Title: AGA Institute Quality Measure Development for the Management of Gastric Intestinal Metaplasia with *Helicobacter pylori*

Short Title: *Helicobacter pylori* Gastric Intestinal Metaplasia Quality Measure

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Grant support: The AGA Institute provided funding for creation of this document.

Abbreviations: American Gastroenterological Association (AGA), clinical guidelines committee (CGC), current procedural terminology (CPT), gastric intestinal metaplasia (GIM), *Helicobacter pylori* (*H pylori*), International Classification of Diseases tenth revision (ICD-10), merit-based incentive payment system (MIPS), quality committee (QC), United States (US)

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This is the author's manuscript of the article published in final edited form as:

Hung, K. W., Maratt, J. K., Cho, W. K., Shah, B. J., Anjou, C. I., & Leiman, D. A. (2022). AGA Institute Quality Measure Development for the Management of Gastric Intestinal Metaplasia with Helicobacter pylori. Gastroenterology. https://doi.org/10.1053/j.gastro.2022.03.023

Disclosures: The authors have no conflicts of interest to disclose.

Acknowledgments: We would like to particularly acknowledge the work of David Godzina and members of the AGA Quality Committee who participated in generating and evaluating this measure.

Writing Assistance: No writing assistance was used for this manuscript.

Author contributions: **Kenneth W. Hung**: Conceptualization, Drafting, Review/Editing; **Jennifer K. Maratt**: Conceptualization, Drafting, Review/Editing; **Won Kyoo Cho**: Conceptualization, Review/Editing; **Brijen J. Shah**: Review/Editing; **Chioma I. Anjou**: Review/Editing; **David A. Leiman**: Conceptualization, Drafting, Review/Editing

Keywords: Quality measures, Gastric intestinal metaplasia, *Helicobacter pylori*

Introduction

Gastric cancer is the third leading cause of cancer-related deaths worldwide, with over 1 million incident cases diagnosed globally[1]. Non-cardia intestinal type gastric cancer, the most common subtype of gastric cancer, develops through the Correa cascade in which chronic inflammation of normal gastric mucosa leads to atrophic gastritis, followed by gastric intestinal metaplasia (GIM), dysplasia, and ultimately gastric cancer[2]. GIM has an estimated prevalence of 4.8% in the United States based on an analysis of gastric biopsies from a large pathology database, but higher rates of GIM have been reported in certain racial and ethnic groups (14.8% in Asian Americans, 18.2% in Native Americans, 25.5% in African Americans, 29.5% in Hispanic Americans)[3, 4]. Additional risk factors for GIM include tobacco use, autoimmune gastritis, and living or immigrating from an endemic area. The annual risk of progression from GIM to non-cardia intestinal-type gastric cancer is 0.16%, and factors such as persistent *Hel cobacter pylori (H pylori)* infection, family history, anatomic extent and location of GIM, and histologic subtypes may confer increased risk of progression to gastric cancer[5]. Studies of US endoscopists show variation in the management of patients with GIM, including use and interval for endoscopic surveillance, prompting the development of guidelines for the management of GIM[6, 7].

H pylori infection is one of the most common causes of atrophic gastritis and GIM and is a major driver of progression along the Correa cascade. The overall prevalence of *H pylori* in the US is 35.6% but has been reported to be much higher in specific racial and ethnic groups, 74.8%, 61.6%, and 52.7% in Alaskan Native Americans, Hispanic Americans, and Non-Hispanic Blacks, respectively, disproportionately affecting such vulnerable populations frequently impacted by healthcare disparities[8, 9]. *H pylori* is readily treatable with a short course of antibiotics, and treatment is cost effective in the prevention of gastric cancer[10]. However, rates of failed *H pylori* eradication are rising, so repeat testing to confirm eradication is recommended[11]. Despite the high prevalence of *H* pylori infection and release of evidence-based guidelines, quality gaps in testing and treatment exist in the management of *H pylori*[12, 13].

The AGA recently published a clinical practice guideline on the management of GIM, which highlights best practices for treatment and eradication of coexistent *H pylori*[5]. Due to the high incidence of gastric cancer, widespread prevalence of GIM and concomitant *H pylori* infection, and variation in practice patterns, development of quality measures for the management of GIM will provide meaningful aspirational care targets, promote adherence to evidence-based, effective care, and allow benchmarking for quality practice to improve the care of patients with GIM.

Measure Evaluation and Development

This document presents the official recommendations of the American Gastroenterological Association (AGA) regarding quality measures related to the diagnosis and management of GIM. The current report outlines the process by which the Quality Committee (QC) evaluates guidance statements published by the AGA's Clinical Guidelines Committee (CGC) to inform measure development. The following recommendations were developed by the QC in consultation with the CGC. Their development was funded by the AGA Institute, with no additional outside funding.

The recommendation statements from the AGA's GIM guideline were evaluated for development as potential quality measures. A standardized process first implemented by the AGA in 2016 and outlined elsewhere[14] was utilized for this evaluation and concordant with previously employed methods for measure development[15]. Optimal understanding of this measure evaluation process will be enhanced by reading applicable portions of the topic guidelines. Briefly, the AGA QC follows a "guidelines to measures" protocol that has been employed for the creation of other measures.

This process relies on the evaluation of forthcoming guideline recommendations to be reviewed by the QC. Recommendation statements are evaluated as potential measure concepts along several axes, including the strength of the recommendation and quality of the evidence as specified using GRADE methodology. Only those statements with strong recommendations based on high or moderate quality evidence are considered for further measure development, which includes an assessment of their potential utility for practicing gastroenterologists. This assessment involves QC subcommittee analysis of measure importance and, when appropriate, is followed by the formal creation of a measure prioritization brief outlining the decision rationale whereby topics are rated on their meaningfulness, potential magnitude of effect, quality gaps, feasibility, and applicability to gastroenterologists. High priority measure concepts subsequently undergo review and vot ng by all QC members ahead of a 30-day public comment period prior to testing and formal adoption. Finally, measures that receive 60 percent or more of the full QC vote will be recommended for national implementation.

Recommendations

The AGA Clinical Practice Guidelines on Management of GIM were reviewed and each recommendation statement was independently evaluated by the AGA QC for the potential to develop into quality measures[5]. The assessment from this evaluation is outlined in **Table 1**.

Recommendations with low or very low quality of evidence were not considered for quality measure development because of the limited certainty of evidence such that new high-quality studies may change clinical practice recommendations. Conditional recommendations were also not considered for measure development. As a result, the suggestions against the routine use of endoscopic surveillance or routine short-interval repeat endoscopy for the purpose of risk stratification in patients with GIM were not developed. Indeed, there are no prospective studies to support nor argue against the

routine performance of endoscopic surveillance in patients with GIM in preventing gastric cancer, mortality, or other patient-related outcomes. There are patient-specific factors, such as family history of gastric cancer, race/ethnicity, smoking, autoimmune gastritis/pernicious anemia, anatomic extent of GIM, and histologic subtype of GIM within the stomach that may affect the risk of developing gastric cancer[4]. Balancing this significantly increased risk of GIM progression in some groups (up to 4.5-fold higher) with the uncertain evidence in US populations, AGA guidelines recommended against the routine surveillance of GIM (conditional recommendation, very low quality of evidence) but commented that there are high-risk populations for whom a shared discussion regarding the potential benefit of endoscopic surveillance at regular intervals should be considered[5]. However, because of the conditional recommendation provided against GIM surveillance among all patients diagnosed with GIM, irrespective of additional risk factors, the AGA QC cannot generate a quality measure on routine endoscopic GIM surveillance. There are also insufficient data to indicate that routine short-interval repeat endoscopy for risk stratification in patients with GIM impacts gastric cancer detection or treatment.

In contrast, recommendations with moderate or strong quality of evidence were reviewed for suitability of quality measure development In this case, the recommendation for patients with GIM to have testing for *H pylori* followed by eradication over no testing and eradication was assessed and developed as a fully specified measure. *H pylori,* a class I ca cinogen per the World Health Organization, is a major risk factor for GIM and non-cardia gastric cancer. *H pylori* infection can be detected by stool antigen, breath testing, gastric biopsies, or serology. GIM may lower the sensitivity of *H pylori* detection in gastric biopsies, so repeat *H pylori* testing with either stool or breath testing, off proton pump inhibitor therapy for at least 2 weeks, is recommended. *H pylori* eradication in individuals with or without GIM has been associated with a 32% pooled relative risk reduction in the risk of developing gastric cancer[16]. However, *H pylori* antibiotic resistance is increasing, and post-treatment confirmation of eradication is recommended due to rising rates of *H pylori* eradication failure[17, 18]. Serology cannot reliably distinguish between active or prior infection, therefore methods other than serology are recommended to confirm *H pylori* eradication. Ensuring adequate assessment and eradication of *H pylori* in patients with GIM is of critical importance and addresses a significant quality gap because 1) gastric cancer incidence and mortality are high, 2) a strong association exists between *H pylori*, GIM, and gastric cancer, 3) *H pylori* eradication is associated with decreased gastric cancer incidence and mortality, 4) *H pylori* eradication failure rates are rising resulting in the need for multiple courses of antibiotics that may further worsen antibiotic resistance, and 5) *H pylori* antibiotic resistance testing is difficult to obtain. We therefore proposed the development of a quality measure to ensure *H pylori* testing and confirmation of eradication in patients with GIM. The recent publication of ICD-10 codes specific for GIM in October 2021 allowed the QC to proceed with development of a GIM quality measure (**Figure 1**).

Following its development, the measure specification was posted for public comment in November 2021. Comments and suggestions that were received included the addition of CPT code descriptions into the measure specifications and revision of the measure

specifications to emphasize testing for *H pylori* 4 weeks after completion of therapy. In response to these comments, we updated CPT codes with descriptions and emphasized the timing of repeat *H pylori* testing 4 weeks after completion of treatment. Comments in support of this measure were also received from the College of American Pathologists. The finalized measure reflects these comments.

Discussion and Future Directions

The AGA CGC has systematically reviewed data and issued recommendations for the management of GIM based on the quality of available evidence. The AGA QC develops quality measures based on CGC guidelines with moderate or high quality of evidence and strong recommendations. Quality measure development entails a rigorous process of measure specification, testing, and submission to quality programs such as the Merit-based Incentive Payment System (MIPS).

Data on long-term outcomes of GIM and endoscopy for isk stratification or surveillance in a US population are lacking. Factors such as family history, histologic features, and anatomic extent of GIM all affect risk of progression of GIM to gastric cancer. International guidelines recommend endoscopic surveillance of GIM at varying intervals depending on anatomic extent of GIM and presence or absence of additional risk factors for gastric cancer[19, 20]. However, in the absence of high-quality data regarding the role of endoscopic surveillance of GIM and optimal surveillance intervals with respect to patient-related outcomes, current evidence is not strong enough to support the development of quality measures for endoscopic surveillance of GIM. Until more evidence is available regarding endoscopic surveillance for GIM, ensuring eradication of *H pylori* is an attainable goal that would improve patient outcomes. Given the disparate impact of gastric cancer, GIM, and *H pylori* on certain portions of the US population, there may be a role for future measure development or measure stratification for high risk populations when additional data are available.

In the meantime, studies have shown non-adherence to *H pylori* testing guidelines and knowledge gaps in the management of patients at increased risk for gastric cancer[12, 13]. Beyond GIM, *H pylori* assessment and eradication have been shown to improve outcomes in peptic ulcer disease-associated gastrointestinal bleeding and dyspepsia[21-23]. Wide variations of care exist, so efforts to confirm eradication are important opportunities for improvement in the care of patients with GIM. Future quality improvement opportunities will include creating mechanisms to identify patients with *H pylori* and GIM, with a focus on tracking and increasing rates of *H pylori* eradication confirmation within a confined episode of care to reduce the risk of gastric cancer.

Importantly, there are no other quality measures related to the management of *H pylori*. The current measure therefore represents an opportunity to improve the quality of care for patients with the most common bacterial infection worldwide, affecting over half of the world's population, disproportionately affecting vulnerable populations frequently impacted by healthcare disparities[8]. Because of the strong relationship between *H pylori* and atrophic gastritis, dyspepsia, and peptic ulcer disease, development of quality measures to promote *H pylori* testing, treatment, and confirmation of eradication in

these conditions is a potential next step. The development of a broader quality measure for *H pylori* treatment and confirmation of eradication in all individuals who test positive for *H pylori* is another potential future direction in improving care of patients with *H pylori* in general. This will require thorough review and grading of the quality of available evidence with respect to *H pylori* testing and treatment and patient-related outcomes, including benefits and harms, will be critical to determine the appropriateness and magnitude of the effect of a broader *H pylori* measure.

Management of *H pylori* infection is beyond the scope of this document and has been discussed in numerous guidelines, consensus documents, and clinical practice updates[18, 24, 25]. Successful eradication on the initial treatment attempt is imperative due to declining eradication rates with subsequent treatment regimens. A renewed focus on the treatment and eradication of *H pylori* has the potential to greatly improve global health and emphasizing the need to confirm eradication will result in a greater understanding of current resistance patterns. This may have the potential to create a virtuous cycle whereby other best practices can be recognized, including tailoring treatment to local antimicrobial resistance and improving antibiotic stewardship[11, 25].

In conclusion, the AGA QC has created a novel quality measure for *H pylori* testing and eradication in patients with GIM. Future inclusion of this measure in a Quality Payment Program or endorsement by organizations such as the National Quality Forum will depend on real-world usage, testing, and refinement. In the meantime, the measure may be used for ongoing quality improvement interventions and continued measurement will be essential to address the quality gap and improve the care of patients who are at risk for gastric cancer.

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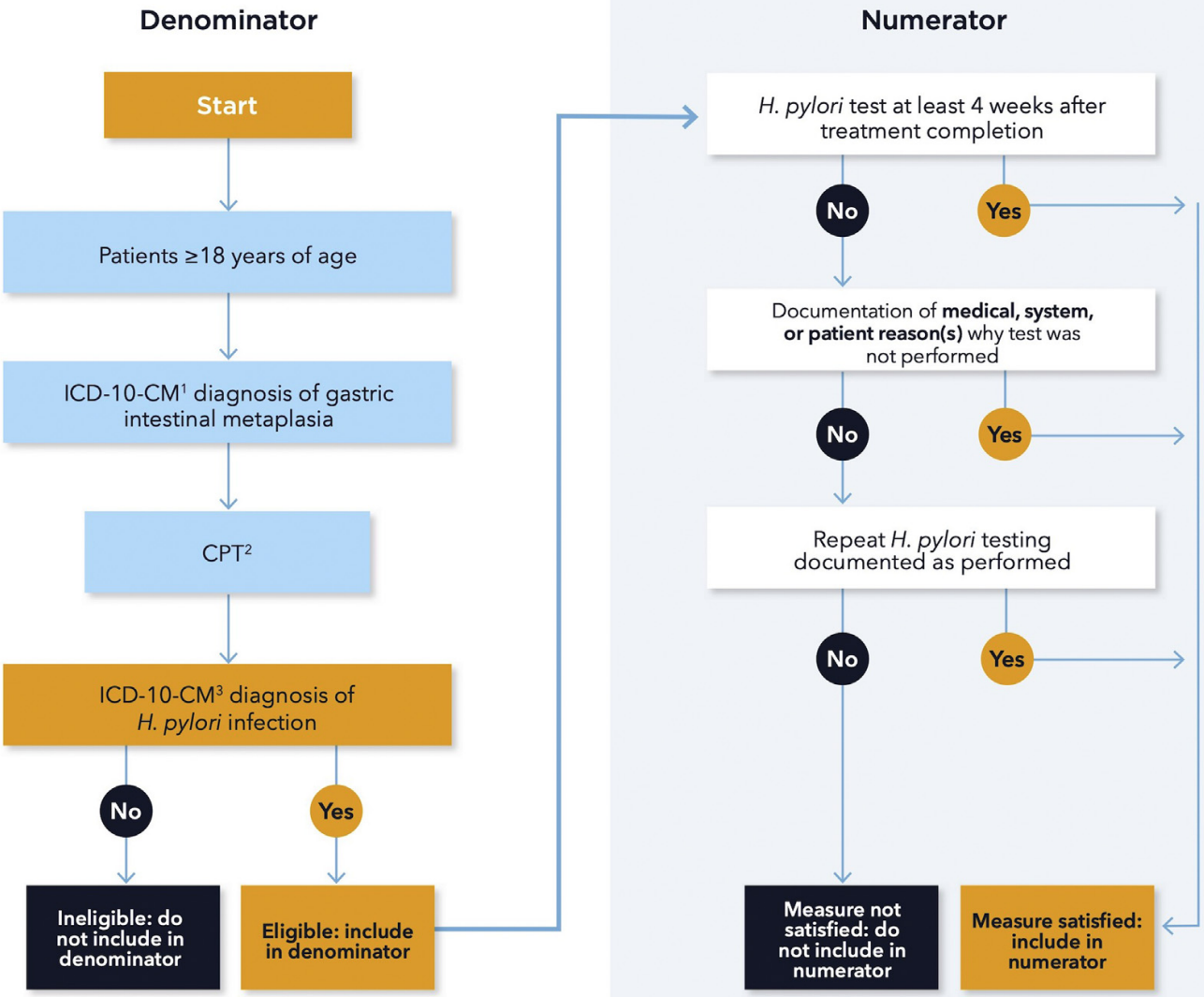
Figure 1. *H pylori* assessment and eradication in gastric intestinal metaplasia measure flow diagram

Table 1. Summary of recommendations and rationale for quality measure development

Statement	GRADE	Decision	Rationale
Guideline on the Management of Gastric Intestinal Metaplasia (GIM)			
In patients with GIM, the AGA recommends testing for *H pylori* followed by eradication over no testing and eradication.	Strong recommendation, moderate quality of evidence	Proceed with measure concept development	Quality gap in confirmation of *H pylori* eradication
In patients with GIM the AGA suggests against routine use of endoscopic surveillance.	Conditional recommendation, very low quality of evidence	No measure concept to develop	Insufficient strength of recommendation and certainty of evidence
In patients with GIM, the AGA suggests against routine short-interval repeat endoscopy for the purpose of risk stratification.	Conditional recommendation very low quality of evidence	No measure concept to develop	Insufficient strength of recommendation and certainty of evidence

Abbreviation: GIM – gastric intestinal metaplasia



Patients must meet denominator eligible criteria first before considering patient for numerator eligibility.

[1]ICD-10-CM: K31A0, K31A11, K31A12, K31A13, K31A14, K31A15, K31A19, K31A21, K31A22, K31A29
[2]CPT: 43239, 99201, 99202, 99203, 99204, 99205, 99212, 99213, 99214, 99215
[3]ICD-10-CM: B96.81