Complete Summary

GUIDELINE TITLE

Identification, diagnosis, and management of anemia in adult ambulatory patients treated by primary care physicians: evidence-based and consensus recommendations.

BIBLIOGRAPHIC SOURCE(S)

Dubois RW, Goodnough LT, Ershler WB, Van Winkle L, Nissenson AR. Identification, diagnosis, and management of anemia in adult ambulatory patients treated by primary care physicians: evidence-based and consensus recommendations. Curr Med Res Opin 2006 Feb;22(2):385-95. [56 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- July 31, 2008, Erythropoiesis Stimulating Agents (ESAs): Amgen and the U.S. Food and Drug Administration (FDA) informed healthcare professionals of modifications to certain sections of the Boxed Warnings, Indications and Usage, and Dosage and Administration sections of prescribing information for Erythropoiesis Stimulating Agents (ESAs). The changes clarify the FDA-approved conditions for use of ESAs in patients with cancer and revise directions for dosing to state the hemoglobin level at which treatment with an ESA should be initiated.
- November 8, 2007 and January 3, 2008 Update, Erythropoiesis Stimulating Agents (ESAs): The U.S. Food and Drug Administration (FDA) notified healthcare professionals of revised boxed warnings and other safety-related product labeling changes for erythropoiesis-stimulating agents (ESAs) stating serious adverse events, such as tumor growth and shortened survival in patients with advanced cancer and chronic kidney failure.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Anemia (excluding anemia related to nutritional deficiencies, cancer/chemotherapy, or chronic renal failure)

GUIDELINE CATEGORY

Diagnosis
Management
Risk Assessment
Screening

CLINICAL SPECIALTY

Family Practice
Geriatrics
Internal Medicine
Obstetrics and Gynecology
Preventive Medicine
Rheumatology

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

Provide evidence based and consensus recommendations for the identification, diagnosis, and management of ambulatory patients with anemia not related to nutritional deficiencies, cancer/chemotherapy, or chronic renal failure

TARGET POPULATION

Adult ambulatory patients treated by primary care physicians who have or may have anemia not related to nutritional deficiencies, cancer/chemotherapy, or chronic renal failure

INTERVENTIONS AND PRACTICES CONSIDERED

Screening/Risk Assessment

1. Routine complete blood count at time of office visit in select populations
2. Assessment of risk based on age, presence or absence of cardiovascular disease or symptoms, presence or absence of anemia symptoms, and hemoglobin levels

Diagnosis

1. Stool for occult blood
2. Additional optional tests, such as reticulocyte count, iron, total iron binding capacity, folate, B12, ferritin, creatinine, or chest x-ray

Note: Guideline developers considered but recommended against referral to a gastroenterologist or hematologist for initial diagnostic work-up

Management

1. No intervention (observation only)
2. Referral
3. Trial of empiric iron therapy
4. Transfusion
5. Erythropoietic growth factors (epoetin alfa, epoetin beta, or darbepoetin)

MAJOR OUTCOMES CONSIDERED

Among patients with anemia, what impact does treatment have on:

- Mortality
- Morbidity
- Quality of life and functioning

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Guideline developers conducted a search of the literature using the PubMed database, from 1990 through 2003. The search terms and strategies were

developed in conjunction with clinical experts in anemia and included, but were not limited to, 'anemia', 'therapy', 'quality of life', 'mortality', 'survival', 'prevalence', 'disease progression',' outcome assessment', 'treatment outcome', 'referral', 'consultation', 'diagnostic tests', 'etiology', epidemiology', and 'mass screening'. Additional articles were identified from among the reference lists of papers selected for review. Panelists reviewed the reference lists and recommended additional relevant references.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Clinicians or epidemiologists trained in health services research extracted all the data from the studies to create evidence tables. These tables underwent subsequent review by two physicians with training in health services research. The nine-member expert panel also reviewed the evidence synthesis for completeness and accuracy.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Guideline developers used a validated evidence-based but not evidence-constrained consensus process (the RAND/UCLA Appropriateness Method) to develop recommendations for the identification, diagnosis, and management of patients with anemia in an ambulatory environment.

The panelists received the literature review and an initial set of scenarios by mail. They were requested to carefully study the synthesis of the literature and to rate each scenario using a scale of 1 to 9 (1 = extremely inappropriate, 5 = uncertain, 9 = extremely appropriate). 'Appropriateness' was defined as the expected health benefits of the therapy exceeding its expected negative health consequences by a sufficiently wide margin to justify prescribing the therapy.

After having accomplished this task independently, the results of the initial rating were compiled. Finally, the group was convened for a 2-day meeting. During the meeting, the panelists reviewed the summarized first-round ratings, revised the structure of the clinical scenarios, ensured that all panelists were working from the same definition of key terms, and discussed reasons for the degree of agreement or disagreement in the ratings from the first round. Panelists then independently and confidentially re-rated all indications.

The final rating was the median score of the nine panelists. Guideline developers considered that indications were 'appropriate' for median ratings between 7 and 9 (without disagreement), 'inappropriate' for median ratings between 1 and 3 (without disagreement), and 'uncertain' for median ratings between 4 and 6 or if panelists disagreed. The consensus method did not force agreement. Guideline developers defined disagreement as occurring when at least two panelists rated the indication 'appropriate' and at least two rated the indication 'inappropriate', regardless of the median rating.

Clinical Scenarios

Guideline developers attempted to create a comprehensive list of all possible clinical scenarios for the identification, diagnosis, and management of anemic patients in an ambulatory setting. Preliminary scenarios were constructed by the authors, and subsequently underwent a two-round review process by the expert panel. Patients with cancer- or chemotherapy-related anemia, or chronic kidney disease related anemia, were excluded from consideration. Scenarios pertained to three clinical situations described in the original guideline document.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The RAND/UCLA Appropriateness Method

Appropriate: Median ratings between 7 and 9 (without disagreement)

Uncertain: Median ratings between 4 and 6 or if panelists disagreed (when two panelists rated the indication "appropriate" and at least two rates the indication as "inappropriate)

Inappropriate: Median ratings between 1 and 3 (without disagreement)

Rating Scale of Appropriateness* (1 to 9)

1 = extremely inappropriate

5 = uncertain

9 = extremely appropriate

*'Appropriateness' was defined as the expected health benefits of the therapy exceeding its expected negative health consequences by a sufficiently wide margin to justify prescribing the therapy.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of recommendation (Appropriate, Uncertain, Inappropriate) are defined at the end of the "Major Recommendations" field.

Identification

The panel rated it 'appropriate' to perform a routine complete blood count (CBC) at the time of an office visit in patients with an underlying chronic condition (e.g., rheumatoid arthritis, congestive heart failure) who had not received a CBC in the past year. In patients without an underlying chronic condition, it was rated 'appropriate' to perform a CBC if a CBC had not been done in the past 5 years for all women, men aged 50 and older, or those with anemia symptoms (Table 1).

***Table 1**. Appropriateness of a Routine Complete Blood Count at the Time of an Office Visit*

Comorbidity	Interval	Population	Consensus
No chronic comorbidity	Every 5 years	Men aged 18 to 49 without anemia symptoms	Uncertain
		All women	
		Men aged 50 and older	Appropriate
		Men with anemia symptoms	
Chronic comorbidity	Yearly	All	Appropriate

Diagnosis

In women aged 18 to 49 with a hemoglobin (Hb) > 12 g/dL, the panel rated it 'inappropriate' to perform any diagnosis and 'appropriate' to just observe. The corresponding threshold for men or women aged 50 and older was a hemoglobin of > 13 g/dL (Table 2).

***Table 2**. Appropriateness of a Diagnosis Given Patient Characteristics*

Population	Hb level (g/dL)	No intervention (just observe)	Perform basic diagnosis	Empiric iron	Refer for GI diagnosis	Refer for Hematologic work-up
Women 18 to 39 years old	≤12	Inappropriate*	Appropriate	Uncertain	Inappropriate	
	>12	Appropriate	Inappropriate			
Women aged 40 to 49 years old	≤12	Inappropriate*	Appropriate	Inappropriate		
	>12	Appropriate	Inappropriate			
Women aged ≥50 (or post-menopausal and 18 to 49) years old or any man	≤13	Inappropriate	Appropriate	Inappropriate		
	>13	Appropriate	Inappropriate			

*Uncertain is Hb 11-12 g/dL and no comorbid chronic disease

GI= gastrointestinal

A diagnosis was rated 'appropriate' in women aged 18 to 50 with hemoglobin ≤12 g/dL (or ≤13 g/dL in men or post-menopausal women). When an evaluation was indicated, the panel rated the performance of a basic evaluation 'appropriate' (e.g., test stool for occult blood and obtain routine labs or chest x-ray). However, referral to a gastroenterologist or hematologist for a work-up was rated 'inappropriate' (Table 2). The use of an empiric trial of iron therapy in the absence of a diagnostic workup was rated 'inappropriate' in all situations except for women aged 18 to 39.

Management

With respect to management, the panel rated it 'appropriate' to just observe and 'inappropriate' to transfuse or give erythropoietic growth factors in patients with a hemoglobin of ≥11 g/dL and no anemia symptoms or underlying cardiovascular disease (Table 3).

Table 3*. Appropriateness of anemia management options given patient characteristics (non-nutritional anemia)*

Hb (g/dL)	Cardiovascular disease	Anemia symptoms	Age	Management options		
				Observe	Transfuse	Epo/darbo
<8.0				Inappropriate	Appropriate*	Appropriate
8 to 9.4	–	–	18 to 69	Uncertain	Uncertain	Appropriate+
	–	–	70 or	Inappropriate	Appropriate	
	Either CVD or symptoms				Appropriate++	Appropriate

9.5 to 10.9	–	–	older	Uncertain	Inappropriate	Uncertain
	–	+		Inappropriate	Uncertain	Appropriate
	+	–	18 to 49		Inappropriate	Uncertain
	+	+			Appropriate	
	–	–		Uncertain	Inappropriate$	Uncertain
	–	+		Inappropriate	Uncertain	Appropriate
	+	–	50 or older			
	+	+			Appropriate	
11 to 11.9**	–	–		Appropriate	Inappropriate	Inappropriate
	–	+		Uncertain		Uncertain
	+	–		Appropriate		Inappropriate
	+	+		Uncertain		Uncertain
12 or greater +++				Appropriate	Inappropriate	

*Uncertain if age 18 to 49, no CVD, and no anemia symptoms

+Uncertain if age 18 to 49

++Uncertain if no anemia symptoms

$Uncertain if age ≥70 years

**11 to 12.9 if age ≥70 years

+++ ≥13 if age ≥70 years

CVD = cardiovascular disease; epo = epoetin; darbo = darbepoetin

For patients with hemoglobin of 9.5 to 10.9 g/dL, it was rated 'inappropriate' to just observe the patient if the patient had anemia symptoms or cardiovascular disease. If the patient had anemia symptoms, the use of erythropoietic growth factors was rated 'appropriate' (or 'uncertain' if no anemia symptoms were present). The use of blood transfusion was rated 'inappropriate' if the patient had no anemia symptoms, 'uncertain' in the presence of just anemia symptoms, and 'appropriate' if the patient had anemia symptoms and underlying cardiovascular disease.

In patients with hemoglobin < 9.5 g/dL, it was rated 'inappropriate' to just observe (unless the patient had no symptoms, no cardiovascular disease, and was younger than age 70 in which case it was rated 'uncertain'). The use of an erythropoietic growth factor was rated 'appropriate'. Transfusion was considered appropriate in patients aged 70 and older and in those presenting with either anemia symptoms or underlying cardiovascular disease.

In patients with hemoglobin < 8 g/dL, the use of either transfusion or erythropoietic growth factor was rated 'appropriate' and observation was rated 'inappropriate'.

Definitions:

Rating Scheme for Strength of Recommendations

Appropriate: Median ratings between 7 and 9 (without disagreement)

Uncertain: Median ratings between 4 and 6 or if panelists disagreed (when two panelists rated the indication 'appropriate' and at least two rates the indication as 'inappropriate')

Inappropriate: Median ratings between 1 and 3 (without disagreement)

Rating Scale of Appropriateness* (1 to 9)

1 = extremely inappropriate

5 = uncertain

9 = extremely appropriate

*'Appropriateness' was defined as the expected health benefits of the therapy exceeding its expected negative health consequences by a sufficiently wide margin to justify prescribing the therapy.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate identification, diagnosis, and management of anemia to improve outcomes in ambulatory patients with anemia (specifically, anemia not related to nutritional deficiencies, cancer/chemotherapy, or chronic renal failure)

POTENTIAL HARMS

Risks associated with diagnostic tests including venipuncture and colonoscopy

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This recommendation does not address the issue of population identification or when patients should visit a physician to have an anemia assessment performed. Rather, this recommendation addresses the somewhat narrower issue of whether to obtain a routine complete blood count (CBC) when the patient had already sought medical care.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Dubois RW, Goodnough LT, Ershler WB, Van Winkle L, Nissenson AR. Identification, diagnosis, and management of anemia in adult ambulatory patients treated by primary care physicians: evidence-based and consensus recommendations. Curr Med Res Opin 2006 Feb;22(2):385-95. [56 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Feb

GUIDELINE DEVELOPER(S)

National Anemia Action Council - Private Nonprofit Research Organization

SOURCE(S) OF FUNDING

National Anemia Action Council

GUIDELINE COMMITTEE

Panel of Experts

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

National Anemia Action Council (NAAC) has received unrestricted educational grants from Amgen, Inc.

Robert W. Dubois is Senior Vice President of Cerner Health Insights, which provided consulting services to Amgen, Inc. Kirkwood F. Adams is a member of NAAC and has received grants and research support from Amgen Inc. William Ershler is a member of NAAC. Allen Nissenson is President of NAAC. L. Tim Goodnough was Vice President of NAAC at the time the guidelines were developed, and has received honoraria for teaching and speaking from the following companies: Amgen, Watson, and American Regent.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available to subscribers in Portable Document Format (PDF) from the Current Medical Research and Opinion Web site.

Print copies: Available from Robert W. Dubois, MD, PhD, Senior Vice President, Cerner Health Insights, 9100 Wilshire Blvd, Suite 655 East Tower, Beverly Hills, CA 90212; Phone: +1-310-598-4563; Fax: +1-816-936-1963; Email: rdubois@cerner.com

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on January 15, 2007. The information was verified by the guideline developer on February 5, 2007. This summary was updated by ECRI Institute on July 9, 2007, following the FDA advisory on erythropoiesis stimulating agents. This summary was updated by ECRI Institute on March 21, 2008 following the FDA advisory on Erythropoiesis Stimulating Agents. This summary was updated by ECRI Institute on August 15, 2008 following the U.S. Food and Drug Administration advisory on Erythropoiesis Stimulating Agents (ESAs).

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