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Prioritising Summary

Rapid test for *Helicobacter pylori* diagnosis of patients presenting with symptoms of dyspepsia

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PRIORITISING SUMMARY

REGISTER ID: **000416**

NAME OF TECHNOLOGY: **RAPID TEST FOR HELICOBACTER PYLORI**

PURPOSE AND TARGET GROUP: **DIAGNOSIS OF PATIENTS PRESENTING WITH SYMPTOMS OF DYSPEPSIA OR FOR FOLLOW UP OF ERADICATION.**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

- ☐ Yet to emerge
- ☐ Experimental
- ☒ Investigational
- ☐ Nearly established
- ☐ Established
- ☐ Established *but* changed indication or modification of technique
- ☐ Should be taken out of use

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- ☐ Yes — ARTG number
- ☒ No[1]
- ☐ Not applicable

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
US		✓	
UK		✓	
Australia	✓		
Several other countries	✓	✓	

IMPACT SUMMARY:

Local medical clinics could use *H pylori* rapid diagnostic tests to cheaply diagnose patients with low resource investment. This would be an important arm of any eradication scheme for *H pylori*.

BACKGROUND

Helicobacter pylori is a bacteria which has been accepted as a major contributor to the development of gastric cancer (Fock et al 2008). There are calls to investigate the potential to eradicate *H pylori* in high risk populations (Talley 2008). The accurate diagnosis of a subject's *H pylori* status is important for correct therapy and additionally for eradication programmes. For broad application, *H pylori* testing

[1] Only one H pylori diagnostic test was found on the TGA database. As this was not a product reviewed in this prioritising summary its ARTG number was deemed irrelevant.

should be effective, rapid, cheap and widely available. There are several diagnostic tests with a variety of modalities to evaluate a patient's *H pylori* status. Rapid faecal *H pylori* antigen tests are becoming more widely used due to their low equipment requirements and ease of use. These tests are generally based on immunochromatographic reactions between monoclonal antibodies to *H pylori* and *H pylori* antigens that may be present in the patient stool sample. Stool samples are diluted in a specific diluent and subsequently applied to a support matrix. A positive test for *H pylori* infection is indicated by the appearance of both a control line and a test line on the support matrix. A negative test is indicated by the appearance of only the control line. Any other combination or lack of lines on the matrix indicates an invalid result. Several manufacturers have versions of this diagnostic test, which all follow the same principles. Additionally, enzyme-linked immunoassays can also be used to diagnose *H pylori* infection from stool samples, however these tests are more intensive regarding resources and are not as rapid.

CLINICAL NEED AND BURDEN OF DISEASE

The prevalence of *H pylori* in Australia varies with the population tested. A general epidemiological study found that across a wide subset of the Australian population the prevalence was 15.4 per cent (Moujaber et al 2008). Previous studies in smaller and more local populations found that the prevalence was as high as 38 per cent in an Anglo-Celtic population residing in Melbourne (Lin et al 1998) and 76 per cent in a Western Australian aboriginal population (Windsor et al 2005).

Stomach cancer incidence has been in decline in developed countries for several decades and Australia is no exception. From 1983 to 2003 the age standardised incidence of stomach cancer has dropped from 15.8 per to 9.2 per 100,000 population. This drop may be attributed to improved living standards reducing the prevalence of *H pylori* with an increase in fruit and vegetable consumption combined with a reduced intake of salt and smoke preserved food (AIHW 2007; Fock et al 2008).

DIFFUSION

Some Australian studies have used stool based *H pylori* detection tests. There are limited indications that these tests are being used in some clinical settings for research purposes (Day et al 2004).

COMPARATORS

The current non-invasive diagnostic gold standard is the Urea Breath Test (UBT). This test relies on the ability of *H pylori* to breakdown urea. The breakdown releases carbon dioxide which is absorbed into the blood and passes out of the body in the subject's breath. The urea is labelled with an isotope of carbon and can be quantitated in the subject's breath. There are two main types of UBT which use either carbon-13 or carbon-14 labelled urea. While this test is rapid it is also equipment intensive and expensive. In addition several factors such as bleeding ulcers, or antibiotic treatments

reduce the effectiveness of the UBT resulting in false negatives (Stenstrom et al 2008). Compared to histology it is estimated that the UBT is 95% sensitive and 95% specific when diagnosing *H pylori* infections (Vaira & Vakil 2001).

SAFETY AND EFFECTIVENESS ISSUES

There is a significant amount of recent literature published evaluating immunochromatographic tests for detection of *H pylori* antigens in stool samples. Due to the space constraints of prioritising summaries only the studies which included larger populations or compared several tests were analysed in this summary.

A study compared four *H pylori* stool antigen tests to UBT in their ability to confirm the eradication of *H pylori* after therapy in 97 patients. The tests evaluated were two rapid imunochromatographic tests (RAPID Hp StAR[2] and ImmunoCard STAT! HpSA[3]) a monoclonal EIA[4] test (Amplified IDEIA Hp StAR[5]), and a polyclonal EIA test (Premier Platinum HpSA[6]). After the eradication therapy, patients were tested for *H pylori* and the results compared to the reference standard (not stated). The sensitivities and specificities are summarised in Table 1. Of all the tests, the ImmunoSTAT! performed the best with a sensitivity and specificity of 91 and 97 per cent, respectively (Quesada et al 2006) (Level III-2 diagnostic evidence).

Table 1 Test results compared to reference standard

Test name	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
RAPID Hp StAR	73	96-98	73-80	96
ImmunoCard STAT! HpSA	91	97	77	99
Amplified IDEIA Hp StAR	73	97	73	97
Premier Platinum HpSA	91	79	35	98

Two stool tests, an EIA (Novitec EIA[7]) and a rapid immunochromatographic test (Stick H. pyl[8]) were compared to three reference tests: histology, rapid urease test and urea breath test. The study prospectively recruited 100 patients (50 *H pylori* positive and 50 *H pylori* negative). The patients were classified as positive if diagnosed positive by ≥2 reference tests and as negative if diagnosed negative by all reference tests. The results of the two experimental tests compared to the reference tests are summarised in Table 2 (Kyrlagkitsis et al 2007) (Level III-2 diagnostic evidence).

[2] DakoCytomation, Cambridge, UK
[3] Meridian Diagnostics, Cincinnati, OH
[4] Enzyme-linked immunoassay
[5] DakoCytomation, Cambridge, UK
[6] Meridian Diagnostics, Cincinnati, OH
[7] HiSS Diagnostics GmbH, Freiburg, Germany
[8] Operon S.A. Zaragoza

Table 2 Test results compared to the reference standards

Test name	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Novitec EIA	82	94	93	84
Stick H. pyl	78	78	76	78

Six *H pylori* stool antigen tests (3 EIA and 3 immunochromatographic tests) were evaluated in a population of 98 patients undergoing routine upper gastrointestinal endoscopy. The reference standards were histology, rapid urease test and urea breath test. Positive patients were classified as such if diagnosed positive ≥2 reference tests and as negative if diagnosed negative in all reference tests. The EIA tests were: Premier Platinum HpSA EIA test[9], Immundiagnostik ELISA[10], Amplified IDEIA™ HpStAR™[11]. The immunochromatographic tests were Letitest *H pylori* CARD[12], ImmunoCard STAT! HpSA[13], RAPID HpStAR™[14]. The results of the tests are summarised in Table 3 (Blanco et al 2008) (Level III-2 diagnostic evidence).

Table 3 Test results compared to the reference standards

Test name	Sensitivity % (test positive/reference positive)	Specificity % (test negative/reference negative)
EIA Tests		
Immundiagnostik ELISA	87.3 (69/79)	83.3 (15/18)
Premier Platinum HpSA EIA	92.5 (74/80)	72.2 (13/18)
Amplified IDEIA™ HpStAR™	95.0 (76/80	66.6 (12/18)
Immunochromatographic tests		
H. pylori Letitest	83.8 (67/80)	66.6 (12/18)
ImmunoCard STAT! HpSA	52.5 (42/80)	94.4 (17/18)
RAPID HpStAR™	78.8 (63/80)	55.5 (10/18)

A study with a population of 240 patients evaluated two stool based *H pylori* tests against histology, rapid urease test, urea breath test and bacterial culture. Patients were deemed positive if the culture results were positive or if two or more of the histology, rapid urease test or urea breath tests were positive. The patients were tested both before and after *H pylori* eradication therapy. The tests used were the ImmunoCard STAT! HpSA (immunochromatographic test) and the Premier Platinum HpSA (EIA). The post-eradication testing was performed 2-4 months after the completion of the eradication therapy. The results compared to the reference standards are shown in Table 4 (Wu et al 2006) (Level III-2 diagnostic evidence).

[9] Meridian Diagnostics, Cincinnati, OH
[10] Immundiagnostik, Bensheim, Germany
[11] Dako, Cambridge, UK
[12] (Laboratorios Leti, Barcelona, Spain)
[13] (Meridian Diagnostics),
[14] Dako, Cambridge, UK

Table 4 Test results compared to the reference standards

Test name	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Pre-eradication (n=176)				
ImmunoCard STAT! HpSA	95.2	87.0	90.4	93.1
Premier Platinum HpSA	83.8	90.9	92.2	81.4
Post-eradication (n=100)				
ImmunoCard STAT! HpSA	100	91.0	84.6	100
Premier Platinum HpSA	84.9	92.5	84.8	92.5

In summary, the *H pylori* rapid diagnostic stool tests reviewed in these studies performed with similar levels of sensitivity and specificity. Overall the best performer seemed to be the ImmunoCard STAT! HpSA although in one study this test did show a significantly lower sensitivity. In the hands of different researchers there were significant differences in the performance of some tests. To some extent this variability is expected due to different population sources and different treatments for the patients, for example whether they were undergoing eradication therapy. Additionally, there are many more studies that could not be reviewed for this prioritising summary. Overall most of the rapid stool tests compared well to the established diagnostic standards.

COST IMPACT

The cost per test using the Premier Platinum HpSA Plus kit or the ImmunoCard STAT! HpSA kit is US$50 and US$55, respectively. Additional costs, apart from labour, are not expected as the kits contain all required materials for use.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified/raised in the sources examined.

OTHER ISSUES

No issues were identified/raised in the sources examined.

SUMMARY OF FINDINGS

Based on the small subsection of the literature reviewed in this prioritising summary, the *H pylori* rapid diagnostic stool tests showed good sensitivity with excellent specificity. The ImmunoCard STAT! HpSA was the best performer in most cases. A large amount of studies are available on these diagnostic tests.

HEALTHPACT ACTION:

Given the potential links to gastric cancer and lymphoma, HealthPACT recommended that a Horizon Scanning report be commissioned, combining an assessment of rapid testing for *Helicobacter pylori* and screening for *Helicobacter pylori* in targeted populations.

NUMBER OF INCLUDED STUDIES

Total number of studies

Level III-2 Diagnostic evidence 4

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Wu, D. C., Wu, I. C. et al (2006). 'Comparison of stool enzyme immunoassay and immunochromatographic method for detecting Helicobacter pylori antigens before and after eradication', *Diagn Microbiol Infect Dis,* 56 (4), 373-378.

SEARCH CRITERIA TO BE USED:

Dyspepsia/etiology/ microbiology/pathology

Immunoassay/ methods

Helicobacter Infections/diagnosis

Chromatography/ methods