

Adherence to Guidelines for Asymptomatic Iron Deficiency Anemia in Outpatient Primary Care

Anna Goebel¹, Abraham Segura², Ahlaam Abdulwali³, Shivan J Mehta², Michael Harhay⁴, Ravy Vajravelu⁵ and Shazia M Siddique²

¹Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA

²Division of Gastroenterology and Hepatology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA

³Macalester College, St Paul, Minnesota, USA

⁴Department of Biostatistics, Epidemiology, and Informatics, University of Pennsylvania

⁵Division of Gastroenterology, Hepatology and Nutrition, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA

*Corresponding author:

Anna Goebel, MD,
Department of Medicine University of Pennsylvania
3400 Civic Center Blvd Philadelphia, PA 19104, USA

Received: 29 Sep 2025

Accepted: 10 Oct 2025

Published: 26 Oct 2025

J Short Name: WJGHE

Copyright:

©2025 Anna Goebel, MD. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and build upon your work non-commercially

Keyword:

Iron Deficiency Anemia; Endoscopy; Clinical Guideline Implementation; Primary Care

Citation:

Anna Goebel, MD, Adherence to Guidelines for Asymptomatic Iron Deficiency Anemia in Outpatient Primary Care. World Jour of Gastro and Hepatology® 2025; V10(5): 1-10

1. Abstract

1.1. Background and Aims

In 2020, the American Gastroenterological Association (AGA) published guidelines for the gastrointestinal evaluation of asymptomatic iron deficiency anemia (IDA), strongly recommending bidirectional endoscopy for post-menopausal women and men, with a conditional recommendation for pre-menopausal women. This study evaluated adherence to these guidelines in an academic outpatient primary care setting.

1.2. Methods

1.3. Design

Retrospective Cross-Sectional Study

1.4. Setting

Thirty outpatient primary care clinics at an academic health system

1.5. Participants

Adults ≥ 18 years meeting IDA criteria (hemoglobin < 13 g/dL in men or < 12 g/dL in non-pregnant women; ferritin ≤ 45 ng/mL), with no gastrointestinal (GI) bleeding, menorrhagia, pregnancy, or hematologic malignancy. Menopause was defined as age ≥ 51 . Exclusion criteria included pregnancy, hematologic malignancy, gastrointestinal bleeding, and menorrhagia.

1.6. Exposure

A registry of eligible patients was created; 168 patients were randomly selected for manual chart abstraction. Data included demo-

graphics, non-invasive testing, and endoscopy utilization.

1.7. Analysis

Multivariable logistic regression identified factors associated with ordering guideline-directed testing.

1.8. Results

Of 168 eligible patients, bidirectional endoscopy was ordered for 40% of men and 34% of post-menopausal women, compared to 10% of pre-menopausal women. Non-invasive testing was underutilized: celiac serologies in 16.1% and H. pylori in 7.1%. Premenopausal women had 86% lower odds of undergoing bidirectional endoscopy than men (OR 0.14; 95% CI 0.03–0.55), after adjusting for age, family history, medication use, and anemia severity. Bidirectional endoscopy completion rates were 75% in men, 73.7% in postmenopausal women, and 70.0% in premenopausal women.

1.9. Conclusions

Guideline-concordant evaluation of IDA is inconsistently implemented, particularly in pre-menopausal women. Further research to determine criteria for diagnostic evaluation is needed.

2. Introduction

Asymptomatic iron deficiency anemia (IDA) is a prevalent condition that warrants careful clinical attention. It can result from serious underlying causes such as malnutrition, chronic malabsorption, or occult gastrointestinal bleeding from both benign and malignant sources, necessitating thorough evaluation of the gastrointestinal

(GI) tract.[1] Gastrointestinal lesions are common in patients with IDA; one study found that 61% of those with GI bleeding had iron deficiency anemia, underscoring the strong link between GI blood loss and IDA. [2] Despite this, there is considerable uncertainty regarding the proper definition of IDA and the appropriate diagnostic pathway. In 2020, The American Gastroenterological Association (AGA) released new clinical practice guidelines directed at healthcare professionals, including primary care clinicians, to standardize the approach to GI evaluation of asymptomatic IDA. These guidelines strongly recommend a higher ferritin threshold of 45 ng/mL to define IDA, strongly recommend bidirectional endoscopy for asymptomatic IDA for post-menopausal women and men, and conditionally recommend non-invasive testing for celiac disease and *Helicobacter pylori* (*H. pylori*) infection in certain settings. For pre-menopausal women, these guidelines conditionally recommend a similar endoscopic and non-invasive diagnostic approach, except they also suggest an initial course of iron replacement therapy without bidirectional endoscopy for patients who have a high value of avoid the small risk of endoscopy, may have other plausible reasons for IDA, and place low value on the small risk of missing gastrointestinal malignancy [3]. Clinician adherence to these guidelines for the evaluation of IDA is unknown. This study aims to assess adherence to the AGA's 2020 guidelines within multiple primary care sites in a large academic medical center, identifying gaps in implementation. Additionally, this study aimed to evaluate the association between clinician ordering of guideline-directed diagnostic testing with patient risk factors to explore potential variation in care.

3. Methods

3.1. Study Design and Population

A retrospective cross-sectional study of outpatient encounters was conducted across 30 diverse primary care clinics (internal medicine and family medicine) within the University of Pennsylvania Health System (UPHS) from July 1, 2022, to June 30, 2023. Participants were randomly selected from an electronic registry of patients with IDA with the following inclusion criteria: 1) adults older than 18 years old with at least 1 prior visit with a UPHS primary care provider in the past 3 years, AND 2) a prior encounter with a diagnosis code for IDA secondary to blood loss (ICD-10 code D50.0), OR 3) a hemoglobin <12 g/dL for non-pregnant women and <13 g/dL for men and ferritin ≤45 ng/mL within the last 3 years. Patients were excluded if they had, at the time of the last primary care office visit encounter: (1) an active problem list entry or encounter diagnosis associated with gastrointestinal bleeding (ICD-10 codes: K92., K29.01, K62.5, K31.811, K57, K29, K25–28); (2) an active diagnosis of menorrhagia (N92.); (3) a diagnosis of celiac disease (K90) or chronic liver disease (K74); (4) undergone colonoscopy in the past year; (5) an active prescription for ferrous sulfate, ferrous gluconate, or intravenous iron prior to the PCP visit; or (6) active gastrointestinal symptoms (e.g., abdominal pain, diarrhea, constipation, bloating, or change in bowel habits). Registry patients were randomized using a random number generator and the first 180 were selected for manual chart review to further exclude 7)

patients with pregnancy in the last three months and 8) any known malignancy. The study was reviewed by the Institutional Review Board at the University of Pennsylvania and deemed exempted.

3.2. Covariables and Outcomes

Demographics, clinical history, test selection (e.g. type of endoscopy, non-invasive *H. pylori* or celiac disease testing), and diagnostic results were obtained by manual review of the electronic health record. Covariables of interest included age, sex, menopausal status, self-reported race, family history of colorectal cancer, iron supplementation, and use non-steroidal anti-inflammatory (NSAID), aspirin (ASA), or anticoagulants. Menopausal status was determined using an aged-based cutoff of 55 years old: female individuals younger than 55 years old were considered to be pre-menopausal, and women 55 years and older were classified as post-menopausal [4,5]. The women did not have a chart history of menorrhagia. Prior endoscopy was not considered as covariant. These variables were selected to capture key demographic characteristics and clinical factors likely considered by primary care providers when evaluating the etiology of iron deficiency anemia and determining the need for further diagnostic workup [6-8].

The primary study outcome was clinician ordering of bidirectional endoscopy for evaluation of IDA during the encounter. Secondary outcomes included clinician ordering of unidirectional endoscopy (i.e. esophagogastroduodenoscopy [EGD] or colonoscopy alone); patient completion and diagnostic yield of endoscopy; clinician ordering, patient completion and diagnostic yield of non-invasive testing (e.g. *H. pylori* stool antigen testing, serum tissue transglutaminase IgA for celiac disease). Study data were collected, managed, and securely stored using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at University of Pennsylvania.

4. Statistical Analysis

Descriptive statistics were performed with categorical variables reported as counts with percentages and continuous variables presented as medians with interquartile range (IQR). Multivariable logistic regression was performed to evaluate the association between patient-level variables and clinician ordering practices for endoscopic evaluation. The model adjusted for factors likely to influence clinical decision, including age, combined sex and menopausal status (man, post-menopausal woman, pre-menopausal woman), NSAID use, ASA use, anticoagulant use, severity of anemia – categorized as mild (Hgb 11–12.9 g/dL), moderate (Hgb 8–10.9 g/dL), and severe (Hgb <8 g/dL) – and family history of colorectal cancer (yes vs. no). All statistical analyses were performed using STATA version 17 (College Station, TX, USA).

5. Results

Cohort characteristics are presented in Table 1. A total of 168 patients met inclusion criteria, with a median age of 47 years (IQR 39–61.5). The cohort consisted of 20 men (11.9%), 58 postmenopausal women (34.5%), and 90 premenopausal women (53.6%). Racial distribution was 32.1% White, 51.8% Black, 7.1% Asian, and 8.9% classified as other. A family history of colorectal cancer

was documented in 9.5% of the total cohort, with highest prevalence among men (25%). The overall median hemoglobin was 10.95 g/dL (IQR 10–11.5), and median ferritin was 14 ng/mL (IQR 7–24.5). Hemoglobin was comparable between men (median 11.35 g/dL, IQR 9.85–11.9), post-menopausal women (median 10.7 g/dL, IQR 9.7–11.3), and pre-menopausal women (median 11.05 g/dL, IQR 10.2–11.6). Ferritin levels were highest among men (median 25.85 ng/mL, IQR 13.5–36.2) and lowest among premenopausal women (median 9.85 ng/mL, IQR 6–20). Half (50.0%) all patients were classified as having mild anemia, 44.6% had moderate anemia, and 5.4% of the cohort was classified with severe anemia. Severity of anemia varied by sex and menopausal status: moderate anemia was most common among postmenopausal women (52.2%), while men had the highest proportion of mild anemia (65.0%). Regarding high-risk medication use, aspirin was used in 11.9% of patients, anticoagulants in 1.8%, and NSAIDs in 8.3%. A larger proportion of men were taking aspirin (50%) or anticoagulants (5%) compared to post- and pre-menopausal women at the time of IDA diagnosis. There were no patients on thienopyridine antiplatelet agents in this cohort. Clinician ordering of bidirectional endoscopy (n=37 orders) varied significantly by sex and menopausal status (Figure 1). Among men, 40% had an order for bidirectional (EGD and colonoscopy) endoscopy ordered as part of their diagnostic evaluation, compared to 41.3% of post-menopausal women and only 9.8% of pre-menopausal women. A total of 37 patients completed bidirectional endoscopy, with completion rates of 75% for men, 73.7% for postmenopausal women, and 70.0% for premenopausal women. Overall, there were more pre-menopausal women (n = 64; 62.8%) without any diagnostic endoscopy orders than men (n = 5; 25.0%) and post-menopausal women (n = 11; 23.9%). Among pre-menopausal women

without any endoscopy orders, 42 (65.6%) were prescribed oral iron supplementation. Endoscopic yield by sex and menopausal status is summarized in Figure 2. When stratified by sex and menopausal status, positive findings were identified in 3 men (20%), 14 post-menopausal women (40.0%) and 5 pre-menopausal women (13.2%). Men and post-menopausal women were diagnosed exclusively lower GI lesions (e.g. adenoma, angiodysplasia), and 1 case of inflammatory bowel disease was diagnosed in a single man. All 3 cases of celiac disease in this cohort were diagnosed in pre-menopausal women. There were no patients diagnosed with *H. pylori* based on gastric biopsies, and there were no patients diagnosed with CRC via lower endoscopy.

Non-invasive *H. pylori* testing regardless of bidirectional endoscopy testing status was low and varied by menopausal status (Figure 3a). In the full cohort, 12 patients had orders for non-invasive *H. pylori* testing. Among 9 premenopausal women with orders for *H. pylori* testing, 6 completed testing and 1 was positive for *h. pylori*. All 3 post-menopausal women who received orders for *H. pylori* testing completed it and all results were negative. No men were tested for *H. pylori* in this cohort. Of the non-invasive *H. pylori* ordered only one was ordered after bidirectional endoscopy. Non-invasive celiac disease testing was also infrequent but more evenly distributed across groups (Figure 3b). Among 12 premenopausal women who had non-invasive celiac disease testing ordered, 11 completed testing with all negative results. Eight postmenopausal women were ordered for and completed testing, and 1 tested positive for celiac disease. There were 7 men ordered for testing, 6 completed testing and all were negative for celiac disease. Of the non-invasive celiac testing ordered 22 tests were ordered prior to upper endoscopy being ordered.

Table 1: Cohort Characteristics.

	Total	Men	Post-menopausal	Pre-menopausal
			women	women
	N=168	n=20	n=46	n=102
Age in years, median (IQR)	47 (39-61.5)	60.5 (39.5-74.5)	72 (58-80)	41.5 (34-47)
Race, n (%)				
White	54 (32.1%)	6 (30%)	25 (54.3%)	23 (22.5%)
Black	87 (51.8%)	11 (55%)	21 (45.7%)	55 (53.9%)
Asian	12 (7.1%)	1 (5%)	0 (0.0%)	11 (10.8%)
Other	15 (8.9%)	2 (10%)	0 (0.0%)	13 (12.7%)
CRC family history, n (%)	16 (9.5%)	5 (25%)	2 (4.3%)	9 (8.8%)
NSAID use, n (%)	14 (8.3%)	2 (10%)	8 (17.4%)	4 (3.9%)
Aspirin use, n (%)	20 (11.9%)	10 (50%)	7 (15.2%)	3 (2.9%)
Anticoagulant use, n (%) ^a	3 (1.8%)	1 (5%)	1 (2.2%)	1 (1.0%)
Hemoglobin in g/dL, median (IQR)	10.95 (10-11.5)	11.35 (9.85-11.9)	10.7 (9.7-11.2)	11.05 (10.2-11.6)
Ferritin in ng/mL, median (IQR)	14 (7-24.5)	25.85 (13.5-36.2)	18.5 (11.7-28)	9.85 (6-20)
Anemia by severity, n (%) ^b				
Mild anemia	84 (50.0%)	13 (65%)	19 (41.3%)	52 (51.0%)
Moderate anemia	75 (44.6%)	6 (30%)	24 (52.2%)	45 (44.1%)
Severe anemia	9 (5.4%)	1 (5%)	3 (6.5%)	5 (4.9%)

a. Anticoagulants include vitamin K antagonists and direct oral anticoagulants

b. Classification of anemia by severity as defined by WHO 2024.

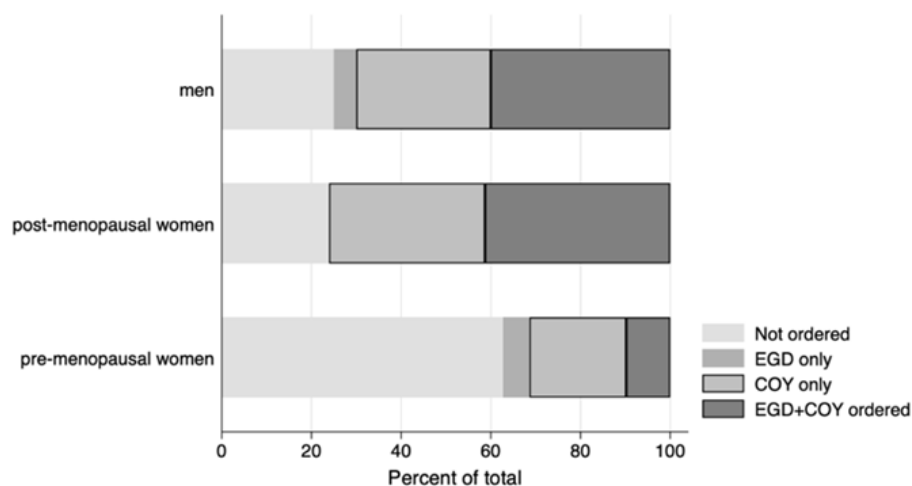


Figure 1: Type of endoscopy ordered at PCP visit by sex/menopausal status.

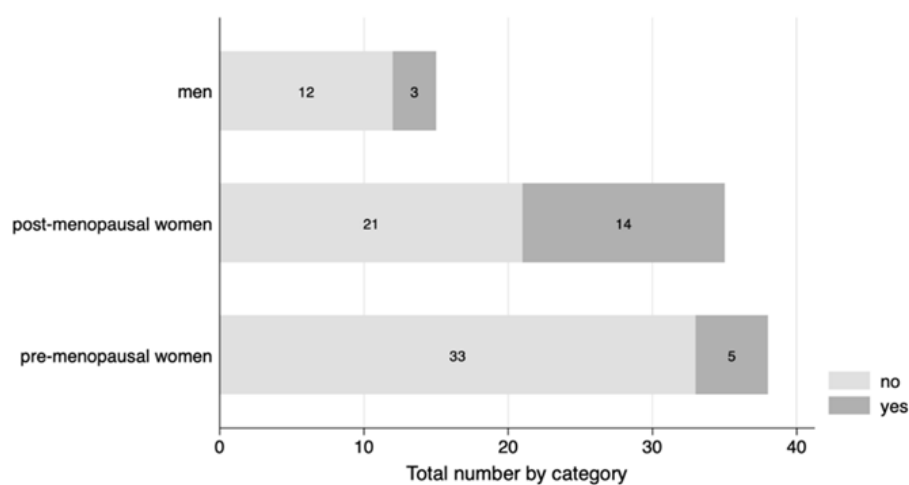


Figure 2: Positive endoscopic findings by sex and menopausal status and endoscopic findings in patients with iron deficiency anemia using ferritin threshold of ≤ 45 .

Finding	Men	Post-menopausal women	Pre-menopausal women
Celiac disease	0	0	3
Low-risk adenoma (LRA) ^a	1	5	1
High-risk adenoma (HRA) ^b	0	2	0
Sessile polyp (SP) ^c	0	1	0
Other notable lesions ^d	0	3	1
HRA + SP	1	3	0
LRA + other	1	0	0

a. 1-2 nonadvanced adenomas <10mm in size

b. ≥ 3 adenomas OR adenoma ≥ 10 mm in size OR tubulovillous/villous histology OR high-grade dysplasia or CRC

c. sessile serrated adenoma/polyp OR traditional serrated adenoma OR hyperplastic polyp

d. angiodysplasia, diverticular disease, inflammatory bowel disease, internal hemorrhoids

* 0 patients with gastric biopsies positive for H. pylori

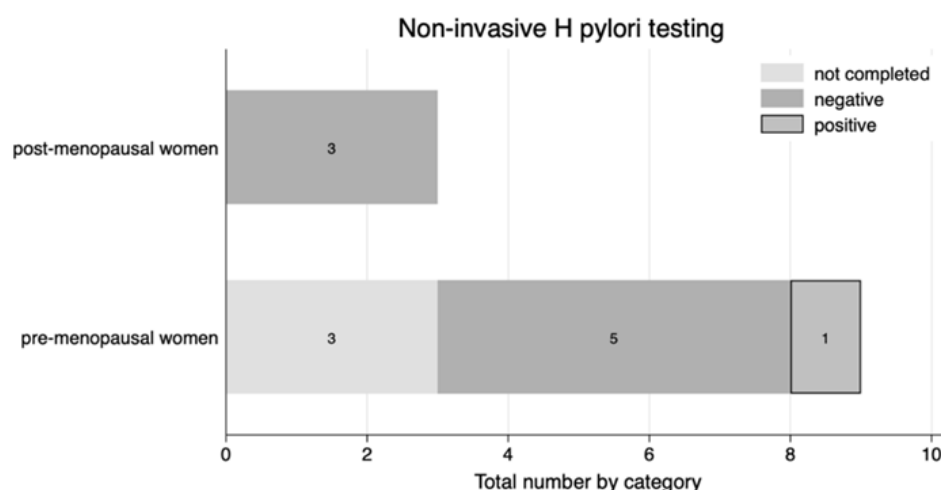


Figure 3a: Non-invasive H. pylori testing ordered by sex and menopausal status.

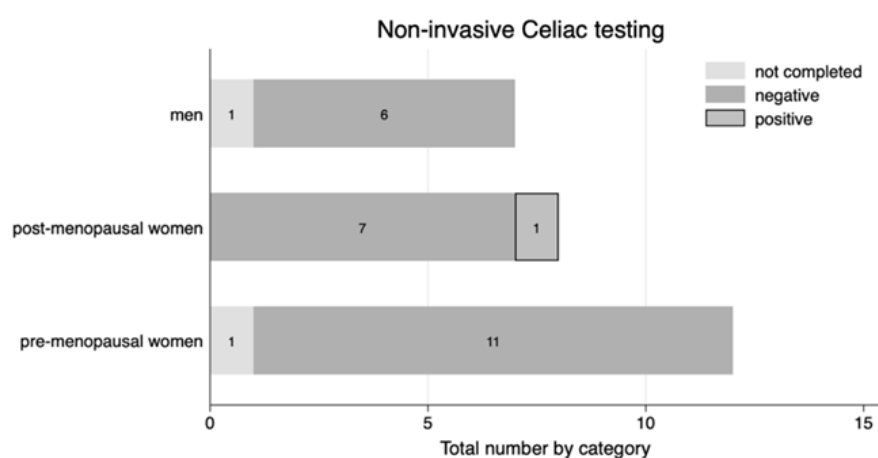


Figure 3b: Non-invasive celiac disease testing ordered by sex and menopausal status.

5.1. Factors affecting likelihood of clinician ordering of endoscopy:

Multivariable logistic regression identified significant associations between sex/menopausal status and clinician ordering of bidirectional endoscopy (Figure 4 and Supplemental Table 1). Compared to men, premenopausal women had significantly lower odds of being referred for bidirectional endoscopy (OR 0.11, 95% CI 0.03–0.42). Postmenopausal women also had lower odds, though the association did not reach statistical significance (OR 0.86, 95% CI 0.22–3.29). Other variables including age, anemia severity, family history of CRC, and use of NSAIDs, aspirin, or anticoagulants were not significantly associated with clinician ordering practices. A secondary analysis was performed to evaluate the predictors of

any diagnostic testing modality (endoscopy or non-invasive testing) for iron deficiency anemia (Supplemental Figure 1 and Supplemental Table 2). In this analysis, sex and menopausal status remained significantly associated with clinician ordering. Compared to men, pre-menopausal women had significantly lower odds of undergoing any testing (OR 0.19, 95% CI 0.05–0.81), while post-menopausal women also showed lower odds that did not reach statistical significance (OR 0.39, 95% CI 0.08–1.88). Increasing age was marginally associated with higher odds of testing (OR 1.03, 95% CI 1.00–1.07). Other factors including family history of colorectal cancer (OR 3.51, 95% CI 0.83–14.8), NSAID or aspirin use, anticoagulant use, and anemia severity were not significantly associated with ordering of testing.

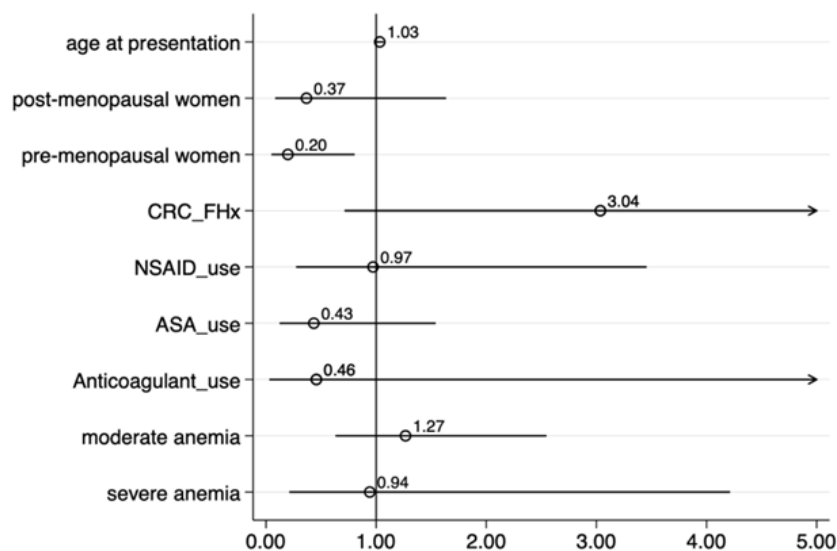


Figure 4: coefficient plot of multivariable logistic regression model evaluating factors association with clinician ordering of bidirectional endoscopy.

Supplemental Table 1: Primary analysis multivariable logistic regression estimates.

Risk factor	Estimate (OR)	95% confidence interval
Age in years	1.03	1.00 – 1.07
Sex and menopausal category ^a		
Post-menopausal women	0.37	0.0 – 1.63
Pre-menopausal women	0.20	0.05 – 0.80
CRC family history	3.04	0.71 – 12.9
NSAID use	0.97	0.27 – 3.46
Aspirin use	0.43	0.12 – 1.54
Anticoagulant use	0.46	0.03 – 6.74
Anemia severity ^b		
Moderate anemia	1.27	0.63 – 2.55
Severe anemia	0.94	0.21 – 4.21

a. Reference category is Men

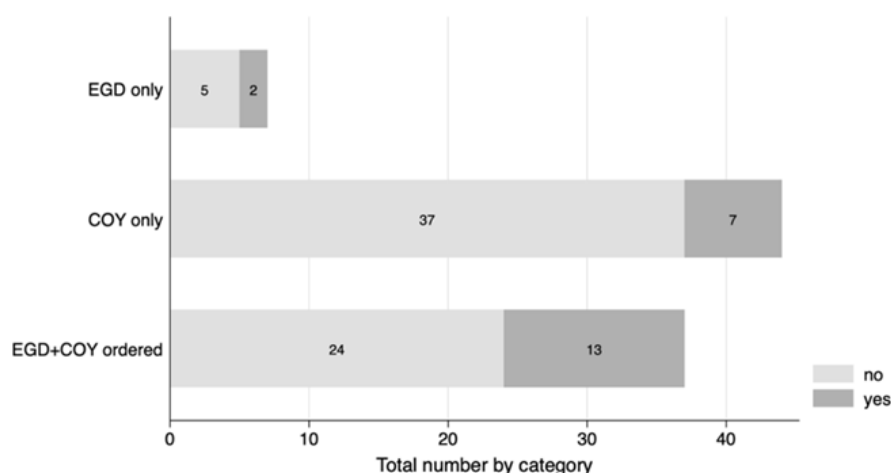
b. Reference category is mild anemia

Supplemental Table 2: Secondary analysis multivariable logistic regression estimates.

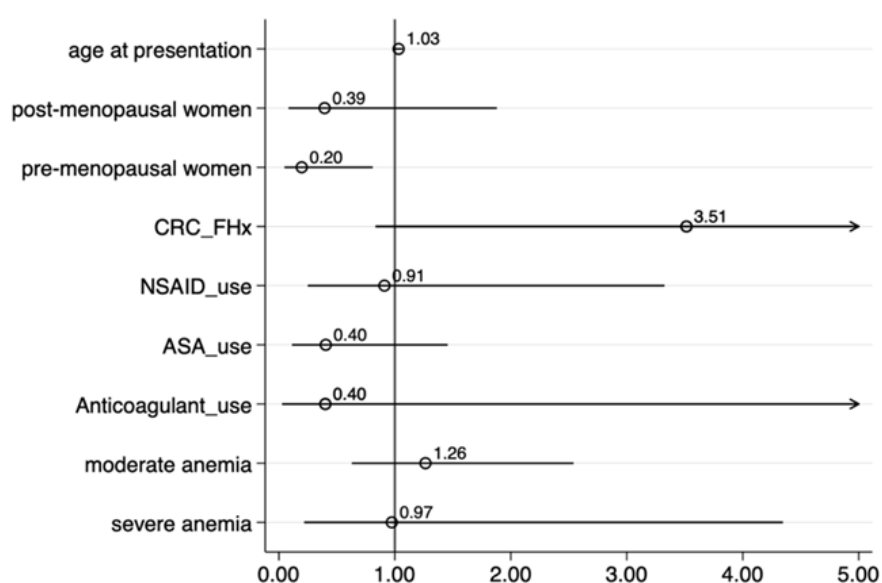
Risk factor	Estimate (OR)	95% confidence interval
Age in years	1.03	0.99 – 1.07
Sex and menopausal category ^a		
Post-menopausal women	0.39	0.08 – 1.88
Pre-menopausal women	0.20	0.05 – 0.80
CRC family history	3.51	0.83 – 14.8
NSAID use	0.91	0.25 – 3.33
Aspirin use	0.40	0.11 – 1.46
Anticoagulant use	0.40	0.02 – 5.90
Anemia severity ^b		
Moderate anemia	1.26	0.63 – 2.54
Severe anemia	0.97	0.22 – 4.35

a. Reference category is Men

b. Reference category is mild anemia



Supplemental Figure 1: Diagnostic yield by type of endoscopy.



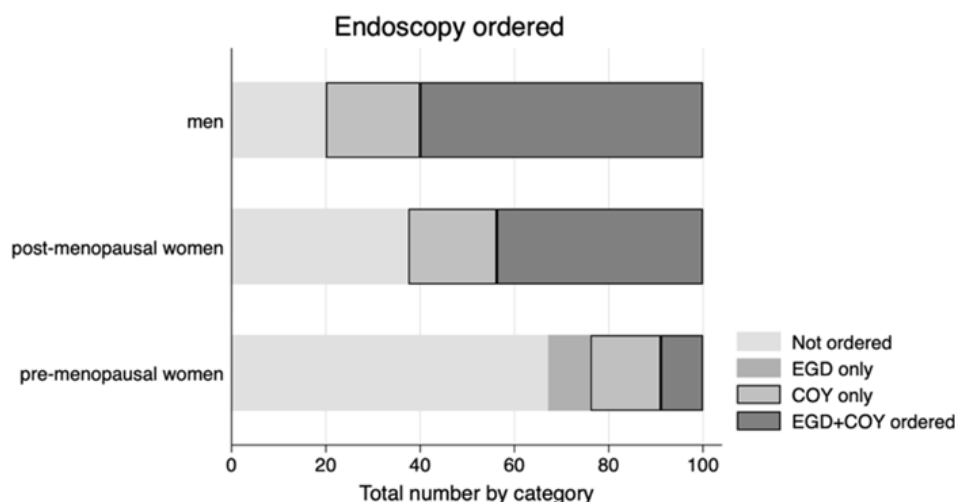
Supplemental Figure 2: Secondary analysis coefficient plot of multivariable logistic regression model evaluating factors association with clinician ordering of any endoscopic or non-invasive testing for IDA.

Supplemental Table 3: Cohort characteristics using ferritin ≤ 15 as IDA threshold.

	Total	Men	Post-menopausal women	Pre-menopausal women
	N=88	N=5	N=16	N=67
Age in years, median (IQR)	43.5 (36.5-52.5)	54 (41-75)	75 (61.5-85.5)	41 (34-47)
Race, n (%)				
White	29 (33%)	1 (20%)	12 (75%)	16 (24%)
Black	42 (48%)	4 (80%)	4 (25%)	34 (51%)
Asian	8 (9%)	0 (0%)	0 (0%)	8 (12%)
Other	9 (10%)	0 (0%)	0 (0%)	9 (13%)
CRC family history, n (%)	7 (8%)	2 (40%)	0 (0%)	5 (7%)
NSAID use, n (%)	5 (6%)	1 (20%)	1 (6%)	3 (4%)
Aspirin use, n (%)	5 (6%)	2 (40%)	2 (12%)	1 (1%)
Anticoagulant use, n (%) ^a	1 (1%)	0 (0%)	1 (6%)	0 (0%)
Hemoglobin in g/dL, median (IQR)	10.4 (9.55-11.25)	9.3 (9.2-10)	10.05 (8.5-11)	10.5 (9.9-11.5)
Ferritin in ng/mL, median (IQR)	7 (5-10)	6 (4.4-8.1)	9.05 (5.6-12.2)	7 (5-9.7)
Anemia by severity, n (%) ^b				
Mild anemia	32 (36%)	1 (20%)	5 (31%)	26 (39%)
Moderate anemia	49 (56%)	4 (80%)	9 (56%)	36 (54%)
Severe anemia	7 (8%)	0 (0%)	2 (12%)	5 (7%)

a. Anticoagulants include vitamin K antagonists and direct oral anticoagulants

b. Classification of anemia by severity as defined by WHO 2024



Supplemental Figure 3: Type of endoscopy ordered at PCP visit by sex/menopausal status using ferritin threshold of ≤ 15 .

6. Discussion

This study revealed variable clinical practice in the diagnostic evaluation of IDA by primary care clinicians. Bidirectional endoscopy was only ordered in 40% of men and 41.3% of post-menopausal women despite a strong recommendation for this group, with lower rates amongst pre-menopausal women without menorrhagia (10%). Endoscopy order rates improved to 75% and 76.1% among men and post-menopausal women, respectively, when we included those that received any type of endoscopy; this increase was primarily due to a significant proportion of patients receiving unidirectional colonoscopy in both groups which may have been in the context of routine cancer screening. Notably, clinician ordering practices for bidirectional endoscopy or any diagnostic testing did not significantly vary based on patient clinical factors such as anemia severity, CRC family history, and use of high-risk medications, such as NSAIDs, aspirin, or anticoagulants. However, this lack of association may reflect limited power due to the small sample size, wide confidence intervals, or unmeasured confounding, such as prior diagnostic evaluation before the IDA diagnosis, that could obscure true clinical decision-making patterns. Despite strong guideline recommendations, adherence to ordering bidirectional endoscopy remains under 50% across all groups and completion rates are even lower. Read et al. conducted a national online survey of internal medicine PCPs to assess self-reported testing practices for anemia and found that overuse of screening labs, misinterpretation of iron studies, and underuse of bidirectional endoscopy were common.[9] The rising incidence of colorectal cancer in younger populations may also influence PCPs to prioritize colonoscopy while deferring upper endoscopy [10,11]. However, upper GI tract causes of IDA, such as peptic ulcers, celiac disease, and *H. pylori* infection, are also common and may be underdiagnosed. Time constraints, patient preferences, and lack of streamlined referral systems likely further contribute to incomplete workup.[23] Further evaluation of other provider and organizational factors is needed to fully test this assumption. Pre-menopausal women consistently had the lowest rates of diagnostic testing for IDA. In our cohort, only 37.2% received orders for any endoscopic evaluation from their primary care provider. While pre-menopausal had more

orders for non-invasive *H. pylori* or celiac disease testing than men and post-menopausal women, frequency was relatively low. This discrepancy in practice may be explained by long-standing clinician belief that extraintestinal causes of anemia, such as abnormal uterine bleeding, are more common in women of childbearing age than in men [14]. However, our cohort was reviewed to ensure that included patients did not have documented menorrhagia. Additionally, some primary care providers may still be influenced by older guidelines that advised against initial endoscopic evaluation in pre-menopausal women with IDA, based on the assumption that menstrual blood loss is the predominant etiology in this group [15]. Yet our findings revealed that the proportion of positive endoscopic findings was similar between pre-menopausal women (13.2%) and men (20%). Our findings are consistent with prior work evaluating endoscopic yield among pre-menopausal women with IDA [16]. Our findings challenge the notion that pre-menopausal women are less likely to have GI pathology than men, revealing an opportunity to address status quo bias in clinical decision making. Use of guideline-directed iron supplementation anemia also appeared limited in this cohort. Among pre-menopausal women with no orders for or documentation of diagnostic endoscopy, two-thirds were prescribed oral iron supplementation. Thus, over 20% of pre-menopausal women in our cohort did not receive guideline-directed diagnostic endoscopy nor treatment for IDA. This raises the concern that pre-menopausal women with IDA are a vulnerable group. IDA is a major health concern among women, particularly in premenopausal populations where causes are often multifactorial, and if left untreated, it is associated with fatigue, impaired physical endurance, reduced cognitive performance, and increased risk of maternal mortality [12]. Among women of childbearing age, the global prevalence of anemia is 30.2%, significantly higher than the overall population prevalence of 24%, highlighting the disproportionate burden of IDA in this group [13]. Given the high prevalence, appropriate evaluation and treatment are critical. Yet, while there are no universally established benchmarks for treatment rates in outpatient settings, these proportions raise concern for missed opportunities to initiate guideline-concordant therapy. Notably, oral iron supplementation lacks standardized dosing rec-

ommendations especially in patients with comorbidities such as kidney disease, and high doses often result in poor absorption, gut irritation, and inflammation [17,18]. These findings highlight the need for clearer prescribing guidance.

Despite recommendations supporting diagnostic evaluation for IDA, non-invasive testing for celiac disease and *H. pylori* was infrequently performed in our cohort. Only 16.1% of patients underwent celiac serologies, and just 7.1% were tested for *H. pylori*, even though both conditions are recognized contributors to iron deficiency. While no formal benchmark exists for expected testing rates, these proportions suggest that non-invasive evaluations are not routinely incorporated into workups, even in academic primary care settings. This is particularly concerning given that the prevalence of *H. pylori* infection increases with age and that *H. pylori* is a known risk factor for gastric cancer [19]. U.S. data have shown rising morbidity and mortality from gastric cancer, underscoring the potential long-term benefits of broader *H. pylori* screening in patients with IDA [20]. Similarly, the incidence of celiac disease has increased over time, with women diagnosed at nearly twice the rate of men—though underdiagnosis in men may partially account for this disparity [21]. Evidence also suggests that non-invasive testing may help uncover clinically significant gastrointestinal pathology. In an Italian study of 59 premenopausal women with IDA, 67.8% had positive non-invasive tests that prompted endoscopic evaluation, ultimately revealing bleeding-associated or non-bleeding lesions in the vast majority [22]. In contrast, among our 90 premenopausal patients, only 8.9% were tested for *H. pylori* and 12.2% underwent celiac testing, with just a single positive result. Nonetheless, the diagnostic yield of endoscopy remained notable. These findings emphasize the importance of considering early non-invasive testing and endoscopic evaluation when IDA is persistent or unexplained, particularly in younger women, and highlight missed opportunities for timely diagnosis.

This study has several strengths. To our knowledge, it is one of the first to evaluate adherence to guideline-recommended evaluation for iron deficiency anemia in an academic primary care setting. We also used manual chart review for data abstraction to reduce the risk of information bias, validate a priori inclusion and exclusion criteria, and accurately collect risk factors for this study. This study has several limitations. The ordering practices from an urban primary care practice may be different from practices across the country, but it may be even lower at non-academic practices that do not have access to the same degree of specialty input. As an exploratory study, group sample sizes obtained were small and are at risk for being underpowered to detect differences between groups in our multivariable analysis. We addressed this by performing secondary analyses, as previously described, with larger sample sizes that did not significantly differ from our primary analysis. As a retrospective analysis relying on electronic health records, we are not able to fully capture provider rationale or over-the-counter medication use (e.g. NSAIDs). This is an inherent limitation of this type of research. Finally, insurance status and socioeconomic factors were not analyzed, which could have influenced adherence

and procedure completion rates. Delays in scheduling, high out-of-pocket costs, and lack of transportation are well-documented barriers to completing endoscopic evaluations. This work provides a basis for future research to explore whether socioeconomic disparities played a role in guideline adherence and evaluate interventions aimed at improving access and completion rates for necessary evaluations.

7. Conclusion

Despite AGA recommendations, guideline adherence for the evaluation of asymptomatic IDA in academic primary care remains variable, and pre-menopausal women are at risk of receiving sub-standard care. Many patients who met criteria for diagnostic testing did not undergo endoscopic or non-invasive evaluation. Inadequate adherence to AGA guidelines may result in missed diagnoses of GI malignancies, celiac disease, and *H. pylori* infection, leading to delays in treatment and increased morbidity. In the context of rising rates of early-onset colorectal cancer and known diagnostic delays, identifying opportunities for earlier detection of clinically significant gastrointestinal pathology is a priority. Improving provider awareness, refining clinical decision support tools, behavioral interventions, clarifying criteria for endoscopic evaluation in premenopausal women, and patient navigation support could be leveraged to optimize patient outcomes.

References

1. Short MW, Domagalski JE. Iron deficiency anemia: evaluation and management. *Am Fam Physician*. 2013; 87(2): 98-104.
2. Planella de Rubinat M, Teixidó Amorós M, Ballester Clau R, Trujillano Cabello J. Incidence and predictive factors of iron deficiency anemia after acute non-variceal upper gastrointestinal bleeding without portal hypertension] *Gastroenterol Hepatol*. 2015; 38: 525-533.
3. Ko CW, Siddique SM, Patel A. AGA Clinical Practice Guidelines on the gastrointestinal evaluation of iron deficiency anemia. *Gastroenterology*. 2020; 159(3): 1085-1094.
4. Phipps AI, Ichikawa L, Bowles EJ. Defining menopausal status in epidemiologic studies: A comparison of multiple approaches and their effects on breast cancer rates. *Maturitas*. 2010; 67(1): 60-6.
5. US Preventive Services Task Force. Mangione CM, Barry MJ. Hormone Therapy for the Primary Prevention of Chronic Conditions in Postmenopausal Persons: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2022; 328(17): 1740-1746.
6. Spencer M, Lenhart A, Baker J. Primary Care Physicians Are Under Testing for Celiac Disease in Patients with Iron Deficiency Anemia: Results of a National Survey. *PLoS One*. 2017; 12(9): e0184754.
7. Lanier JB, Park JJ, Callahan RC. Anemia in Older Adults. *Am Fam Physician*. 2018; 98(7): 437-442.
8. Snook J, Bhala N, Beales ILP, Cannings D, Kightley C, Logan RP, Pritchard DM. British Society of Gastroenterology guidelines for the management of iron deficiency anaemia in adults. *Gut*. 2021; 70(11): 2030-2051.
9. Read AJ, Waljee AK, Sussman JB, et al. Testing Practices, Interpretation, and Diagnostic Evaluation of Iron Deficiency Anemia by US Primary Care Physicians. *JAMA Netw Open*. 2021; 4(10): e2127827.

10. Ahnen DJ, Wade SW, Jones WF. The increasing incidence of young-onset colorectal cancer: a call to action. *Mayo Clin Proc.* 2014; 89(2): 216-224.
11. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2023. *CA Cancer J Clin.* 2023; 73(1): 17-48.
12. Horton S, Ross J. The economics of iron deficiency. *Food Policy.* 2003; 28(1): 51-75.
13. McLean E, Cogswell M, Egli I, Wojdyla D, de Benoist B. World-wide prevalence of anemia, WHO Vitamin and Mineral Nutrition Information System, 1993–2005. *Public Health Nutr.* 2009; 12(4): 444-454.
14. Kepczyk T, Cremins JE, Long BD, Bachinski MB, Smith LR, McNally PR. A prospective, multidisciplinary evaluation of premenopausal women with iron-deficiency anemia. *Am J Gastroenterol.* 1999; 94(1): 109-15.
15. Goddard AF, James MW, McIntyre AS, Scott BB; British Society of Gastroenterology. Guidelines for the management of iron deficiency anemia. *Gut.* 2011; 60(10): 1309-16.
16. Bini EJ, Micale PL, Weinshel EH. Evaluation of the gastrointestinal tract in premenopausal women with iron deficiency anemia. *Am J Med.* 1998; 105(4): 281-6.
17. Moretti D, Goede JS, Zeder C. Oral iron supplements increase hepcidin and decrease iron absorption from daily or twice-daily doses in iron-depleted young women. *Blood.* 2015; 126(17): 1981-1989.
18. Daly A, Egan B, Ryan M, Galvin K, Gaffney P. Tolerability and efficacy of different iron supplementation regimens in primary care: a randomized clinical trial. *BMJ Open Gastroenterol.* 2020; 7(1): e000376.
19. Eusebi LH, Zagari RM, Bazzoli F. Epidemiology of *Helicobacter pylori* infection. *Helicobacter.* 2014; 19(S1):1-5.
20. Rawla P, Barsouk A. Epidemiology of gastric cancer: global trends, risk factors and prevention. *Prz Gastroenterol.* 2019; 14(1): 26-38.
21. King JA, Jeong J, Underwood FE. Incidence of Celiac Disease Is Increasing Over Time: A Systematic Review and Meta Analysis. *Am J Gastroenterol.* 2020; 00(00): 1-19.
22. Lebowitz B, Rubio-Tapia A, Lee AR. Epidemiology, Presentation, and Diagnosis of Celiac Disease. *Gastroenterology.* 2021; 160(1): 63-75.
23. Annibale B, Lahner E, Chistolini A, Gailucci C, Di Giulio E. Endoscopic evaluation of the upper gastrointestinal tract is worthwhile in premenopausal women with iron-deficiency anaemia irrespective of menstrual flow. *Scand J Gastroenterol.* 2003; 38(3): 239-45.
24. Sarkar U, Bonacum D, Strull W, Spitzmueller C, Jin N, López A, Giardina TD. Challenges of making a diagnosis in the outpatient setting: a multi-site survey of primary care physicians. *BMJ Qual Saf.* 2012; 21(8): 641-8.