



Topic Brief: Diagnosis and Staging of Non-Metastatic Gastric Cancer

Date: 1/24/2024

Nomination Number: 1070

Purpose: This document summarizes the information addressing a nomination submitted on November 9, 2023 ([link to nomination](#)) through the Effective Health Care Website. This information was used to inform the Evidence-based Practice Center (EPC) Program decisions about whether to produce an evidence report on the topic, and if so, what type of evidence report would be most suitable.

Issue: The nominators are interested in a systematic review of modalities for diagnosing and staging non-metastatic gastric cancer to develop guidelines.

Findings: The EPC Program will not develop a new systematic review because we found several systematic reviews addressing the topic, including one large comprehensive review published in December 2023, as well as a clinical guideline which was published in 2022.

Background

Gastric cancer affects approximately 27,000 people in the United States,¹ and has a 5-year survival rate of 27% largely due to late-stage diagnosis.² When gastric cancer is diagnosed early, the 5-year survival rate jumps to 90%.² Current gold standard diagnostic tools include radiographic imaging and computed tomography (CT) scanning, upper endoscopy, and traditional tumor biomarkers (CEA, CA19-9, and CA72-4).³ The continued evolution and technological improvements of diagnostic tools make it imperative that these “gold standard” approaches are continuously evaluated against other tools in order to ensure these standards are still, in fact, the best.

The nominator, the American Society of Clinical Oncology (ASCO), would like to use a review on the diagnosis and staging of non-metastatic gastric cancer to create a treatment guideline, to raise awareness for evidence-based diagnosis options, and highlight areas of uncertainty for which more evidence and research are needed.

Scope

Key Questions (KQs):

1. For suspected non-recurrent, non-metastatic gastric cancer, what is the diagnostic and staging accuracy of:
 - a. Minimally- or non-invasive procedures
 - b. Precision medicine (e.g., biomarkers and liquid biopsies)
 - c. Imaging

Table 1. Questions and PICOS (population, intervention, comparator, outcome, study design)

Key Question(s) For suspected non-recurrent, non-metastatic gastric cancer, what is the diagnostic and staging accuracy of:	a) Minimally- or non-invasive procedures	b) Precision medicine (e.g., biomarkers and liquid biopsies)	c) Imaging
Populations	Include: Adults with suspected non-recurrent, primary non-metastatic gastric cancer Exclude: Suspicion of recurrent cancer or metastatic cancer		
Interventions	Minimally- or non-invasive procedures for diagnosis and staging (e.g., endoscopic ultrasound, endoscopic ultrasound-guided fine needle aspiration, endoscopic ultrasound-guided fine needle biopsy, confocal laser endomicroscopy, diagnostic laparoscopy, diagnostic lymph node dissection)	Blood and other fluid tests for diagnosis and staging (e.g., immunohistochemistry tests, liquid biopsy, next generation sequencing [NGS], and other biomarker tests)	Imaging for diagnosis and staging (e.g., endoscopic narrow-band imaging, CT/MRI/PET, white light imaging) Exclude: use of artificial intelligence with imaging
Comparators	Any other intervention as a comparator. Exclude studies with no comparator		
Outcomes	Diagnostic and staging accuracy, direct (procedure-induced) harms or adverse events		
Study Design	Exclude: pilot and feasibility studies, case series/case reports		Exclude: pilot and feasibility studies, case series, white papers, network modeling, simulation studies

Assessment Methods

See Appendix A.

Results

Summary of Literature Findings

We identified 22 completed systematic reviews and/or meta-analyses, one protocol for a systematic review & meta-analysis, and one set of guidelines.

We identified guidelines published in 2022 from the European Society for Medical Oncology examining evidence and recommending diagnostic and staging procedures for gastric cancer.⁴ While these guidelines were developed in Europe, they consider US Food and Drug Administration (FDA) regulations and approvals. Most of the systematic reviews we identified examined evidence within a single modality type (interventions of interest were all procedures, all biomarkers, or all imaging, rather than examining across each “bucket”); however one systematic review (2023) looked across all of our nominator’s interventions of interest for gastric cancer diagnosis,³ and one examined endoscopic ultrasound vs. computed tomography (CT) for staging.⁵

Reviews examining evidence on minimally- or non-invasive procedures for diagnosing and staging (KQ 1a; 3 reviews) examine staging laparoscopy,⁶ confocal laser endomicroscopy,⁷ and magnifying endoscopy.⁸ Endoscopy is the current standard of practice,⁴ though most of the recent systematic reviews examine the efficacy of using artificial intelligence and machine learning in conjunction with endoscopy, an emerging technology that is *not* part of the nominator’s scope of this brief.

Question 1b addresses precision medicine which is a quickly advancing field, and these systematic reviews and meta-analyses aimed to examine diagnostic accuracy as well as their clinical utility and feasibility as diagnostic, staging, and prognostic tools (13 reviews). Beyond diagnosis and staging, the importance of this technology and its implications on *treatment* pathways cannot be understated. Though several novel biomarkers are examined in these reviews, reviews of microRNA studies⁹⁻¹² make up around a third of the identified reviews.

Reviews of imaging techniques for diagnosing gastric cancer (KQ 1c) yielded five completed systematic reviews and meta-analyses, and one protocol for a SR & MA on narrow band imaging.¹³ The completed reviews examine PET imaging,^{14,15} CT vs endoscopic ultrasound,^{14,15} magnifying narrow-band imaging,¹⁶ and blue laser imaging vs narrow-band imaging.¹⁶

See Appendix B for detailed assessments of all EPC selection criteria.

Table 2. Systematic reviews by key question

Questions: For suspected non-recurrent, non-metastatic gastric cancer, what is the diagnostic and staging accuracy of:	Systematic Reviews (January 2020 – December 2023)
a) Minimally- or non-invasive procedures	Guidelines: 1 ⁴ Systematic Review: 2 ^{3,6} Meta-Analysis: 1 ⁸ Systematic Review & Meta-Analysis: 1 ⁷
b) Precision medicine (e.g., biomarkers and liquid biopsies)	Guidelines: 1 ⁴ Systematic Review: 3 ^{3,12,17} Meta-analysis: 2 ^{9,18} Systematic Review & Meta-Analysis: 8 ^{10,11,19-24}
c) Imaging	Guidelines: 1 ⁴

	Systematic Review: 1 ³ Meta-analysis: 2 ^{5,25} Systematic Review & Meta-Analysis: 3 ¹⁴⁻¹⁶ Protocol for Systematic Review & Meta-Analysis: 1 ¹³
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Summary of Selection Criteria Assessment

The nominators are interested in a systematic review examining the efficacy and comparative efficacy of modalities for diagnosing gastric cancer to develop guidelines. This is an important topic, and appropriate for the Evidence-based Practice Center program. We identified a set of guidelines (2022⁴), 22 completed reviews (including one review from December 2023³ examining the interventions of interest), and 1 review protocol. A new AHRQ review on this topic would be duplicative of the evidence available.

Please see Appendix B for detailed assessments of individual EPC Program selection criteria.

References

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Conflict of Interest: None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

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Appendix A: Methods

We assessed the nomination for priority for a systematic review or other AHRQ Effective Health Care report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one. See Appendix B for detailed description of the criteria.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance.

Desirability of New Review/Absence of Duplication

Ovid MEDLINE ALL <1946 to December 19, 2023>

Date searched: December 20, 2023

1 *Stomach Neoplasms/ (97632)

2 ((antrum or cardia or fundic or fundus or gastric or "lamina propria" or "muscularis mucosae" or "muscularis propria" or pylorus or stomach or submucosa) adj2 (adenocarcinoma or cancer* or carcin* or malignan* or neoplas* or tumo?r\$1)).ti,kf,kw. (86042)

3 or/1-2 (115129)

4 exp *Diagnosis/ or *Neoplasm Staging/ (2798905)

5 (biopsy or biopsies or diagnos* or stage\$1 or staging).ti,kf. (1083580)

6 or/4-5 (3600989)

7 Diagnostic Imaging/ or "Endoscopic Ultrasound-Guided Fine Needle Aspiration"/ or Image-Guided Biopsy/ or ((Laparoscopy/ or Lymph Node Excision/ or Sentinel Lymph Node Biopsy/) and (diagnos* or stage or staged or staging).ti,ab,kf.) or (CLE or chromoendoscop* or "confocal laser endomicroscop*" or (endoscop* adj5 (ultrasonograph* or ultrasound)) or ((diagnos* or stage or staged or staging) adj3 (laparoscop* or "lymph node"))) or "diffusion weighted" or DWI or FDG-PET).ti,ab,kf. (195596)

8 Biomarkers, Tumor/ or exp Biopsy/ or (biomarker\$1 or immunohistochemistry or immunohistochemistry or "liquid biops*" or "next generation sequencing" or NGS or ((biochemical or biologic\$2 or cancer* or metabolite or neoplas* or tumo?r\$1) adj3 marker\$1)).ti,ab,kf. (1159969)

9 Magnetic Resonance Imaging/ or Narrow Band Imaging/ or Positron-Emission Tomography/ or exp Tomography, X-Ray Computed/ or ((endoscop* adj5 "narrow-band") or "computed tomograph*" or ((CT or PET) adj2 scan\$1) or (("magnetic resonance" or "white light") adj2 imaging) or MRI or "positron emission tomography").ti,ab,kf. (1342915)

10 (("minimally invasive" or noninvasive or non-invasive) adj7 diagnos*).ti,ab,kf. (30114)

11 or/7-10 (2515535)

12 and/3,6,11 (7801)

13 12 not (Feasibility Studies/ or Artificial Intelligence/ or Pilot Projects/ or (animal model* or bitch\$2 or bovine or canine or capra or cat or cats or cattle or cow\$1 or dog\$1 or equine or ewe\$1 or feline or goat\$1 or hamster\$1 or horse\$1 or invertebrate\$1 or macaque\$1 or mare\$1 or mice or monkey\$1 or mouse or murine or nonhuman or non-human or ovine or pig or pigs or porcine or primate\$1 or rabbit\$1 or rat\$1 or rattus or rhesus or rodent* or sheep or simian or sow\$1 or vertebrate\$1 or zebrafish or adjuvant or "case report" or "case study" or ChatGPT or chemotherap* or "deep learning" or feasibility or gastrectom* or intelligence or intelligent or "machine learning" or management or neoadjuvant or pilot or metastat* or recurr* or resect* or therap* or treat* or surger*).ti. or (case reports or comment or editorial or letter or news).pt.) (4263)

14 limit 13 to english language (3554)

15 limit 14 to yr="2020 - 2024" (926)
 16 15 and ((meta-analysis or systematic review).pt. or (meta-anal* or metaanal* or ((evidence or review or scoping or systematic or umbrella) adj3 (review or synthesis))).ti.) (81)
 17 limit 14 to yr="2018 - 2024" (1343)
 18 17 and ((controlled clinical trial or randomized controlled trial).pt. or (random* or trial*).ti,ab,kf.) (125)
 19 18 not 16 (112)
 20 17 and (Cohort Studies/ or Cross-Sectional Studies/ or Longitudinal Studies/ or comparative study.pt. or (cohort or comparative or cross-sectional or longitudinal\$2).ti,ab,kf.) (225)
 21 20 not (16 or 18) (191)

Ovid EBM Reviews - Cochrane Central Register of Controlled Trials <November 2023>

Date searched: December 20, 2023

1 Stomach Neoplasms/ (3529)
 2 ((antrum or cardia or fundic or fundus or gastric or "lamina propria" or "muscularis mucosae" or "muscularis propria" or pylorus or stomach or submucosa) adj2 (adenocarcinoma or cancer* or carcin* or malignan* or neoplas* or tumor?r\$1)).ti. (5865)
 3 or/1-2 (7142)
 4 Diagnosis/ or Neoplasm Staging/ (13671)
 5 (biopsy or biopsies or diagnos* or stage\$1 or staging).ti. (43615)
 6 or/4-5 (54402)
 7 Diagnostic Imaging/ or "Endoscopic Ultrasound-Guided Fine Needle Aspiration"/ or Image-Guided Biopsy/ or ((Laparoscopy/ or Lymph Node Excision/ or Sentinel Lymph Node Biopsy/) and (diagnos* or stage or staged or staging).ti,ab.) or (CLE or chromoendoscop* or "confocal laser endomicroscop*" or (endoscop* adj5 (ultrasonograph* or ultrasound)) or ((diagnos* or stage or staged or staging) adj3 (laparoscop* or "lymph node"))) or "diffusion weighted" or DWI or FDG-PET).ti,ab. (8458)
 8 Biomarkers, Tumor/ or Biopsy/ or (biomarker\$1 or immunohistochemistry or immuno-histochemistry or "liquid biops*" or "next generation sequencing" or NGS or ((biochemical or biologic\$2 or cancer* or metabolite or neoplas* or tumor?r\$1) adj3 marker\$1)).ti,ab. (54101)
 9 Magnetic Resonance Imaging/ or Narrow Band Imaging/ or Positron-Emission Tomography/ or exp Tomography, X-Ray Computed/ or ((endoscop* adj5 "narrow-band") or "computed tomograph*" or ((CT or PET) adj2 scan\$1) or ("magnetic resonance" or "white light") adj2 imaging) or MRI or "positron emission tomography").ti,ab. (62871)
 10 ("minimally invasive" or noninvasive or non-invasive) adj7 diagnos*).ti,ab. (694)
 11 or/7-10 (118111)
 12 and/3,6,11 (255)
 13 limit 12 to yr="2018 - 2024" (78)

PROSPERO

Date searched: December 20, 2023

((((antrum OR cardia OR fundic OR fundus OR gastric OR "lamina propria" OR "muscularis mucosae" OR "muscularis propria" OR pylorus OR stomach OR submucosa) AND (adenocarcinoma OR cancer* OR carcin* OR malignan* OR neoplas* OR tumor* OR tumour*)) AND (biops* OR diagnos* OR imaging OR stage* OR staging OR "Endoscopic Ultrasound-Guided Fine Needle Aspiration" OR CLE OR chromoendoscop* OR "confocal laser endomicroscop*" OR (endoscop* AND ("narrow-band" OR ultrasonograph* OR ultrasound)) OR "diffusion weighted" OR DWI OR FDG-PET OR biomarker* OR immunohistochemi* OR immuno-histochem* OR "next generation sequencing" OR NGS OR ((biochemical* OR biologic* OR cancer* OR metabolite OR neoplas* OR tumor* OR tumour*) AND marker*)) OR

"computed tomography" OR ((CT OR PET) AND scan*) OR "magnetic resonance" OR MRI OR "positron emission tomography" OR "white light" OR (("minimally invasive" OR noninvasive OR non-invasive) AND diagnos*)):TI AND (Diagnostic OR Systematic Review OR Meta-Analysis OR Review of reviews):RT AND (cancer):HA WHERE CD FROM 20/12/2020 TO 20/12/2023 (51)

Appendix B. Selection Criteria Assessment

Selection Criteria	Assessment
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes.
1b. Is the nomination a request for an evidence report?	Yes.
1c. Is the focus on effectiveness or comparative effectiveness?	Yes.
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes.
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	27,000 people are affected by gastric cancer annually in the United States, and this number jumps to around 5 million globally. ¹
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	A 27% 5-year survival rate is due largely to late stage diagnosis, making it imperative that the best diagnostic tools are used, and used early on. ²
2c. Incorporates issues around both clinical benefits and potential clinical harms	This topic represents clinical benefits and harms.
2d. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	a 2018 economic impact review of gastric cancer reported the annual cost of gastric cancer in the United States to be over \$3 billion. ²⁶
3. Desirability of a New Evidence Review/Absence of Duplication	
3. A recent high-quality systematic review or other evidence review is not available on this topic	A new review would be duplicative. We identified 21 semi-fragmented SRs and MAs, 1 comprehensive review, 1 SR protocol, and 1 set of recent guidelines.

Abbreviations: AHRQ=Agency for Healthcare Research and Quality; MA=meta-analysis; SR=systematic review.