

Point-of-Care Helicobacter Pylori Testing: Primary Care Technology

Update.

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Clinical question:

In adults attending primary care with upper gastrointestinal symptoms, what is the accuracy and utility of point-of-care testing to detect *Helicobacter pylori* infection?

Background and advantages over existing technology

Helicobacter pylori (HP) infection causes approximately 5% of uninvestigated dyspepsia and a 20% lifetime risk of peptic ulcer disease (1). HP is a grade 1 carcinogen: 5.2% of cancers globally are attributable to HP infection (2). HP eradication results in: reduced gastric cancer incidence; prevention of recurrent duodenal (Number Needed to Treat [NNT]= 2) and stomach (NNT = 3) ulceration; and resolution of dyspepsia (NNT = 13) (3).

Non-invasive *Helicobacter pylori* diagnostic tests are appropriate for point-of-care (POC) use in primary care (Table 1). Only the ¹³C-Urea Breath Test (UBT) is sufficiently accurate to confirm current infection or eradication (4). HP IgG serology cannot differentiate current from past infection. Rapid qualitative stool antigen testing currently lacks diagnostic accuracy.

Details of technology

Isotope ratio mass spectrometry (IRMS) is the most commonly used ¹³C-UBT method in the UK, however, the sampling procedure involves many opportunities for test incompleteness: collection of the test from the pharmacy; returning for a subsequent extended appointment; sending the test to the laboratory; awaiting results. In comparison, Non-Dispersive Isotope selective Infrared Spectroscopy (NDIRS) has potential as a POC device; it can be used by non-specialist staff outside the laboratory setting, it is relatively inexpensive, and gives results in 2-5 minutes (4).

Patient group and use

Adults presenting to primary care with: (1)

- Uninvestigated dyspepsia and no alarm symptoms > 4 weeks.
- Past history of gastric or duodenal ulcer, taking or starting NSAIDS.

- Unexplained iron-deficiency anaemia, idiopathic thrombocytopenic purpura, or B12 deficiency with normal colonoscopy and endoscopy.
- Need for confirmation of eradication following treatment.

Previous research

Accuracy compared to existing technology

A meta-analysis of studies including adult dyspeptic patients assessing the diagnostic accuracy of UBTs compared to HP culture and/or histology from biopsy reported pooled sensitivity and specificity of 95% (95% CI, 93-96%) and 93% (91-95%), respectively, for NDIRS, with no significant difference to studies reporting IRMS (5). A multicentre study including 41 patients, some with dyspepsia who had not undergone eradication therapy and others with gastric ulceration receiving eradication, found a close correlation between NDIRS and IRMS with an AUROC of 0.96. NDIRS was more sensitive (100% vs 90%) and less specific (89% vs 96%) (6).

Prior restriction of therapy

Restricting medication prior to testing is necessary to gain an accurate UBT result. NDIRS had a sensitivity of 68% and specificity of 91% in 41 patients who had taken acid suppression or antibiotic medication within three days, and a sensitivity of 100% and specificity of 95% at a threshold between 4 and 5% in 182 patients not taking medication within three days, when compared to histology (7). Sensitivity was 97% (95% CI 94-100%) and specificity 94% (95% CI 87-100%) in 178 fasted patients who had not received eradication therapy (acid suppression, bismuth preparations, or antibiotics) within 1 month, compared to biopsy culture and stain (8). A sensitivity of 96% and specificity of 99% was reported in 177 patients undergoing endoscopy for dyspepsia if they had taken no eradication therapy within the previous 8 weeks, compared with IRMS (9).

Reported thresholds

NDIRS showed 100% agreement at a threshold of 4.0‰ compared to a combined reference standard of ¹⁴C-UBT, rapid urease test and histology in 53 outpatients with duodenal ulceration (10). At 5‰, NDIRS was 98% sensitive and 99% specific compared to IRMS in 538 asymptomatic volunteers (11); 79% sensitive and 96% specific in 145 patients compared with a composite reference standard of histology, culture, and rapid urease testing (12); and displayed a sensitivity of up to 100% and specificity of 95% compared with IRMS in a study of 134 fasted dyspeptic patients with non-ulcer dyspepsia (97 cases) or duodenal ulceration (37 cases) (13).

Impact compared to existing technology

We retrieved no studies reporting on the impact of POC NDIRS in primary care. One large study included 44,487 patients >45yrs who met test-and-treat criteria. Breath samples were collected at home and mailed to the laboratory for NDIRS analysis (14). One in five patients tested

positive, although 726 samples (1.6%) were not included due to bag errors. The authors concluded a test-and-treat system involving home testing was feasible.

Cost- effectiveness

No cost-effectiveness studies have been carried out on POC testing for HP infection in primary care. ¹³C-UBT testing in dyspeptic patients was found to be cost-effective in one study, with an incremental cost-effectiveness ratio (ICER) of £1000 per quality-adjusted life year compared to not testing at all. (15). However, cost-effectiveness studies in other populations have not found ¹³C-UBT testing to be cost-effective, providing only small health benefits while significantly increasing costs compared to other tests (16).

Relevant guidelines

International guidelines recommend: (1) a 2-week restriction of proton pump inhibitor (PPI) use, and 4 weeks of antibiotics and bismuth compounds, before HP testing; (2) a ¹³C-UBT 'test-and-treat' strategy in patients with uninvestigated dyspepsia without alarm symptoms; (3) testing in aspirin and NSAID users with a history of peptic ulcer; (4) testing and eradication in unexplained iron deficiency anaemia (IDA), idiopathic thrombocytopenic purpura (ITP), and vitamin B12 deficiency; (5) ¹³C-UBT retesting >4 weeks after eradication therapy (1).

What this technology adds

The NDIRS ¹³C-UBT is more accurate than other non-invasive POC tests for the diagnosis of HP infection and confirmation of HP eradication. It has comparable accuracy to laboratory-based IRMS but has the potential to reduce delays in testing by enabling a rapid diagnosis, prior to treatment initiation. However, the health benefit of this reduction compared to non-POC tests is unclear.

The lack of robust evidence on the comparative accuracy of NDIRS in the primary care setting, and the impact of NDIRS testing on endoscopy demand, needs urgent attention.

The available evidence suggests that, for patients with upper gastrointestinal symptoms, primary care based NDIRS testing may reduce diagnostic delay and could reduce inappropriate prescription of eradication therapy by accurately confirming current infection.

Methodology

Standardised methodology was applied in writing this report, using prioritisation criteria and a comprehensive, standardised search strategy, and critical appraisal. Full details of these are available from

<https://www.oxford.dec.nihr.ac.uk/reports-and-resources/horizon-scanning-reports/>

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Table 1: Non-invasive tests to diagnose *Helicobacter pylori* infection.

Test	Example testing procedure	Confirms current infection	Accuracy		Benefits	Drawbacks
			Sensitivity	Specificity		
IgG serology	Venous blood sent to laboratory for Immunoglobulin-G antibody testing.	No	75-85%	79-90%	-Widely available. -Inexpensive.	-A positive test may represent past infection. -Delay for result.
¹³C-Urea Breath test	Breath collected before and 15-30mins after drinking a ¹³ C-urea substrate solution. HP urease hydrolyses ¹³ C-urea. Breakdown products absorbed into circulation. Exhaled as ¹³ CO ₂ . Detected by either: (1) isotope ratio mass spectrometry (IRMS); (2) non-dispersive isotope-selective infrared spectroscopy (NDIRS) comparing the rotation-vibration bands in the infrared range of electromagnetic spectra; (3) laser-assisted ratio analyser (LARA).	Yes	>95%	>95%	-Detects active infection before and after treatment. -IRMS widely available in laboratory setting. -Rapid point-of-care NDIRS devices available.	-Breath collection kits only available on prescription in some settings. -Delay in obtaining laboratory IRMS result. -NDIRS and LARA devices not widely tested in primary care populations.
Monoclonal stool antigen	Stool sample either (1) sent to the laboratory for HP antigen detection using a monoclonal enzyme immunoassay test or (2) HP detected using a rapid point-of-care qualitative immunochromatographic test.	Yes	>95%	>95%	-Detects active infection before and after treatment. -Accurate laboratory (quantitative) tests widely available.	-Delay in laboratory result. -Rapid (qualitative) tests show variable accuracy.

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