



Spring 2004

# ANEMIAWATCH

A Quarterly Publication of the National Anemia Action Council, Inc.

## Anemia News

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### NAAC Mission Statement

The National Anemia Action Council, Inc. (NAAC) is dedicated to raising the awareness of health care professionals and the public regarding the prevalence, symptoms, consequences, and undertreatment of anemia.

### Anemia Watch Vision

In support of NAAC's mission, the vision of AnemiaWatch is to provide an objective educational resource to health care professionals, and act as a quarterly information liaison in relation to anemia.

97-0404-002

Systematic literature review published on anemia in geriatrics, oncology, human immunodeficiency virus infection, inflammatory bowel disease, rheumatoid arthritis, and surgery.

On April 5, 2004, the American Journal of Medicine published a supplement entitled *Anemia and Its Clinical Consequences in Patients with Chronic Diseases*. Members of NAAC contributed to the publication that summarized systematic literature reviews on anemia in 6 clinical areas: geriatrics, oncology, human immunodeficiency (HIV) infection, inflammatory bowel disease (IBD), rheumatoid arthritis (RA), and surgery. Published articles from peer reviewed publications in the above mentioned clinical areas were reviewed, and evaluations were made as to the prevalence and impact of anemia on clinical and functional outcomes.

The literature review identified a knowledge gap in relation to anemia's impact on clinical and functional outcomes in all 6 clinical areas. Inconsistent criteria for defining anemia in published studies were a major contributing factor to this knowledge gap. The supplement details the necessity for revision of criteria utilized for defining anemia, and the need for a paradigm shift to recognizing anemia as a condition which must be properly identified and treated in order to improve healthcare outcomes. "Two accepted classification schemes – the WHO and the National Cancer Institute [anemia] definitions – are a starting point for developing a uniform set of definitions for anemia." NAAC is currently in the process of developing clinical guidelines for anemia management.

#### First Systematic Literature Review – Anemia in Geriatrics

The first literature review entitled *Prevalence and Outcomes of Anemia in Geriatrics: A Systematic Review of the Literature*<sup>1</sup> was performed in order to identify the following: 1) data concerning anemia prevalence in relevant studies, and factors responsible for rate differences; 2) an inventory of contributing pathophysiologic mechanisms in geriatric anemia; 3) a summarization of anemia-associated complications; 4) a discussion of the validity of gender-specific criteria for anemia within the geriatric population; 5) major

gaps in knowledge about geriatric anemia; and 6) recommendations for a future research agenda.

As described in the Methods section, health care outcomes studied included clinical, and functional, patient satisfaction, and direct and indirect costs of care. The 2 databases of the US National Library of Medicine and Excerpta Medica were utilized, and 74 articles focusing on anemia of chronic disease or iron-deficiency anemia in geriatric patients were deemed appropriate for review. Upon reviewing the materials, several recommendations were made for future research.

The authors stated and reiterated, "to improve the diagnosis and treatment of anemia in elderly patients, future research must include studies designed to determine appropriate criteria – based on clinical measures – for defining anemia in elderly men and women." Recommendations were also made for future studies comparing trends of age-related increase in anemia prevalence in healthy community residents to trends in patients within acute care skilled nursing wards or long term skilled nursing facilities. In order to better determine the impact of anemia on clinical and functional outcomes in the elderly, more information must be accumulated on the affects of anemia in relation to health, quality of life, and cost of care.

This systematic literature review on anemia in geriatrics identified the "greatest opportunities for improving the care of these [geriatric] patients lie in identifying and treating the underlying causes [of anemia]." Please note that the authors quoted statistics from a large randomized placebo-controlled trial examining anemia in the geriatric nursing home population. The findings of this study are discussed in this *AnemiaWatch* issue in the article entitled: *Study results available on the characterization of anemia in elderly nursing home residents*.

#### Second Systematic Literature Review – Anemia in Cancer

The second literature review entitled *Prevalence and Outcomes of Anemia in Cancer: A Systematic Review of the Literature*<sup>2</sup> was performed to determine anemia-prevalence associated with certain cancers, and evaluate the impact of anemia as an independent factor on patient survival and quality of life.

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## **Anemia News**, continued from cover

As described in the Methods section, health care outcomes studied included clinical, and functional, patient satisfaction, and direct and indirect costs of care. The 2 databases of the US National Library of Medicine and Excerpta Medica were utilized, and articles were deemed appropriate for review if they focused on anemia of chronic disease and/or iron-deficiency anemia in patients with cancer. Forty-seven studies were reviewed, and upon reviewing the materials, several recommendations were made for future research.

The authors suggest precedence be given to addressing knowledge gaps identified in this systematic literature review in order to enhance the understanding of anemia management in cancer patients. A consistent definition of anemia was not apparent throughout the reviewed literature, with measures of anemia varying throughout the studies. In addition, many data were obtained from studies that were not designed to assess quality of life, survival, mortality, and other aspects of clinical and functional outcomes. Causal relations between anemia and health care outcomes were identifiable in “the areas of radiation therapy effectiveness [head and neck cancers], transfusion requirements, functional status, and quality of life.” Specific questions were provided by the researchers for future review and addressed the impact of anemia correction on disease progression, treatment response, clinical or functional well-being, and health care outcomes.

### Third Systematic Literature Review – Anemia in HIV

The third literature review entitled *Prevalence and Outcomes of Anemia in Human Immunodeficiency Virus: A Systematic Review of the Literature*<sup>3</sup> was performed to identify anemia-prevalence associated with HIV, and determine the impact of anemia as an independent factor on quality of life and clinical outcomes.

As described in the Methods section, health care outcomes studied included clinical, functional, patient satisfaction, and direct and indirect costs of care. The 2 databases of the US National Library of Medicine and Excerpta Medica were utilized, and 31 articles were deemed appropriate which focused on anemia of chronic disease or iron-deficiency anemia in patients with HIV. Upon reviewing the materials, several recommendations were made for future research.

Due to intrinsic differences among studies available in the literature, the true prevalence of anemia in HIV is difficult to calculate. A standard definition of anemia is not utilized throughout studies,

thus findings were not based on consistent diagnostic criteria. Certain studies distinguished between stages of HIV disease and prevalence statistics were reported for each stage, while other studies did not differentiate between HIV disease stages. Notwithstanding, the literature review yielded “the highest rates of anemia occur in patients with advanced HIV disease (AIDS), and often in patients receiving zidovudine.” Anemia prevalence rates in patients with HIV and the absence of AIDS ranged from 46% to 59%.

The presence of anemia with HIV was associated with “increased mortality, disease progression, transfusion requirements, fatigue, and worsened quality of life,” while the correction of anemia was demonstrated to decrease mortality and increase survival rates.

Rates of opportunistic infections, drug toxicity, and patient deterioration were found to correlate directly with anemia as an independent factor. Of interest, highly active antiretroviral therapy (HAART) was demonstrated to possibly lessen anemia in patients with HIV. In order to determine cost-effective treatment options for patients with anemia and HIV, cost-benefit analyses will need to be performed.

### Fourth Systematic Literature Review: Anemia in IBD

The fourth literature review entitled *Prevalence and Outcomes of Anemia in Inflammatory Bowel Disease: A Systematic Review of the Literature*<sup>6</sup> was performed to identify anemia-prevalence rates associated with IBD, and determine the impact of anemia as an independent factor on clinical and functional health care outcomes.

As described in the Methods section, health care outcomes studied included clinical, functional, patient satisfaction, and direct and indirect costs of care. The 2 databases of the US National Library of Medicine and Excerpta Medica were utilized, and 15 articles were deemed appropriate which focused on anemia of chronic disease or iron-deficiency anemia in patients with IBD.

Anemia prevalence in IBD ranged from 8.8% to 73.7%. The review revealed there are two primary causes for anemia with IBD, (1) iron deficiency from intestinal bleeding and (2) anemia of chronic disease. Upon reviewing the materials, several recommendations were made for future research.

There are not much data on the impact of anemia as an independent factor in IBD. The data suggest a direct correlation with clinical and functional health care outcomes and anemia; however, additional

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## **Ask the Expert**

NAAC welcomes clinical questions from health care professionals related to anemia management. Answers will be provided by physicians who are medical experts in the field of anemia. All relevant clinical questions will be posted on the Ask the Expert section of the web site if appropriate, at times via e-mail, and selected questions will be published in AnemiaWatch.

Please e-mail anemia-related clinical questions to [Asktheexpert@anemia.org](mailto:Asktheexpert@anemia.org)

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studies need to be performed utilizing a standard definition of anemia, and to measure how improved hemoglobin levels affect quality of life and the Crohn Disease Activity Index. The authors recommend double-blind placebo-controlled trials be performed to authenticate the findings that refractory anemias treated with erythropoietic agents result in improved hemoglobin and CDAI scores. Patient outcomes and quality of life can be enhanced through a deeper understanding of the impact of anemia as an independent factor on clinical and functional health care outcomes.

### **Fifth Systematic Literature Review – Anemia in RA**

The fifth literature review entitled *Prevalence and Outcomes of Anemia in Rheumatoid Arthritis: A Systematic Review of the Literature*<sup>5</sup> was performed in order to evaluate anemia prevalence in patients with RA, and to evaluate the impact of anemia as an independent factor on health care outcomes in patients with RA.

As described in the Methods section, health care outcomes studied included clinical, functional, patient satisfaction, and direct and indirect costs of care. The 2 databases of the US National Library of Medicine and Excerpta Medica were utilized, and 19 articles were deemed appropriate which focused on anemia of chronic disease or iron-deficiency anemia in patients with RA.

The authors identified there are “significant gaps in comprehension of the true prevalence or consequence of anemia in patients with RA, as well as the benefits to RA, if any, with anemia treatment.” Out of 10 prevalence studies, 90% measured prevalence rates in adults versus children. The review revealed prevalence rates varied across studies based on the definitions used for anemia and the population clinical characteristics.

Recommendations were made for large studies assessing the anemia prevalence in all patients with RA in order to lend support for anemia screening in this patient population. Additional studies are needed to assess the impact of anemia as an independent factor on clinical and functional health care outcomes.

### **Sixth Systematic Literature Review – Anemia in Surgery**

The sixth literature review entitled *Prevalence and Outcomes of Anemia in Surgery: A Systematic Review of the Literature*<sup>6</sup> was performed in order to determine anemia prevalence in surgical patients (focusing on preoperative anemia), as well as to evaluate the impact of anemia as an independent factor on health care outcomes in surgical patients.

As described in the Methods section, health care outcomes studied included clinical, functional, patient satisfaction, and direct and indirect costs of care. The 2 databases of the US National Library of Medicine and Excerpta Medica were utilized. Thirteen articles were deemed appropriate to evaluate anemia prevalence, and focused on anemia of chronic disease or iron-deficiency anemia in surgical patients. Twenty-nine studies were included in the review of the impact of anemia on various health care outcomes. The review revealed anemia prevalence rates in surgical patients ranged from 5% to 75.8%, depending on the clinical characteristics of the population

(5% statistic was calculated in the geriatric population of women with hip fractures, and the 75.8% statistic stemmed from patients awaiting a colectomy for advanced colon cancer).

The definition of anemia was not consistent across studies, with one of the studies determining the diagnosis of anemia via *ICD-9-CM* codes, and other studies basing the anemia diagnosis on hemoglobin or hematocrit values with varying thresholds; therefore, definitive anemia prevalence rates were not able to be determined. After evaluating the materials, recommendations were made for future research.

Studies are needed to determine anemia's impact on clinical and functional health care outcomes. These studies must be designed with a standardized definition of anemia, and the ability to measure clinical as well as functional outcomes. Additional studies are needed to evaluate anemia prevalence in surgical patients, and the impact of anemia on survival rates and healthcare costs.

In order to compare the differences in cost between autologous and allogenic blood transfusions, a cost analysis should be performed. Although autologous blood transfusion appears more costly than allogenic blood transfusion on the surface, the reduced rate of complications may prove cost-effective. Further exploration is necessary in all of the above areas in order to provide preeminent anemia management in surgical patients with anemia.

## **Anemia News**

### **Study results available on the characterization of anemia in elderly nursing home residents**

Findings of a prospective multiinstitutional cohort study were reported in the March 2004 *Journal of the American Geriatrics Society*. The article entitled *Mechanisms of Unexplained Anemia in the Nursing Home*<sup>7</sup> reported the results of a study characterizing anemia in nursing home residents.

The study involved 81 subjects, of which 74% were confirmed to have anemia. Within this anemic population, demographic statistics revealed the median age was 82, 70% were Caucasian, 28% African-American, and 40% were male. Anemia was defined utilizing the World Health Organization criteria<sup>8</sup> (hemoglobin (Hb) <13 g/dL for men and <12 g/dL for women).

The cause of anemia was unknown in 45% of the anemic population. Iron deficiency anemia (IDA) was found in 23% of the studied population, versus previous reports of IDA in up to 40% of nursing home residents. Anemia of chronic disease was found in 13% of patients.

The study data suggest “nursing home residents with IA have a blunted endogenous EPO response... [and appears to be of primary import]... given the high prevalence of IA found in this population.” EPO levels were observed to be low, and these findings are inconsistent with the theory that idiopathic anemia (IA) stemmed from bone marrow unresponsiveness, in which EPO levels are elevated. The authors recommend additional investigations be performed in “the

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# Web Site Redesign & New Resources:

www.anemia.org is about to offer additional valuable anemia resources.

## PROFESSIONAL LINK

The professional link will provide the latest information in anemia to health care professionals. Resources will include:

- The latest findings in anemia research
- The anemia monograph
- Health professional anemia education slide sets
- Anemia Alert (a monthly broadcast e-mail providing news/research updates and web site information)
- Anemia Watch (a quarterly online publication for health professionals)
- Ask the Expert (your questions will either be published in AnemiaWatch, answered by a medical expert, or guidance provided)
- Continuing medical education resources (NAAC programs and other links)
- Reference Library
- Professionals links
- Search Function

## PATIENT LINK

The patient link will provide the latest information in anemia in simplified language. Resources will include:

- Medical Glossary
- Link to Professional Site
- Anemia AQ: Test Your Knowledge
- E-mail Updates with AnemiaAlert
- Patient Education (patients and caregivers will have access to patient education sheets which address anemia in the following clinical settings: aging, cancer, critical illness, diabetes, heart disease, hepatitis C, HIV/AIDS, inflammatory bowel disease, iron deficiency anemia, kidney disease, rheumatoid arthritis, surgery, and vitamin deficiency).
- Frequently asked questions
- Links to other association/NIH sites
- Anemia Monograph
- Research Reports
- In the News
- Search Function

## MEDIA LINK

The media link will provide the latest information in anemia to media professionals. Resources will include:

- Media Sign Up area
- Statistics/Fast Facts
- Public Relations Staff Contact
- National Experts
- NAAC In The News (press releases)
- Back Issues of AnemiaAlert and AnemiaWatch
- Top News (weekly updates)
- Media Kit
  - Phase I:
    - Mission Statement
    - About NAAC
    - Monograph
    - Glossary
    - Press Releases
    - Graphics/Artwork
    - FAQ's
    - PR Contact
    - Patient/Consumer sheets
  - Phase II:
    - Public Initiatives
    - Stock photographs

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mechanism of inadequate EPO response...specifically, applying more sensitive measures of renal function and a complete cytokine evaluation."

The article concludes with the fact that the implication of low EPO levels, versus bone marrow unresponsiveness, within the elderly nursing home population can be demonstrated via improvement of anemia with low-dosed rHuEPO.

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7. Artz, AS, Fergusson D, Drinka P, et al. Mechanisms of Unexplained Anemia in the Nursing Home. *J Am Geriatr Soc* 2004;52(3):423-427.
8. World Health Organization. *Nutritional anemias: report of a WHO scientific group. Technical Report Series No. 405*. Geneva: World Health Organization; 1968.

# Quarterly Clinical Trial of Interest

NAAC is interested in all valid anemia research. AnemiaWatch will highlight clinical trials of interest to NAAC.

The following information is posted at the public domain:  
[www.clinicaltrials.gov](http://www.clinicaltrials.gov)

## Study by the National Heart, Lung, and Blood Institute

**BACKGROUND:** Red blood cell transfusions are an extremely common medical intervention in both the United States and worldwide; over 11 million units are transfused in the United States. Between 60 percent and 70 percent of all blood is transfused in the surgical setting. Despite the common use of red blood cell transfusions, the threshold for transfusion has not been adequately evaluated and is very controversial. A decade ago the standard of care was to administer a peri-operative transfusion whenever the hemoglobin (Hgb) level fell below 10 g/dl (the "10/30 rule"). Concerns about the safety of blood, especially with respect to HIV and hepatitis, and the absence of data to support a 10 g/dl threshold led to current standard of care today to administer blood transfusions based on the presence of symptoms and not a specific Hgb/hematocrit level. However, there are no randomized clinical trials in surgical patients that have tested the efficacy and safety of withholding blood until the patient develops symptoms or the "10/30" approach to transfusion. Patients with underlying cardiovascular disease are at greatest risk of adverse effects from reduced Hgb levels.

**DESIGN NARRATIVE:** Multi-center randomized trial to test if a more aggressive transfusion strategy that maintains postoperative Hgb levels above 10 g/dl improves patient outcome as compared to a more conservative strategy that withholds blood transfusion until the patient develops symptoms of anemia. Eligible patients for the trial will have undergone surgical repair for a hip fracture and have a postoperative Hgb level below 10 g/dl within three days of surgery. Only patients with cardiovascular disease will be entered into the study. Patients will be randomized to one of the two transfusion strategies.

The 10 g/dl threshold strategy will use enough red blood cell units to maintain Hgb levels at or above 10 g/dl through hospital discharge. Symptomatic transfusion strategy patients will receive red blood cell transfusions for symptoms of anemia, although transfusion is also permitted but not required if the Hgb level falls below 8 g/dl. Outcomes will include functional recovery (primary outcome: ability to walk ten feet across a room without human assistance at 60-days post-randomization), long-term survival, nursing home placement, and postoperative complications (death in hospital or within 30 days, pneumonia, myocardial infarction, thromboembolism, stroke, delirium). An estimated 2,600 patients from 25 centers

will be randomized over a 3.5-year period. This will allow detection of a 16 percent relative risk reduction in the loss of ability to walk independently with power about 0.90. A pilot study in 84 patients demonstrated the feasibility of the study.

Ambulation at 60 days is known to be highly predictive of ultimate functional outcome as well as of mortality at one year. Because inability to walk again has such important implications for quality of life, and because, unfortunately, it is a common problem, it far outweighs the remote chance of viral infection or other complications from transfusion in these elderly patients. Also, this study will measure the frequency and 95% confidence intervals of the medical errors that are important in this patient population and are poorly documented in the literature. The medical errors that will be measured are: transfusion errors (blood transfusion to the wrong patient, mislabeling of samples for type and cross match, use of whole blood instead of packed red cells), failure to use thromboembolism prophylaxis, incorrect antibiotic prophylaxis, wrong site surgery and femoral shaft fracture.

### Eligibility

Genders Eligible for Study: Both  
Criteria

Eligible patients for the trial will have undergone surgical repair for a hip fracture and have a postoperative Hgb level below 10 g/dl within three days of surgery. Only patients with cardiovascular disease will be entered into the study.

### Location Information

Study chairs or principal investigators:  
Jeffrey Carson, University Medicine & Dentistry of NJ  
Michael Terrin, Maryland Medical Research Institute, Inc.

### More Information

Study ID Numbers 159  
Study Start Date July 2003; Estimated Completion Date June 2008  
Record last reviewed February 2004  
NLM Identifier [NCT00071032](https://clinicaltrials.gov/ct2/show/study/NCT00071032)

## NAAC Clinical Guidelines for Anemia Management

Clinical guidelines for anemia management are currently being developed and will be disseminated via peer reviewed journals. As soon as these guidelines are available, they will be posted on [www.anemia.org](http://www.anemia.org) in the *Medical Professional Site*.