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Carbon-13 Urea Breath Test for *Helicobacter Pylori* Infection in Patients with Uninvestigated Ulcer-Like Dyspepsia: An Evidence-Based Analysis

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Abstract

Background

Dyspepsia is a condition defined by chronic pain or discomfort in the upper gastrointestinal tract that can be caused by *Helicobacter pylori*. The carbon-13 urea breath test (^{13}C UBT) is a non-invasive test to detect *H. pylori*.

Objectives

We aimed to determine the diagnostic accuracy and clinical utility of the ^{13}C UBT in adult patients with ulcer-like dyspepsia who have no alarm features.

Data Sources

A literature search was performed using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase, the Wiley Cochrane Library, and the Centre for Reviews and Dissemination database, for studies published between 2003 and 2012.

Review Methods

We abstracted the sensitivity and specificity, which were calculated against a composite reference standard. Summary estimates were obtained using bivariate random effects regression analysis.

Results

From 19 diagnostic studies, the ^{13}C UBT summary estimates were 98.1% (95% confidence interval [CI], 96.3–99.0) for sensitivity and 95.1% (95% CI, 90.3–97.6) for specificity. In 6 studies that compared the ^{13}C UBT with serology, the 1^{13}C UBT sensitivity was 95.0% (95% CI, 90.1–97.5) and specificity was 91.6 % (95% CI, 81.3–96.4). The sensitivity and specificity for serology were 92.9% (95% CI, 82.6–97.3) and 71.1% (95% CI, 63.8–77.5), respectively. In 1 RCT, symptom resolution, medication use, and physician visits were similar among the ^{13}C UBT, serology, gastroscopy, or empirical treatment arms. However, patients tested with ^{13}C UBT reported higher dyspepsia-specific quality of life scores.

Limitations

Processing of the ^{13}C UBT results can vary according to many factors. Further, the studies showed significant heterogeneity and used different composite reference standards.

Conclusions

The ^{13}C UBT is an accurate test with high sensitivity and specificity. Compared with serology, it has higher specificity. There is a paucity of data on the ^{13}C UBT beyond test accuracy.

Plain Language Summary

Breath test for detecting bacteria in patients with ulcer-like symptoms

Dyspepsia is a condition that causes long-term pain or discomfort in the upper abdomen. Symptoms can include heartburn, burping, bloating, nausea, or slow digestion. Dyspepsia can be caused by a bacterium that also causes ulcers and stomach cancer. Half of the world's people are believed to be infected with these bacteria. A test has been developed to detect the bacteria in a breath sample. Our review determined the accuracy of this breath test in adults with ulcer-like symptoms.

From 19 studies, the breath test correctly identified 98% of patients with the bacteria and 95% of patients without the bacteria, as determined by a reference standard. Six studies compared the breath test to a blood test that is currently used. Both the breath and blood tests performed well in correctly identifying patients with the bacteria. However, the blood test was incorrectly positive in 20 more patients who did not have the bacteria according to the breath test. This means that more patients would have received unnecessary treatment.

Thus, the breath test is an accurate test to detect the bacteria in adult patients who have ulcer-like symptoms. But the many differences among the studies in our review included several steps taken to perform the breath test and the reference standards used to compare a blood test with the breath test.

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List of Abbreviations

AUC	Area under the curve
C	Carbon
CI	Confidence interval
HQO	Health Quality Ontario
LR	Likelihood ratio
RCT	Randomized controlled trial
SROC	Summary receiver operating characteristic
UBT	Urea breath test

Background

Objective of Analysis

We aimed to determine the diagnostic accuracy and clinical utility of the carbon-13 urea breath test (^{13}C UBT) for detection of *Helicobacter pylori* infection in adult patients with uninvestigated ulcer-like dyspepsia and who have no alarm features, for whom endoscopy is not indicated.

Clinical Need and Target Population

Description of Condition

Dyspepsia is a condition of the upper gastrointestinal tract that causes such symptoms as heartburn, acid regurgitation, excessive belching, abdominal bloating, nausea, abnormal or slow digestion, and early satiety. (1) Dyspepsia can have many underlying causes, including infection with *H. pylori*.

Global Prevalence and Incidence

The prevalence of *H. pylori* in the world has been estimated to be as much as 50%. (2) Developing countries have a higher burden of infection than developed countries. Infection with the bacteria is an important cause of chronic gastritis, peptic ulcer disease, mucosa-associated lymphoid tissue lymphoma, and gastric cancer. *H. pylori* is a class I carcinogen according to the World Health Organization. (3)

Ontario Prevalence and Incidence

In Ontario, the prevalence of *H. pylori* is 23% according to a published study. (4) The study found that men were more likely to be infected than women. Older age and immigration were also important risk factors for infection. Further, dyspepsia has been shown to affect 29% of Canadians in a population-based survey, and half of them reported chronic symptoms. (5) Approximately 30% of dyspeptic patients in primary care are infected with *H. pylori*. (6)

Technology/Technique

Detection of *H. pylori* can rely on invasive, endoscopy-based methods (e.g., culture, histology, or rapid urease test) or non-invasive tests. Endoscopy is clinically indicated for elderly patients or patients of any age who present with alarm features: weight loss, abdominal mass, dysphagia, persistent vomiting, gastrointestinal bleeding, or anemia. (1)

There are 3 main types of non-invasive tests: serology, stool antigen, and UBT. Serologic testing, which relies on the detection of antibodies in the blood, is the currently funded first-line diagnostic test in Ontario. The UBT relies on the ability of *H. pylori* to convert into carbon dioxide urea that has been labelled with isotopes and then ingested by the patient. The difference in carbon dioxide levels between the baseline breath sample (before ingestion of urea) and the postadministration breath sample is detected by specialized measuring equipment (e.g., mass spectrometer or infrared spectrophotometer). (7)

Urea can be labelled with either the ^{13}C or ^{14}C isotope. The ^{14}C isotope is mildly radioactive and not recommended for children or pregnant women. (8) The ^{13}C isotope is not radioactive and thus is more frequently used. Another advantage of the UBT is that it can be used to evaluate the success or failure of eradication therapy, whereas serology results can remain positive for an extended period even after successful treatment. (9)

Regulatory Status

The protocol for performing the ^{13}C UBT can vary according to many factors, including use of a citric acid test meal, dose of urea, time of breath collection, measuring equipment, or test cut-off value. (8) Two commercial kits with standardized protocols are licensed by Health Canada. The Helikit ^{13}C breath test kit is a class 2 device (licence number 805) manufactured by IsoDiagnostika, a division of Paladin Labs Inc. (Edmonton, Alberta) and is licensed to detect *H. pylori* as the causative organism in peptic ulcers. The Dia13-Helico Breath Test Kit (licence number 64105) is a class 2 device manufactured by R.A.D. Diagnostics (St-Laurent, Quebec) and is also licensed to detect *H. pylori*.

Evidence-Based Analysis

Research Question

What is the diagnostic accuracy and clinical utility of the ^{13}C UBT for detecting *H. pylori* in adults with uninvestigated ulcer-like dyspepsia who have no alarm features?

Research Methods

Literature Search

Search Strategy

A literature search was performed on December 14, 2012, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid Embase, the Wiley Cochrane Library, and the Centre for Reviews and Dissemination database, for studies published from January 1, 2003, until December 14, 2012. (Appendix 1 provides details of the search strategies.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria

- full reports in English;
- studies published between January 1, 2003, and December 14, 2012;
- studies that include adult patients with ulcer-like dyspepsia and without alarm features;
- studies that evaluate the ^{13}C UBT as a first-line diagnostic test or post-treatment test;
- studies that used endoscopy-based methods as the reference standard, with agreement on at least 2 tests.

Exclusion Criteria

- studies with only children or elderly patients,
- studies where data to calculate sensitivity and specificity could not be abstracted,
- studies using a single test as the reference standard.

Outcomes of Interest

- sensitivity and specificity,
- effect on patient management or clinical decision-making,
- patient-important outcomes.

Statistical Analysis

We calculated the sensitivity, specificity, positive likelihood ratio (LR+), and negative likelihood ratio (LR−) for cross-sectional studies of accuracy. Sensitivity is the proportion of positive test results among patients with the disease. Specificity is the proportion of negative test results among those without the disease. The LR+ measures how more frequent a positive test is found in diseased versus non-diseased

patients. On the other hand, the LR− measures whether a negative result is more likely to be found in diseased than in non-diseased patients.

Summary estimates were obtained using bivariate random-effects regression analysis in Stata (10) with the user-written program "metandi." (11) This method assumes that the sensitivity and specificity data undergoing logit-transformation from individual studies are normally distributed around a mean value with a certain amount of variability around this mean. (12) The potential presence of a negative correlation between sensitivity and specificity within studies is addressed by explicitly incorporating this correlation into the analysis. The combination of the 2 normally distributed outcomes, the sensitivity and specificity data undergoing logit-transformation, and the possible correlation between them, leads to the bivariate normal distribution. (12)

Summary measures were calculated using this random-effects approach to account for the heterogeneity among studies and to better enable comparisons between different tests. These estimates were also used as inputs into the economic model.

In addition, we performed the summary receiver operating characteristic (SROC) curve analysis. (13) The SROC curve displays each study's sensitivity and specificity within the receiver operating characteristic space. A regression curve is fitted through the distribution of pairs of sensitivity and specificity. The area under the curve (AUC) measures the overall accuracy of diagnostic tests. The forest plots and SROC curves were created using Meta-DiSc software. (14)

Quality of Evidence

The quality of the body of evidence for each outcome was examined according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group criteria. (15) The overall quality was determined to be high, moderate, low, or very lowthrough use of a step-wise, structural method.

Study design was the first consideration; the starting assumption was that randomized controlled trials (RCTs) are high quality, whereas observational studies are low quality. Five additional factors—risk of bias, inconsistency, indirectness, imprecision, and publication bias—were then taken into account. Limitations in these areas resulted in downgrading the quality of evidence. Finally, 3 main factors that could raise the quality of evidence were considered: large magnitude of effect, dose response gradient, and accounting for all residual confounding factors. (15) For more detailed information, please refer to the latest series of GRADE articles. (15)

As stated by the GRADE Working Group, the final quality score can be interpreted using the following definitions:

High	Very confident that the true effect lies close to the estimate of the effect
Moderate	Moderately confident in the effect estimate—the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Confidence in the effect estimate is limited—the true effect may be substantially different from the estimate of the effect
Very Low	Very little confidence in the effect estimate—the true effect is likely to be substantially different from the estimate of effect

Results of Evidence-Based Analysis

The database search yielded 1,761 citations published between January 1, 2003, and December 14, 2012 (with duplicates removed). Articles were excluded on the basis of information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment. Figure 1 shows the breakdown of when and for what reason citations were excluded in the analysis.

Twenty-one studies (19 diagnostic accuracy studies, 1 post-treatment accuracy study, and 1 RCT) met the inclusion criteria. The reference lists of health technology assessments were hand searched to identify any additional potentially relevant studies, and no additional citations were found.

Sensitivity and specificity were calculated against a composite reference standard consisting of at least 2 tests. While several different reference standards were found in the included studies, the most common one was based on the culture result and, if this was negative, then concordance on histology and the rapid urease test. Nine of the 19 diagnostic accuracy studies reported results using this reference standard.

From the 19 diagnostic accuracy studies, the summary estimates of the ^{13}C UBT were 98.1% (95% CI, 96.3%–99.0%) for sensitivity and 95.1% (95% CI, 90.3%–97.6%) for specificity (Figures 2 and 3). The summary LR+ and LR− estimates were 19.9 (95% CI, 9.9–39.9) and 0.02 (95% CI, 0.01–0.04), respectively. The AUC was 98.8% (95% CI, 97.4%–100%).

In 6 studies that compared the ^{13}C UBT to serology in head-to-head trials (16-21), the sensitivity for ^{13}C UBT was 95.0% (95% CI, 90.1%–97.5%) and specificity was 91.6% (95% CI, 81.3%–96.4%). The LR+ and LR− were 11.3 (95% CI, 4.8–26.6) and 0.05 (95% CI, 0.03–0.11), respectively. The AUC was 97.3% (95% CI, 95.2%–99.4%).

The performance of serologic tests was lower when compared directly to the ^{13}C UBT. The sensitivity for serology was 92.9% (95% CI, 82.6%–97.3%) and specificity was 71.1% (95% CI, 63.8%–77.5%). The LR+ and LR− were 3.2 (95% CI, 2.4–4.3) and 0.10 (95% CI, 0.04–0.28), respectively. The AUC was 91.9% (95% CI, 83.7%–100%).

Two studies (including 1 study with both diagnostic and post-treatment accuracy data) evaluated the performance of the ^{13}C UBT to assess treatment eradication, which occurred when culture, histology, and rapid urease test results were all negative. In the first study of 109 patients with dyspepsia who were administered the ^{13}C UBT 4 to 6 weeks after therapy, the sensitivity was 100% (95% CI, 85.2%–100%), and the specificity was 100% (95% CI, 95.8%–100%). (22) In the second study of 325 gastroenterology referrals, the sensitivity was 98.9% (95% CI, 94.2%–100%), and the specificity was 99.6% (95% CI, 97.6%–100%). (23)

In a small RCT that compared management strategies for patients with dyspepsia and no alarm symptoms in a primary care setting, patients were randomized to empirical therapy with a histamine receptor antagonist (n = 11), serologic testing (n = 8), ^{13}C UBT testing (n = 11), or gastroscopy (n = 13). (24) Resolution of symptoms at 6 weeks and 6 months was similar across all the management arms (P = 0.49), and there were also no differences for medication use or number of physician visits. Pairwise comparisons among the various strategies showed that patients in the ^{13}C UBT group had higher dyspepsia-specific, health-related quality of life scores than those receiving empirical therapy (P = 0.007), serology (P = 0.01), and gastroscopy (P = 0.02).

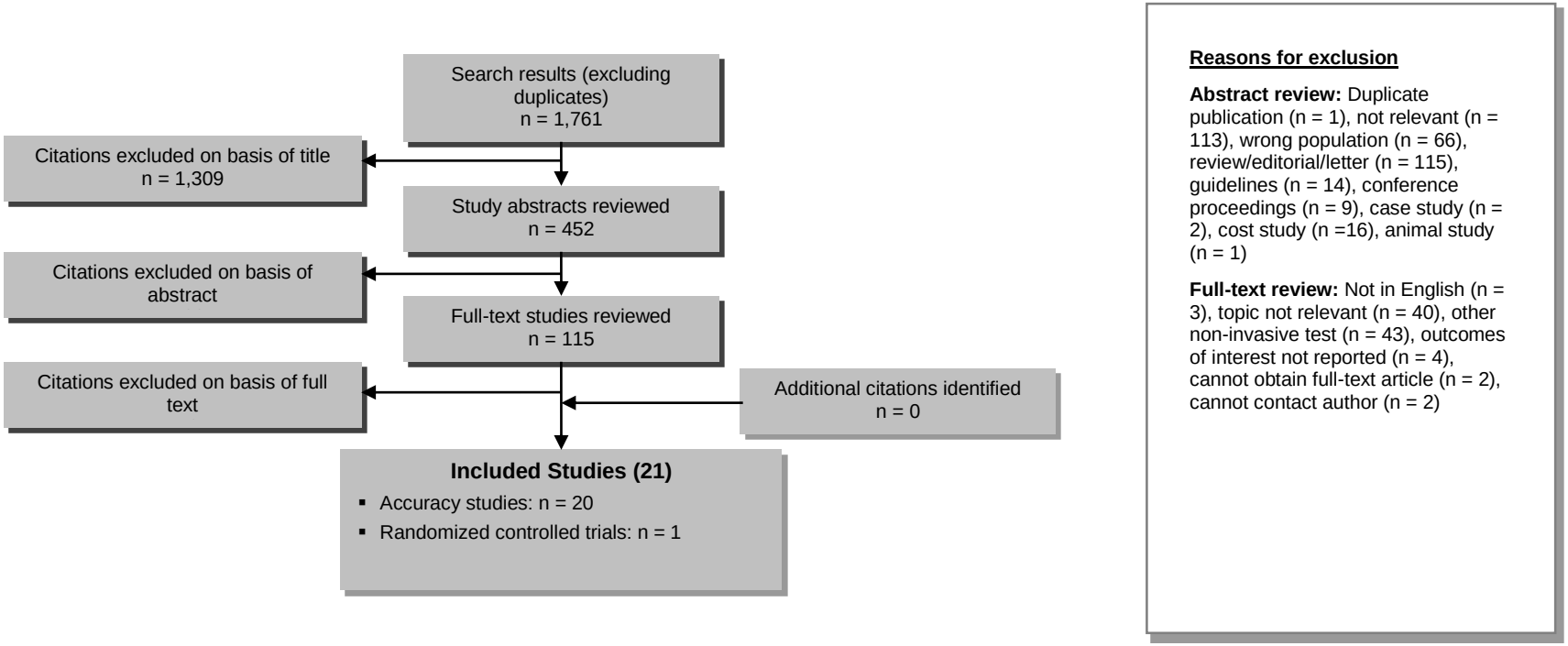

Figure 1: Citation Flow Chart

For each included study, the study design was identified and is summarized below in Table 1, which is a modified version of a hierarchy of study design by Goodman. (25) Table 2 summarizes guidelines for uninvestigated dyspepsia in various countries.

Table 1: Body of Evidence Examined According to Study Design

Study Design	Number of Eligible Studies
RCTs	
Systematic review of RCTs	
Large RCT	
Small RCT	1
Observational Studies	
Systematic review of non-RCTs with contemporaneous controls	
Non-RCT with non-contemporaneous controls	
Systematic review of non-RCTs with historical controls	
Non-RCT with historical controls	
Database, registry, or cross-sectional study	20
Case series	
Retrospective review, modelling	
Studies presented at an international conference	
Expert opinion	
Total	21

Abbreviation: RCT, randomized controlled trial.

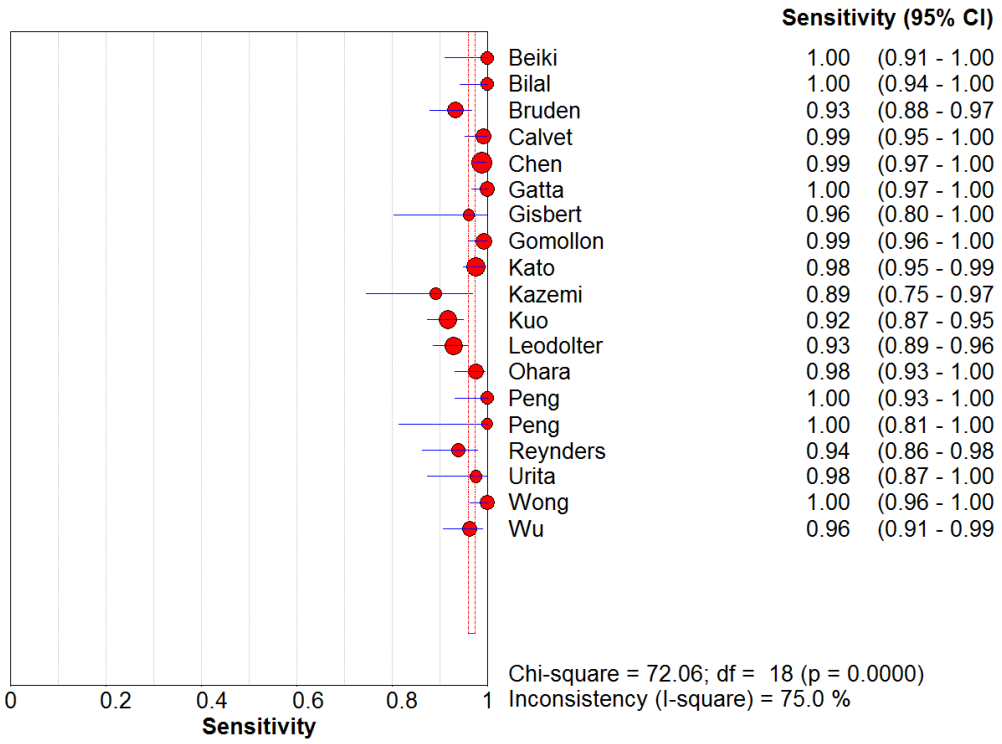

Figure 2: Sensitivity Estimates from 19 Diagnostic Studies of Carbon-13 Urea Breath Test

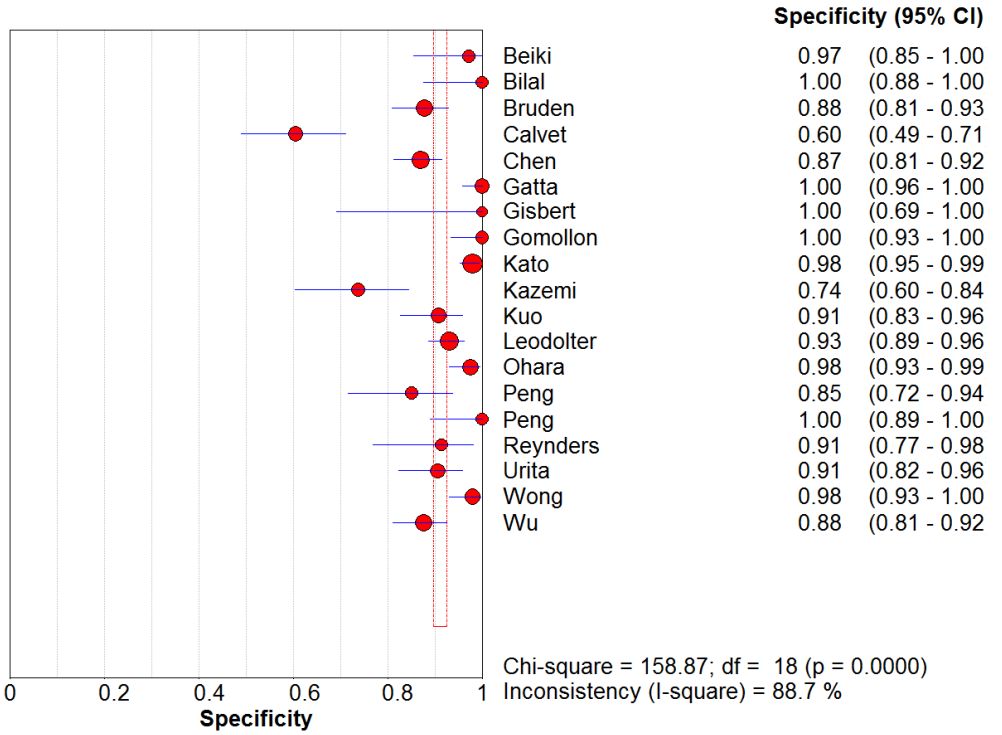

Figure 3: Specificity Estimates from 19 Diagnostic Studies of Carbon-13 Urea Breath Test

Conclusions

- The ^{13}C UBT is an accurate test with high sensitivity and high specificity for both diagnostic and treatment monitoring.
- In head-to-head comparisons with serology, the ^{13}C UBT has comparable sensitivity but higher specificity.
- There is no standardized protocol for performing the non-commercial ^{13}C UBT, and the procedure can vary according to many factors.
- Further, the studies that evaluated the performance of the ^{13}C UBT used different composite reference standards.
- There is a paucity of data on the use of the ^{13}C UBT beyond test accuracy.

Existing Guidelines for Technology

Table 2: Comparison of Guidelines for Uninvestigated Dyspepsia in Various Countries

Country	Guidelines
Canada (26)	Test and treat if patient < 50 years and has no alarm symptoms[a]; UBT is the diagnostic test of first choice, while there is insufficient evidence to recommend the stool antigen test (27)
United States (28)	Test and treat if patient < 55 years of age and has no alarm symptoms; UBT and stool antigen test are the diagnostic tests of choice
Europe (29)	Test and treat if patient has no alarm symptoms; UBT and stool antigen test are the diagnostic tests of choice
Asia Pacific (30)	Test and treat if patient has no alarm symptoms; UBT and stool antigen test are the diagnostic tests of choice

Abbreviation: UBT, urea breath test.

[a]Alarm symptoms include weight loss, presence of abdominal mass, dysphagia, persistent vomiting, gastrointestinal bleeding, or anemia.

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Appendices

Appendix 1: Literature Search Strategies

Search date: December 14, 2012
Databases searched: Ovid MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, Embase, Cochrane Library, Centre for Reviews and Dissemination

Q: What is the diagnostic accuracy and clinical utility of Urea Breath Test in adults with suspected dyspepsia with *Helicobacter pylori*, compared to endoscopy and other tests?
Limits: 2003-current; English; Humans
Filters: None

Database: Ovid MEDLINE® <1946 to November Week 3 2012>, Ovid MEDLINE® In-Process & Other Non-Indexed Citations <December 13, 2012>, Embase <1980 to 2012 Week 49>
Search Strategy:

#	Searches	Results
1	exp Helicobacter pylori/	68439
2	Helicobacter Infections/ use mesz	23191
3	exp Helicobacter infection/ use emez	19241
4	((helicobacter or campylobacter or h) adj2 pylori*).ti,ab.	72636
5	or/1-4	84474
6	exp Breath Tests/ use mesz	10521
7	exp urea breath test/ use emez	1916
8	breath analysis/ use emez	10074
9	(urea adj2 breath*).ti,ab.	5551
10	(carbon* adj2 urea).ti,ab.	434
11	(CUBT* or UBT* or 13C or 14C).ti,ab.	164413
12	(Helikit* or Meretek* UBT or PYtest* or UBIT* or Helibactertest*).ti,ab.	70
13	or/6-12	182311
14	5 and 13	7415
15	limit 14 to english language	6438
16	limit 15 to human	5881
17	limit 16 to yr="2003 -Current"	2955
18	remove duplicates from 17	1795

Cochrane

ID	Search	Hits
#1	MeSH descriptor: [Helicobacter pylori] explode all trees	1829
#2	MeSH descriptor: [Helicobacter Infections] explode all trees	1784
#3	((helicobacter or campylobacter or h) near/2 pylori*):ti (Word variations have been searched)	2676
#4	#1 or #2 or #3	2947
#5	MeSH descriptor: [Breath Tests] explode all trees	1159
#6	(urea near/2 breath*) or (carbon* near/2 urea):ti (Word variations have been searched)	78
#7	(CUBT* or UBT* or 13C or 14C):ti (Word variations have been searched)	204
#8	(Helikit* or Meretek* UBT or PYtest* or UBIT* or Helibactertest*):ti,ab,kw (Word variations have been searched)	1
#9	#5 or #6 or #7 or #8	1314
#10	#4 and #9 from 2003 to 2012	129

Centre for Reviews and Dissemination

Line	Search	Hits
1	MeSH DESCRIPTOR helicobacter pylori EXPLODE ALL TREES	257
2	MeSH DESCRIPTOR helicobacter infections EXPLODE ALL TREES	248
3	((helicobacter or campylobacter or h) adj2 pylori*):TI	229
4	#1 OR #2 OR #3	288
5	MeSH DESCRIPTOR breath tests EXPLODE ALL TREES	50
6	((urea adj2 breath*) or (carbon* adj2 urea)):TI	8
7	(CUBT* or UBT* or 13C or 14C):TI	4
8	(Helikit* or Meretek* UBT or PYtest* or UBIT* or Helibactertest*):TI	0
9	#5 OR #6 OR #7 OR #8	52
10	#4 AND #9	29
11	(#10):TI FROM 2003 TO 2012	18

Appendix 2: GRADE Tables

Table A1: GRADE Evidence Profile for Accuracy Studies

Number of Studies (Design)	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Quality
20 (accuracy)	No serious limitations	Serious limitations (-1)[a]	Serious limitations (-1)[b]	No serious limitations	Undetected	⊕⊕ Low

[a]Significant heterogeneity present in summary estimates of sensitivity, specificity, and likelihood ratios.
[b]Test accuracy is only a surrogate for patient-important outcomes.

Table A2: Risk of Bias Among Randomized Controlled Trials for Comparison of Management Strategies

Author, Year	Allocation Concealment	Blinding	Complete Accounting of Patients and Outcome Events	Selective Reporting Bias	Other Limitations
Cuddihy et al, 2005 (24)	No limitations	Limitations[a]	No limitations	No limitations	Limitations[b]

[a]Blinding of management strategy was impossible for patients and providers.
[b]Outcomes on resolution of symptoms, medication use, physician visits, and dyspepsia-specific quality of life were patient reported.

Appendix 3: Summary Table

Table A3: Data from Studies Included in Review

Author, Year	Country	Study Design	Sample Size	Outcomes
Beiki et al, 2005 (31)	Iran	Cross-sectional	76 patients with dyspepsia	TP = 40, FP = 1, FN = 0, TN = 35
Bilal et al, 2007 (32)	Pakistan	Cross-sectional	90 symptomatic patients	TP = 62, FP = 0, FN = 0, TN = 28
Bruden et al, 2011 (16)	USA	Cross-sectional	280 patients undergoing endoscopy	TP = 139, FP = 16, FN = 10, TN = 115
Calvet et al, 2009 (33)	Spain	Cross-sectional	199 patients with dyspepsia	TP = 117, FP = 32, FN = 1, TN = 49
Chen et al, 2003 (34)	Taiwan	Cross-sectional	554 patients undergoing endoscopy	TP = 365, FP = 24, FN = 4, TN = 161
Gatta et al, 2003 (22)	Italy	Cross-sectional	200 patients with dyspepsia 109 post-treatment patients	TP = 113, FP = 0, FN = 0, TN = 87 TP = 23, FP = 0, FN = 0, TN = 86
Gisbert et al, 2003 (35)	Spain	Cross-sectional	36 patients with dyspepsia	TP = 25, FP = 0, FN = 1, TN = 10
Gomollon et al, 2003 (17)	Spain	Cross-sectional	194 patients with dyspepsia	TP = 139, FP = 0, FN = 1, TN = 54
Kato et al, 2004 (36)	Japan	Cross-sectional	505 patients undergoing endoscopy	TP = 252, FP = 5, FN = 6, TN = 242
Kazemi et al, 2011 (18)	Iran	Cross-sectional	94 patients with dyspepsia	TP = 33, FP = 15, FN = 4, TN = 42
Kuo et al, 2005 (37)	Taiwan	Cross-sectional	317 patients with dyspepsia	TP = 211, FP = 8, FN = 19, TN = 79
Leodolter et al, 2003 (19)	Europe	Cross-sectional	415 patients with dyspepsia	TP = 198, FP = 14, FN = 15, TN = 188
Manes et al, 2005 (23)	Italy	Cross-sectional	325 gastroenterology referrals[a]	TP = 93, FP = 1, FN = 1, TN = 230
Ohara et al, 2004 (38)	Japan	Cross-sectional	251 patients undergoing endoscopy	TP = 125, FP = 3, FN = 3, TN = 120
Peng et al, 2005 (39)	Taiwan	Cross-sectional	50 patients undergoing endoscopy	TP = 18, FP = 0, FN = 0, TN = 32
Peng et al, 2009 (20)	Taiwan	Cross-sectional	100 patients undergoing endoscopy	TP = 53, FP = 7 FN = 0, TN = 40
Reynders et al, 2012 (21)	Belgium	Cross-sectional	117 patients with dyspepsia	TP = 77, FP = 3, FN = 5, TN = 32

Urita et al, 2004 (40)	Japan	Cross-sectional	127 patients undergoing endoscopy	TP = 41, FP = 8, FN = 1, TN = 77
Wong et al, 2003 (41)	Hong Kong	Cross-sectional	200 patients with dyspepsia[b]	TP = 99, FP = 2, FN = 0, TN = 99
Wu et al, 2006 (42)	Taiwan	Cross-sectional	254 patients with dyspepsia[c]	TP = 105, FP = 18, FN = 4, TN = 127
Cuddihy et al, 2005 (24)	USA	Randomized controlled trial	43 patients randomized to 1 of 4 different management strategies	Resolution of symptoms, medication use, and number of visits were similar across all arms; ^{13}C UBT group had higher dyspepsia-specific, quality of life scores than other arms

Abbreviations: FP, false–positive results; FN, false–negative results; TN, true–negative results; TP, true-positive results.
[a]Study evaluated accuracy in post-treatment patients only.
[b]Study included 50 post-treatment patients.
[c]Study included 67 post-treatment patients.

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