low or high-grade dysplasia?

Final Rating: 3.5

Responses included that these tests are primarily designed for detection of Barrett's esopagus (BE) and not differentiation of low- vs. high-grade dysplasia. However, the panelists agreed that there is moderate to good evidence of molecular markers being able to risk stratify BE regarding risk of progression.

2. Does the existing evidence define a patient population that would most benefit from the testing? Have any of the studies included patients >65 years of age?

Final Rating: 3

DNA marker studies have all included the high-risk population as well as >65-yo patients. However, one panelist pointed out that studies have been case controls, and the population-based study BEST3 used a general population with a median age of 69 (but no other population identifiers) on anti-acid medication as a surrogate marker of GERD (Fitzgerald R., Lancet 2020).

3. Is there evidence available to indicate that there are minimally invasive biomarkers tests that would preclude the need for invasive procedures such as endoscopy (EGD)/biopsy by themselves? If so, how confident are you in your decision to use or not use such currently available testing.

Final Rating:2

The consensus was that the evidence is not strong enough to preclude EGD; however, DNA tests have proven valuable to identify patients in need of EGD (i.e., those with a positive minimally invasive test result), as well as identifying those in who an EGD can be precluded (among a general screening population).

4. What evidence is there to indicate that there could be differences between performing molecular biomarker testing on biopsy samples obtained through endoscopy versus samples obtained through less invasive procedures such as a swallowable balloon, sponge, or other cell collection device?

Final Rating:2

The panelists agreed that EGD with biopsies is still the gold standard method. Though there are likely differences between sponge-obtained results and biopsy results, the panelists expressed low confidence that such comparison studies have been performed.

5. What evidence has been published to indicate a reasonable success rate of swallowing for a non-endoscopic device used for molecular biomarker testing?

Final Rating:4

The consensus was that there is confidence that the success rate in selected populations (people who agreed to the test) is high. However, the rate of refusal to take the test is also high (about 70%) so as a screening test, it is not well accepted. Therefore, the confidence level in people willing to swallow the non-invasive is low. Further, the data examining this was from a large population-based study, so there is also high confidence that this high rate of refusal is accurate.

6. What outcomes are there in the literature indicating how to follow a patient with BE with molecular testing instead of endoscopy?

Final Rating: 2

The consensus was that there is very little published evidence to-date. Most patients in sponge studies (or prognostic biopsy marker studies) are still being followed according to standard EGD surveillance protocols.

7. For the outcomes above, how frequently would this test need to be repeated to ensure continued confidence that the patient has not developed disease needing further investigation?

Final Rating: 1.5

The consensus was that there is not much published data on this question.

8. Have studies determined the percentage of patients with BE, dysplasia (low or high grade), or esophageal adenocarcinoma that may be missed by molecular testing and if so, how long is the delay in diagnosis and are there any associated adverse outcomes?

Final Rating: 2.5

The studies have concentrated on finding BE, not cancer. One study identified 131 BE patients (including 11 LGD-HGD-indef. dysplastic patients + 4 stage I EAC patients) in the tested/intervention group who

would not have been found without the sponge test (Fitzgerald R., Lancet 2020). Delay in testing was not specifically studied, but 2 stage IV + 1 stage I cancers developed in the untested control group. Overall, the panelists expressed low confidence that these tests have clearly demonstrated that they result in fewer delays in diagnosis and adverse outcomes.

9. If a clinically validated biomarker test was available, what are additional barriers to its use?

Final Rating: 2

There are not too many studies on this. The consensus was that there is data on patient acceptance but that the data on barriers to adoption is limited. The consensus was that the test must be cost-effective, be used in a well-defined population, must provide cancer control data (ie cancers detected by the test that result in lives saved), and that patients must be willing to take test.

10. Is there evidence defining the clinical setting in which a non-invasive biomarker assay could be performed?

Final Rating: 3

One panelist said that other than in patients with GERD – no. However, studies looking at high risk populations for BE (Ireland DDS, 2020) would provide a higher yield population. Another panelist said that if the test could be made simple enough, the most 'bang for the buck' would be achieved by home administration, with a second person assisting.