The GI FORUM:

MANAGING IRON DEFICIENCY ANEMIA IN CLINICAL GASTROENTEROLOGY

Accredited by

ANNENBERG CENTER FOR HEALTH SCIENCES AT EISENHOWER

Supported by an educational grant from American Regent

Provided by

GastroIntestinal Health Foundation

Disclosure

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Annenberg Center for Health Sciences and the Gastrointestinal Health Foundation.

The Annenberg Center for Health Sciences is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center’s Commission on Accreditation.

A maximum of 1.5 contact hours may be earned for successful completion of this activity.

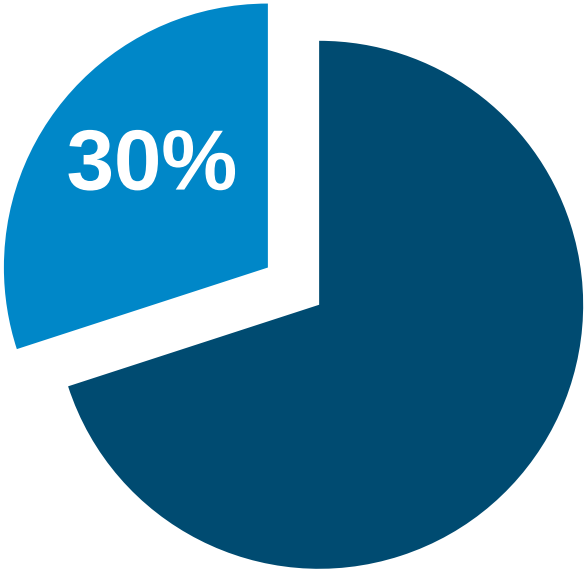
This program is supported by an educational grant from American Regent.

Agenda

- **Introduction and Preliminary Cases**
- Iron Deficiency - How and Why?
- Differential Diagnosis of Anemia
  - Prevalence and Impact of IDA in IBD
- Management of Iron Deficiency Anemia in IBD
  - Oral Iron
  - Intravenous Iron

Iron Deficiency Anemia is One of the Most Common Forms of Anemia in the World

The World Health Organization (WHO) estimates that 30% of the population worldwide has iron deficiency anemia



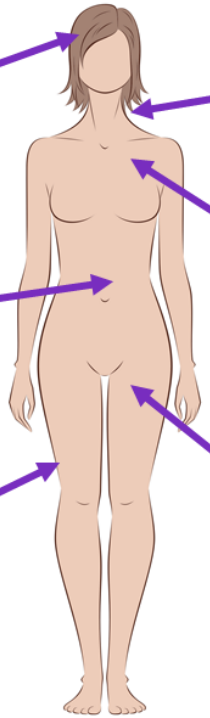
WHO. Available at: http://www.who.int/nutrition/topics/ida/en/. Accessed April 14, 2014.

Why is Iron Deficiency Anemia Important?

Central Nervous System
Fatigue and depression
Impaired cognitive function

Gastrointestinal System
Anorexia
Nausea
Motility disorders

Vascular System
Hypothermia
Pallor of skin



Immune System
Impaired ROS production
Alterations in T cell and macrophage function

Cardiorespiratory System
Exertional dyspnea
Tachycardia, palpitations
Cardiac hypertrophy
Systolic ejection murmur
Risk of cardiac failure

Genital Tract
Menstrual problems
Loss of libido

Gosh K. *Indian J Med Sci.* 2006;60:30-37.
Beard J. *J. Nutr.* 2001; 131:568S-580S.

Case Study #1: Martin W. Patient Characteristics

- 34-year-old male with a 4-year history of moderately severe UC presents to his PCP with primary complaints of fatigue and rapid heart beat x ~30 days
- **Prior clinical remission x 2 years with mesalamine**
  - Recently admitted for IV corticosteroid treatment of a UC flare
  - Discharged home on regimen of taper-dose oral prednisone
  - Follow-up colonoscopy: Mayo Sub-score 0

CBC With Differential	
Hemoglobin	12.5 g/dL
MCV	76 fl/cell

Concomitant Medications
Lansoprazole 15 mg

How Would You Manage This Patient's Anemia?

Case Study #2: Sandra B. Patient Characteristics

- 25 year-old African American female, S/P fistulotomy for perianal fistula presents to her gastroenterologist with c/o anorexia, lethargy, hypothermia, and dysmenorrhea
- Crohn's disease stabilized on current maintenance therapy

CBC With Differential	
Hemoglobin	9 g/dL
MCV	74 fl/cell

Maintenance Medications
Infliximab, IV 5 mg/kg, q8 weeks
6-MP*, 2.5 mg/kg, PO, QD

How Would You Manage This Patient's Anemia?

*6-MP: 6-mercaptopurine

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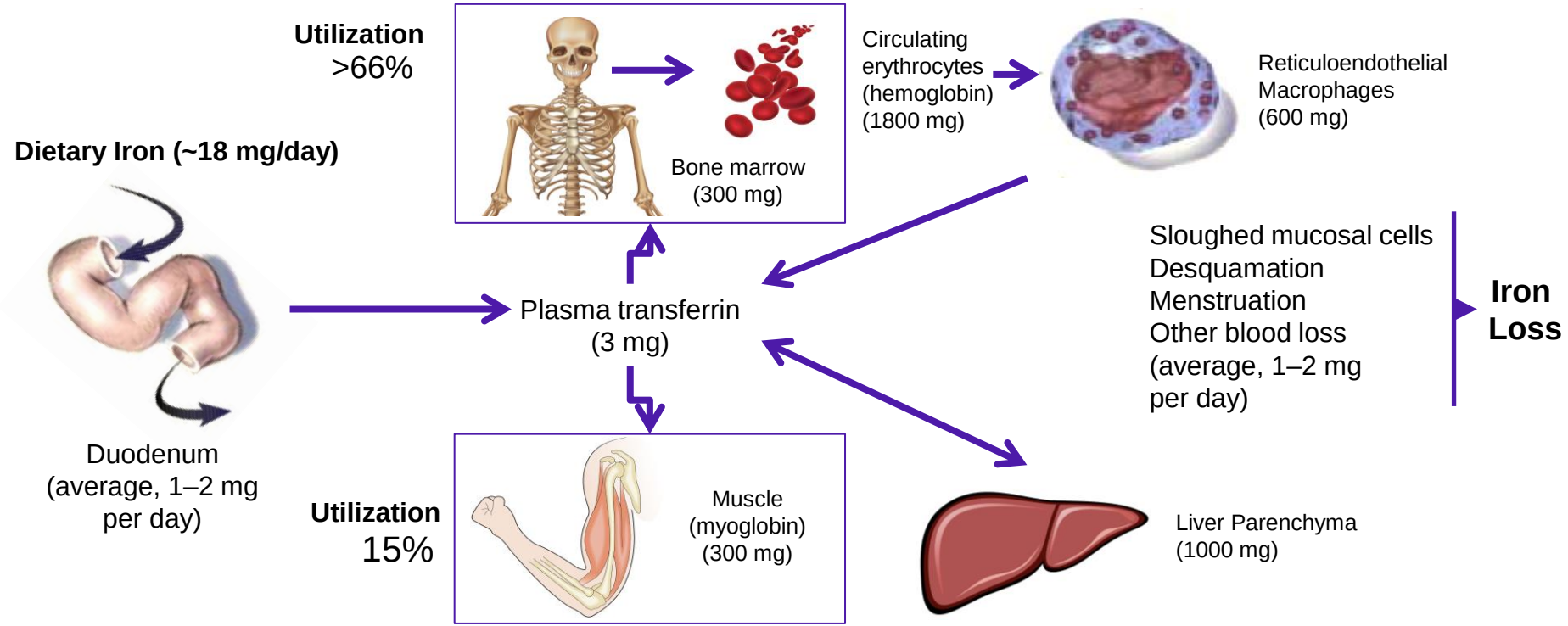
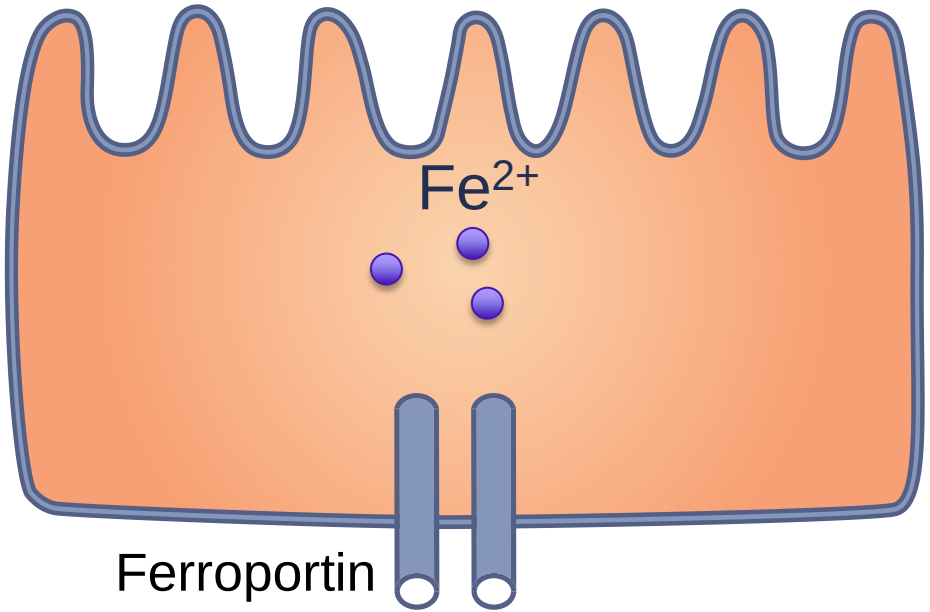
Normal Distribution of Iron in Adults



Andrews NC. *N Engl J Med*. 1999;341:1986-1995.

Hepcidin: The Master Regulator of Iron Absorption



Stein J, Dignass AU. *Ann Gastroenterol*. 2012;26:1-10.

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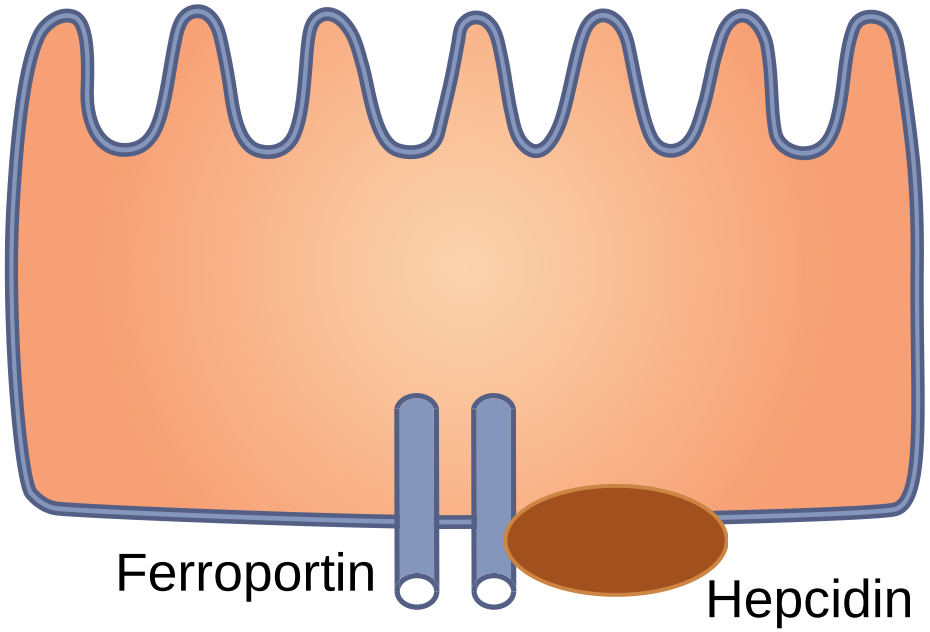
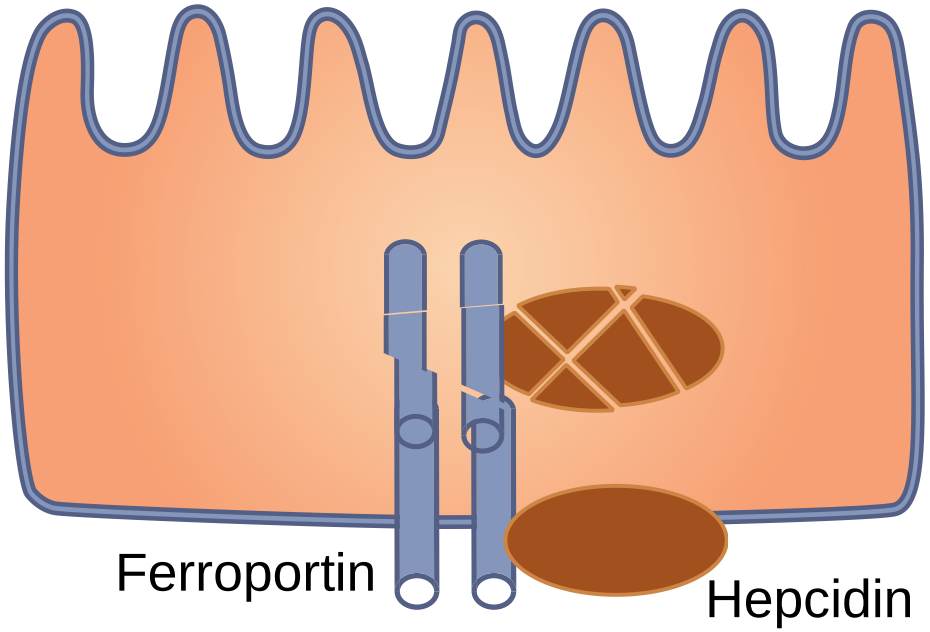


Stein J, Dignass AU. *Ann Gastroenterol*. 2012;26:1-10.

Hepcidin: The Master Regulator of Iron Absorption

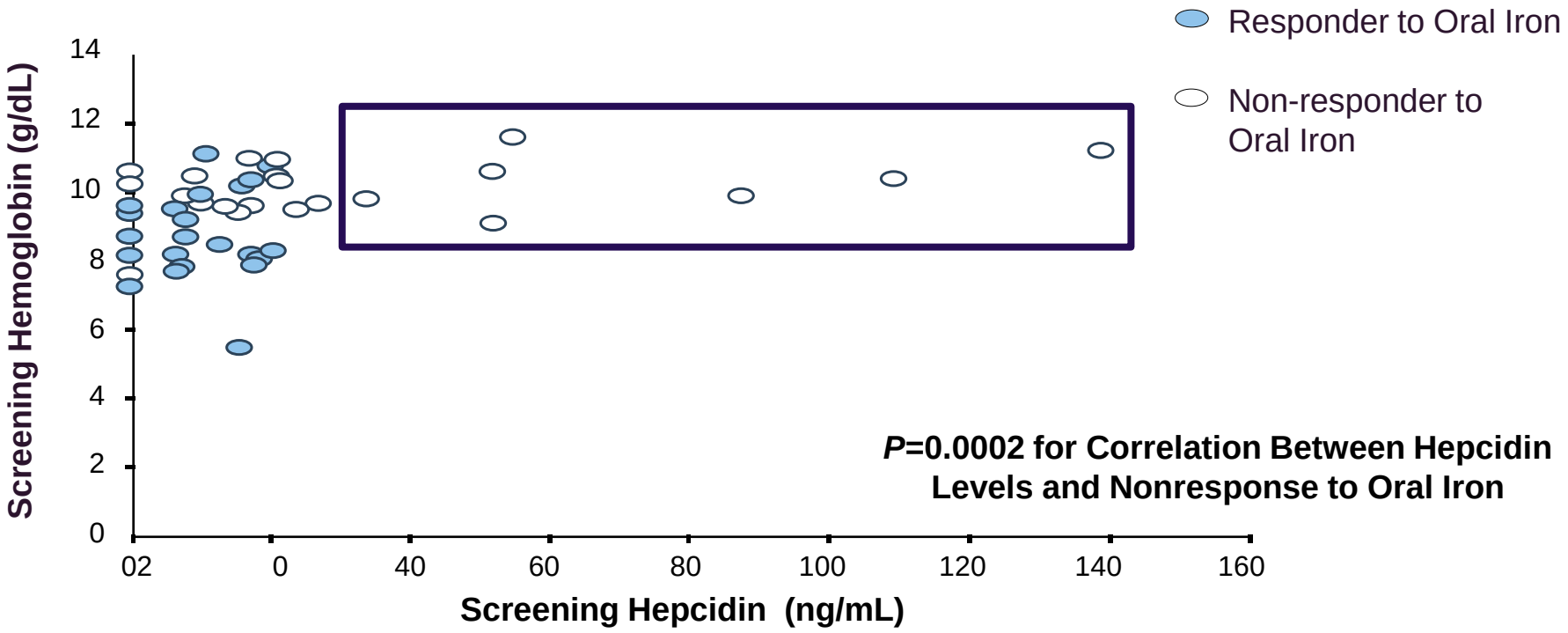
↓Hepcidin
Iron export through ferroportin



↑Hepcidin
Ferroportin degradation: Iron locked in cell

Stein J, Dignass AU. *Ann Gastroenterol*. 2012;26:1-10.

Hepcidin Level: A Greater Predictor of Response to Oral Iron Than Severity of Anemia

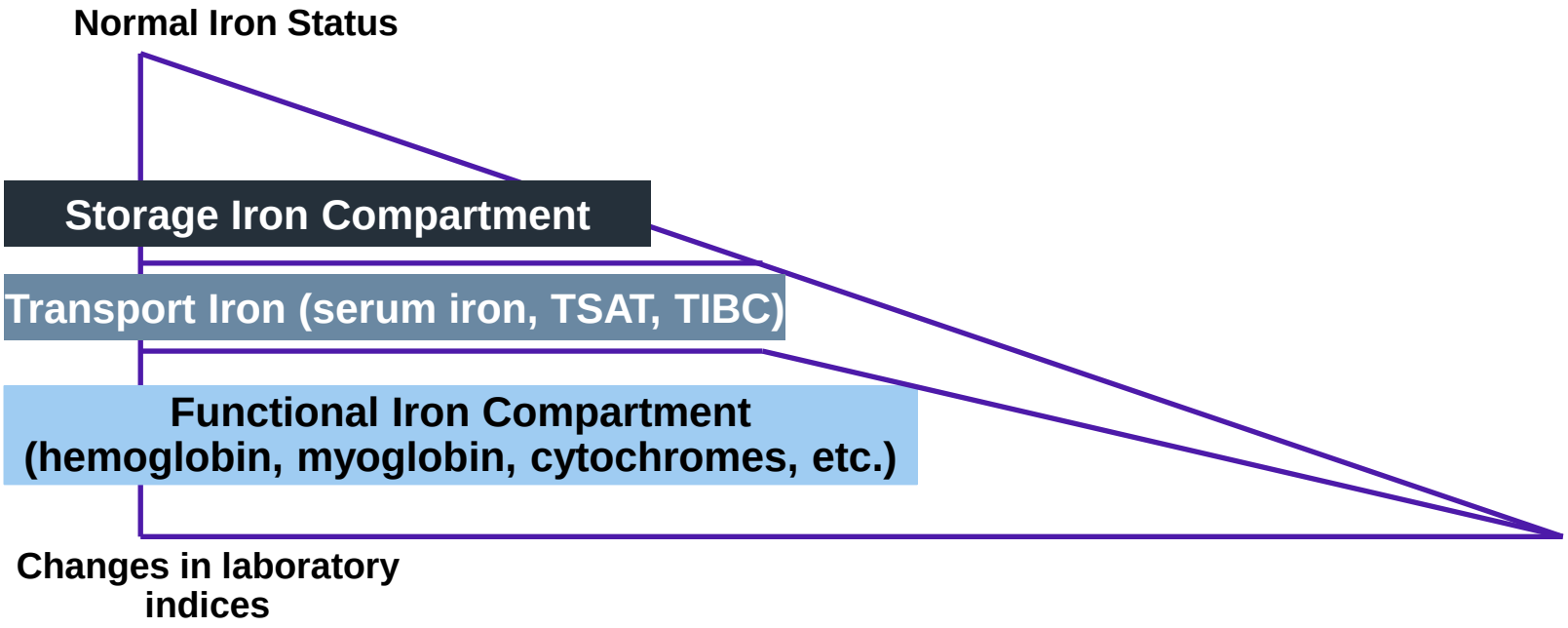


Bregman DB, et al. *Am J Hematol*. 2013;88:97-101.

Summary: Iron Homeostasis

- In a balanced state, 1 to 2 mg of iron enters and leaves the body each day
  - Dietary iron is absorbed by duodenal and upper jejunal enterocytes and circulates in plasma bound to transferrin
- Inflammation increases expression of hepcidin
- Hepcidin levels influence iron absorption and transport by modulating ferroportin
  - Decreased hepcidin enhances absorption
  - Increased hepcidin reduces absorption

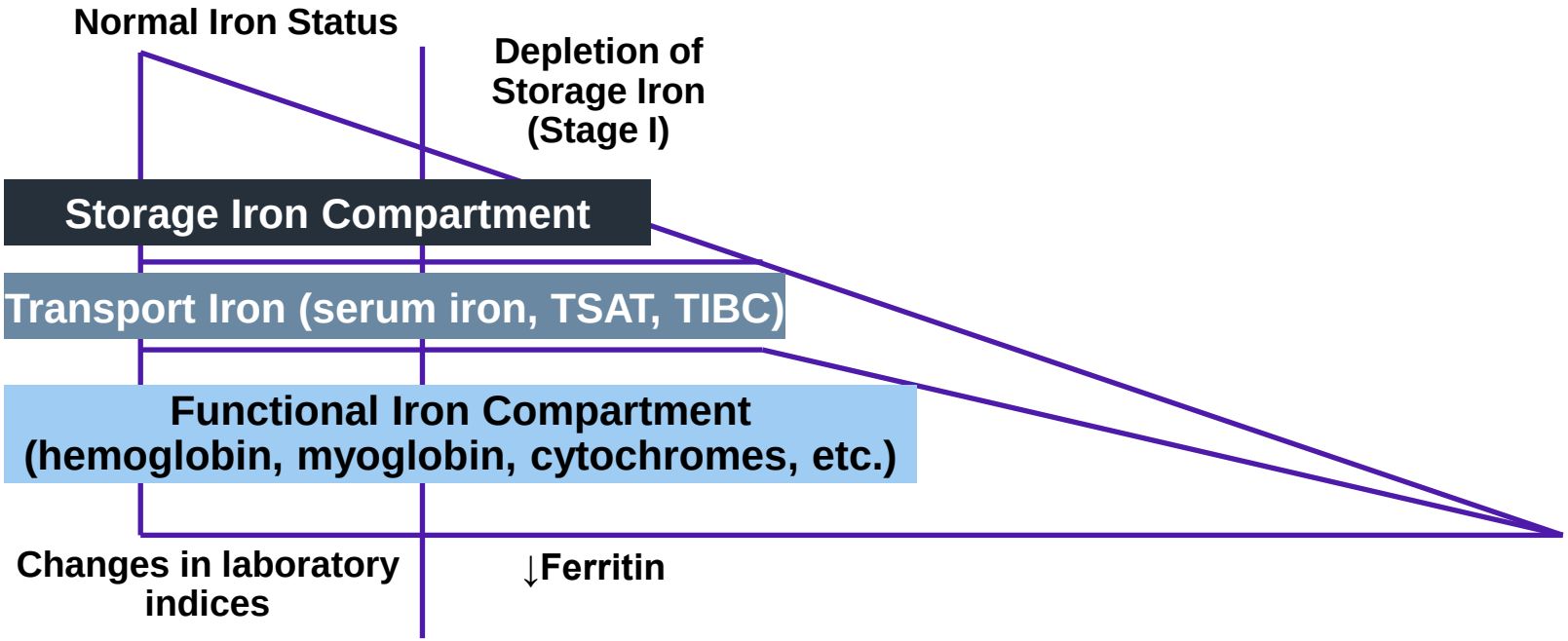
Stages of Iron Deficiency Anemia (IDA)



TSAT= Transferrin Saturation
TIBC = Total Iron Binding Capacity
MCV = Mean Corpuscular Volume
sTfR = Soluble Transferrin Receptor

Tussing-Humphreys L, et al. *J Acad Nutr Diet.* 2012;112:391-400.

Stages of Iron Deficiency Anemia (IDA)



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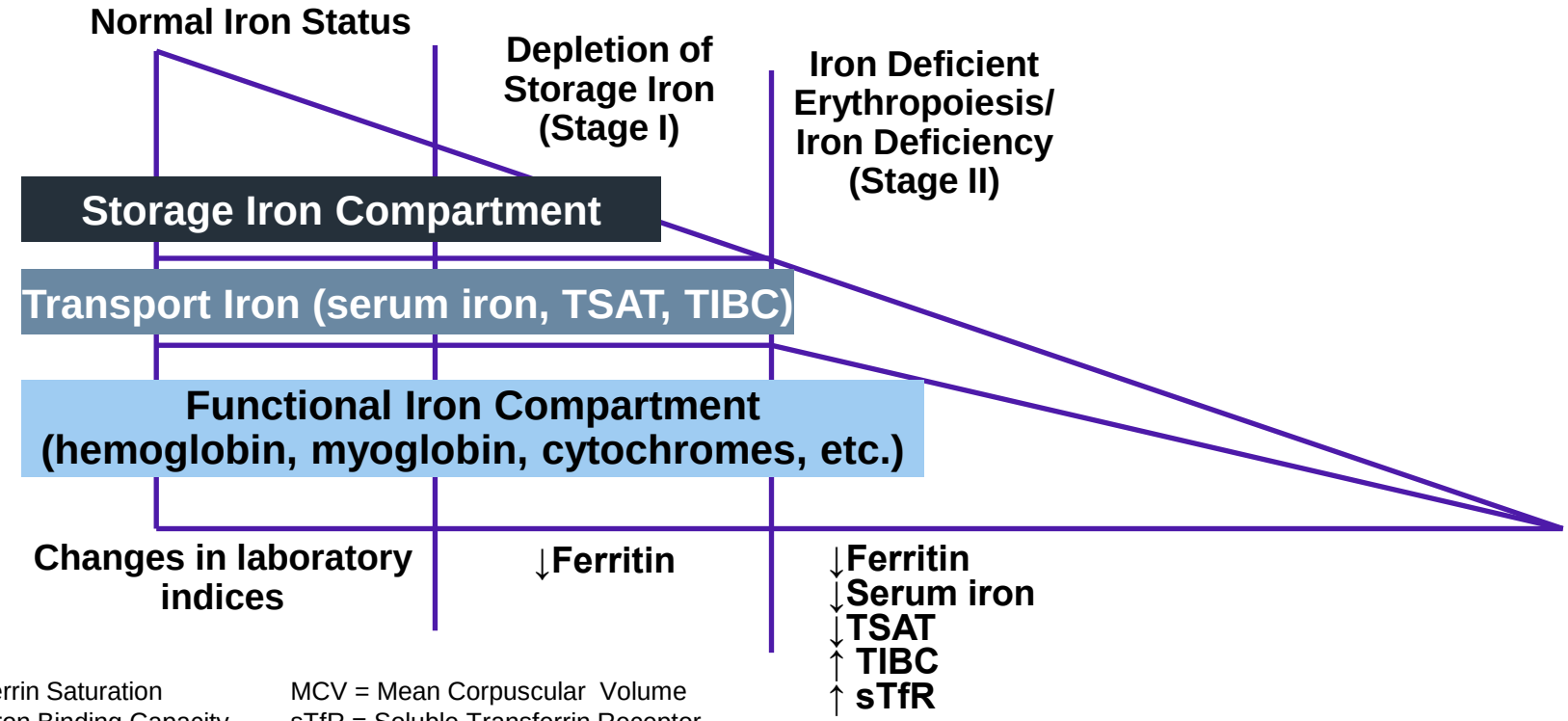

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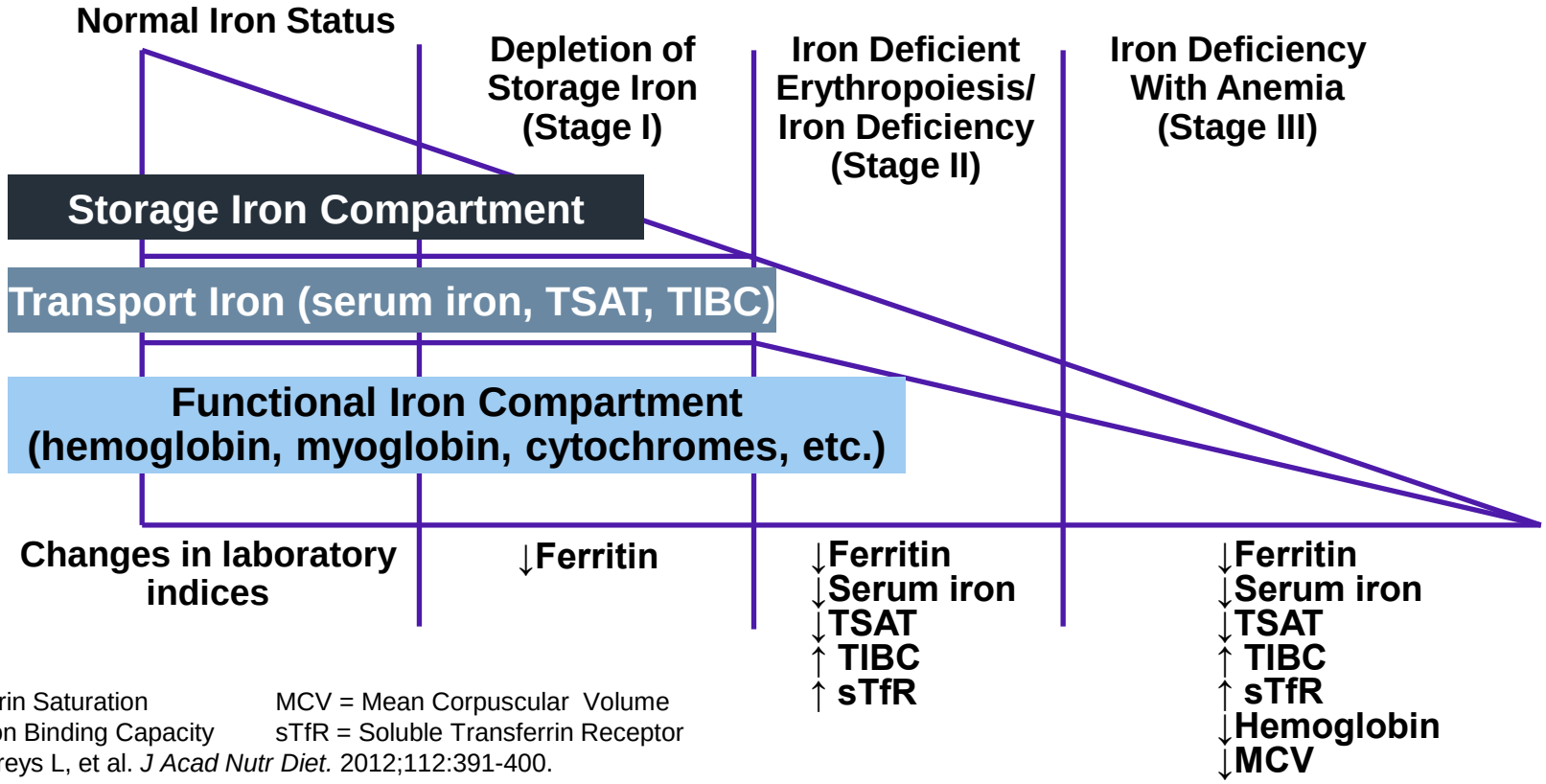

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Causes of Anemia in IBD

Common	• Iron deficiency • Anemia of chronic disease
Occasional	• Vitamin B12 deficiency • Folate deficiency • Drug-induced (sulfasalazine, thiopurines)
Rare	• Hemolysis • Myelodysplastic syndrome • Aplasia (often drug-induced) • Innate hemoglobinopathies or disorders of erythropoiesis

Gasche C, et al. *Inflamm Bowel Dis.* 2007;13:1545-1553.

Common Causes of Iron Deficiency Anemia in Gastrointestinal Disorders

Increased iron loss[1-6]

- Inflammatory Bowel Disease (IBD)
- Gastrointestinal Ulcers
- Gastrointestinal Neoplasia
- Significant Post-Operative Blood Loss
- Hookworms
- Angiodysplasia (AV Malformations)
- Aspirin/NSAID Use
- Diverticular Bleeding
- GERD
- Large Hiatal Hernias (Cameron lesions)

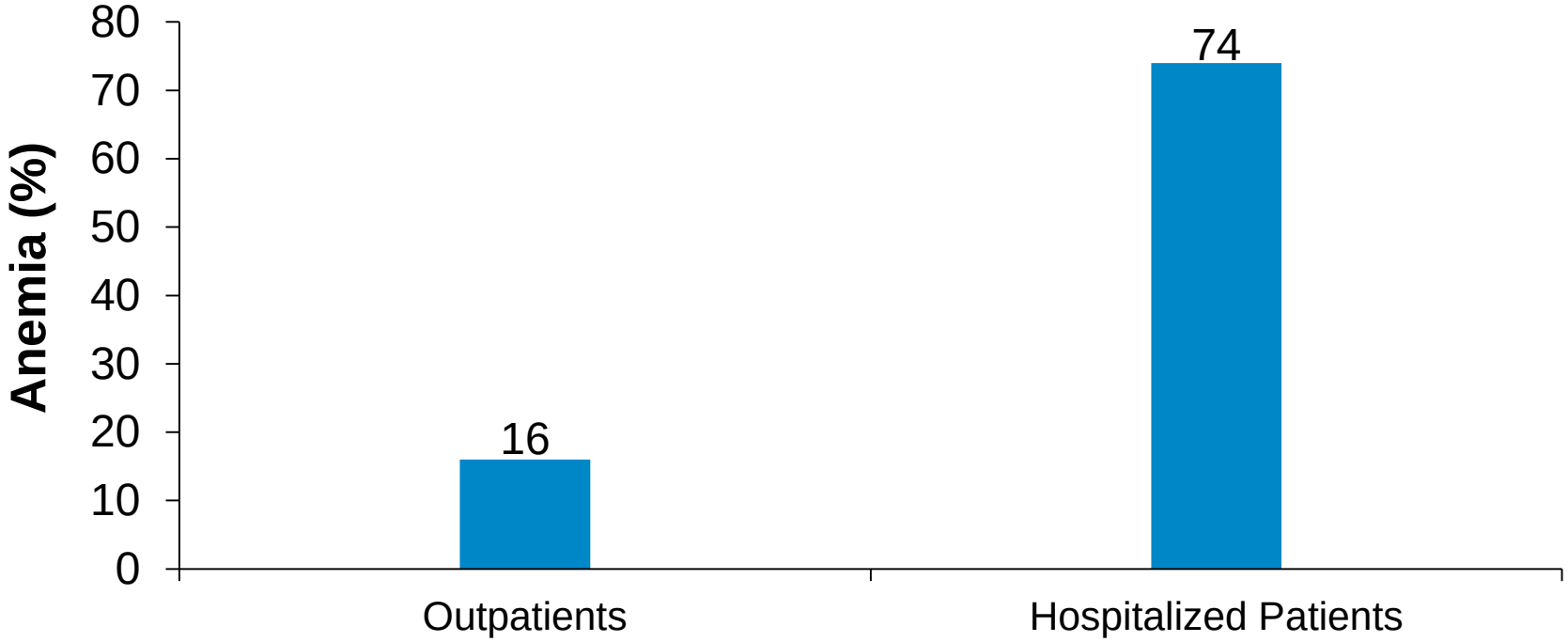
Decreased iron absorption[1-6]

- Inflammatory Bowel Disease (IBD)
- Celiac disease
- Chronic gastritis (*H pylori* and autoimmune)
- Achlorhydria
- Gastric Lymphoma
- Gastrectomy
- Intestinal Bypass
- Duodenal Pathology
- Short Bowel Syndrome
- Gastrojejunostomy
- Giardiasis (Pediatrics)
- Bacterial Overgrowth

CD = Crohn's Disease; UC = Ulcerative Colitis; NSAID: Nonsteroidal Anti-inflammatory Drug

1. Gasche C, et al. *Gut*. 2004;53:1190-1197; 2. Ott C, et al. *Gastroenterol Res Pract*. 2012;2012:595970. doi:10.1155/2012/595970;
3. Ruz M, et al. *Am J Clin Nutr*. 2009;90: 527–532; 4. Hershko C, Patz J. *Haematologica*. 2008;93:1761-1765.;
5. Annibale B, et al. *Am J Med*. 2001;111:439-445; 6. Goldberg N. *Clin Exp Gastroenterol*. 2013;6:61-70.

Prevalence of IDA in Adults With IBD by Hospitalization Status



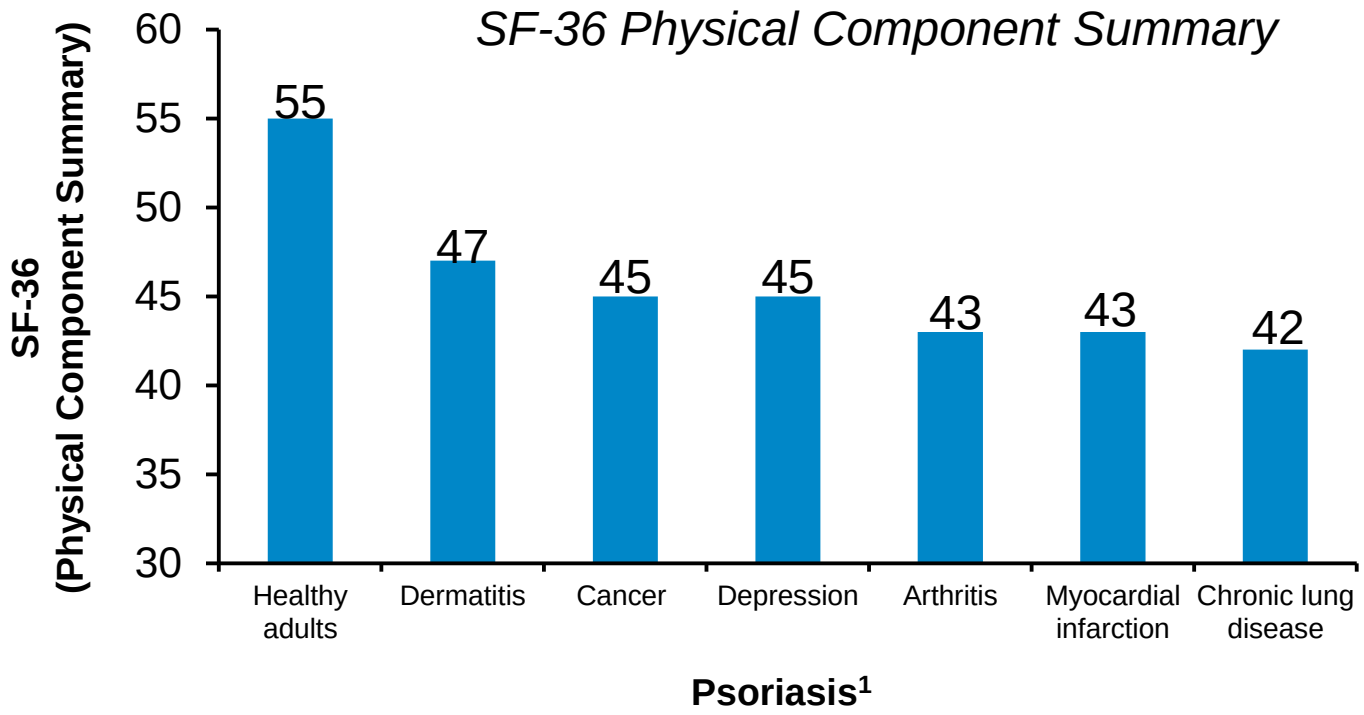
Gisbert JP, Gomollon F. *Am J Gastroenterol.* 2008;103:1299-1307.

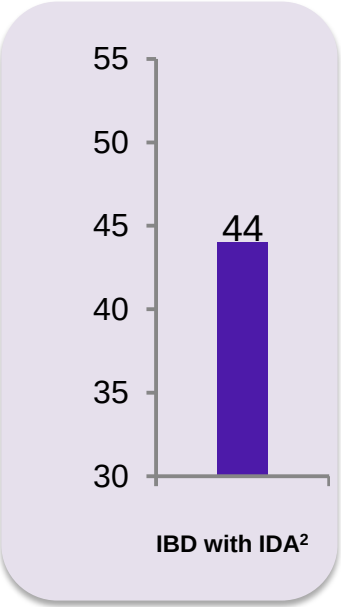
Consequences of IDA in IBD

- IDA in patients with IBD:
  - Associated with increased hospital visits[1,2]
  - Frequently delays hospital discharge[1,2]
  - Is associated with profoundly decreased quality of life[3,4]

1. Kulnigg S, Gasche C. *Aliment Pharmacol Ther.* 2006;24:1507-1523.
2. Gasche C, et al. *Inflamm Bowel Dis.* 2007;13:1545-1553.
3. Wells CW, et al. *Inflamm Bowel Dis.* 2006;12:123-130.
4. Gasche C, et al. *Ann Intern Med.* 1997;126:782-787.

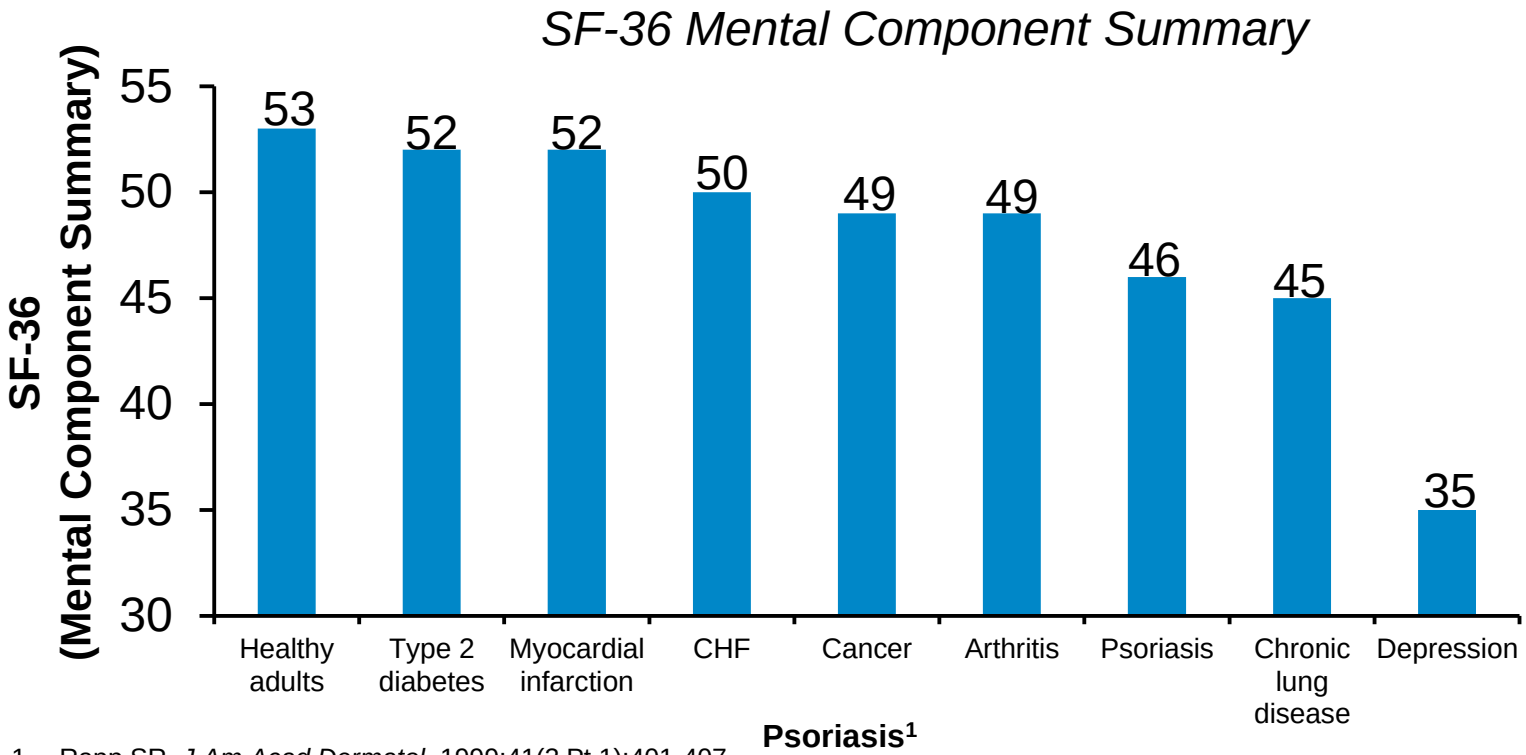
IDA Has a Severe Impact on Physical Function

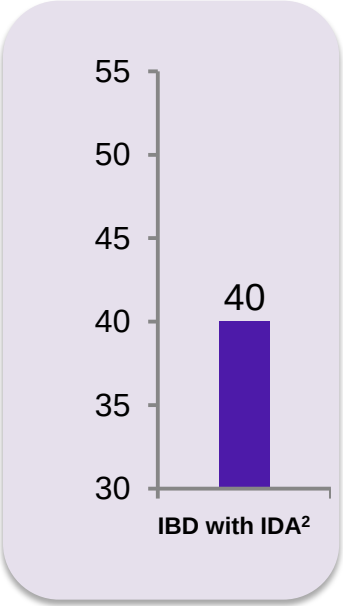




1. Rapp SR. *J Am Acad Dermatol*. 1999;41(3 Pt 1):401-407.
2. IDA Data Derived From: Evastatiev R, et al. *Gastroenterology*. 2011;140:846-853.

IDA Has a Severe Impact on Mental Health Quality of Life





1. Rapp SR. *J Am Acad Dermatol*. 1999;41(3 Pt 1):401-407.
2. IDA Data Derived From: Evastatiev R, et al. *Gastroenterology*. 2011;140:846-853.

Summary: Impact of IDA in IBD

- Broad range of clinically consequential effects
  - Neurologic
  - Gastrointestinal
  - Vascular
  - Immune
  - Cardiorespiratory
  - Sexual
- Profound impact on patient quality of life
  - Physical impact is comparable to depression and arthritis
  - Mental impact is greater than CHF, cancer, chronic lung disease

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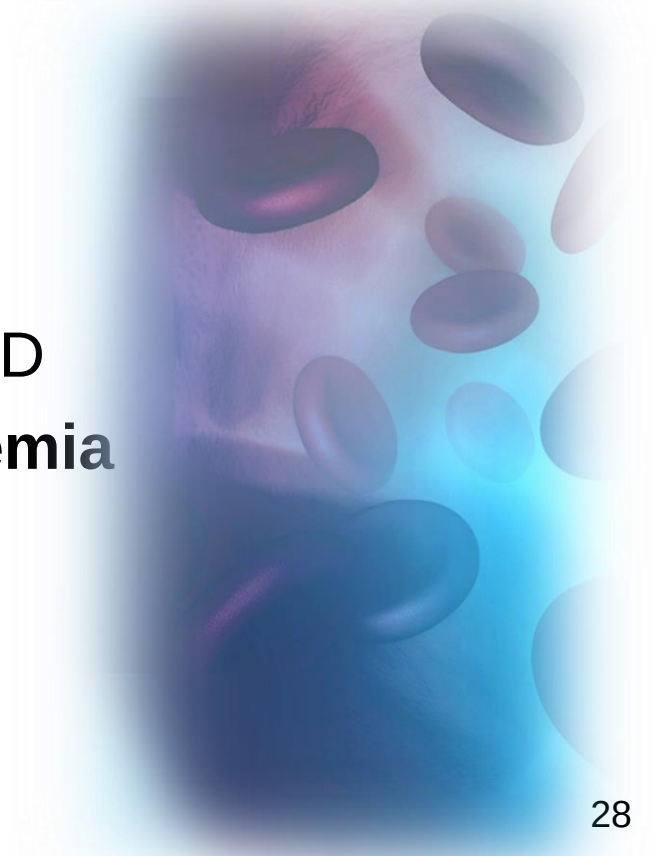
  - **Oral Iron**
  - Intravenous Iron



Oral Iron in Gastrointestinal Disease

- Considered standard for patients with hemoglobin concentrations ≥10 g/dL and CRP <5.0 mg/L due to lower cost and ease of administration
- Limitations in IBD:
  - Intolerance
    - Nausea, vomiting, diarrhea/constipation, abdominal pain
  - Increased hepcidin due to inflammation
    - Reduced absorption

Oral Iron Formulations

Formulation	Elemental Iron	Dosage Forms Available	Additional Information
Carbonyl iron	15-45 mg	Tablets, chewable tablets, suspension	• Not an iron salt • Slow release
Ferric ammonium citrate	25 mg	Capsules	• Less bioavailable than ferrous salts
Ferrous bisglycinate	27 mg	Capsules, tablets	• May be less likely to cause GI intolerance
Ferrous fumarate	50-150 mg	Tablets, chewable tablets	• Similar efficacy/tolerability as ferrous sulfate • Almost tasteless
Ferrous gluconate	27-38 mg	Tablets	• Similar efficacy/tolerability as ferrous sulfate
Ferrous sulfate	65 mg	Oral solution, tablets, EC-tablets, film-coated tablets	• Common formulation
Heme-iron polypeptide	12 mg	Capsules	• Animal origin
Polysaccharide-iron complex	150 mg	Capsules, solution, film-coated tablets	• Promoted to cause less GI irritation (unproven)

Tom W-C. *Pharmacist's Letter / Physician's Letter.* 2008;44: No.240811.

Limitations of Oral Iron

- A significant fraction of ingested iron remains unabsorbed[1]
- Intolerance due to GI adverse effects results in treatment discontinuation in up to 20% of patients[2]
  - Diarrhea
  - Abdominal Pain
  - Constipation
  - Melena-like Stools
- Specific Limitations in IBD:
  - Intolerance due to above symptoms
  - Increased hepcidin from inflammation --> reduces absorption

1. Goldberg N. *Clin Exp Gastroenterol*. 2013;6:61-70.
2. Lindgren S, et al. *Scand J Gastroenterol*. 2009;44:838-845.

Predictors of Response to 14-day Trial Course of Ferrous Sulfate

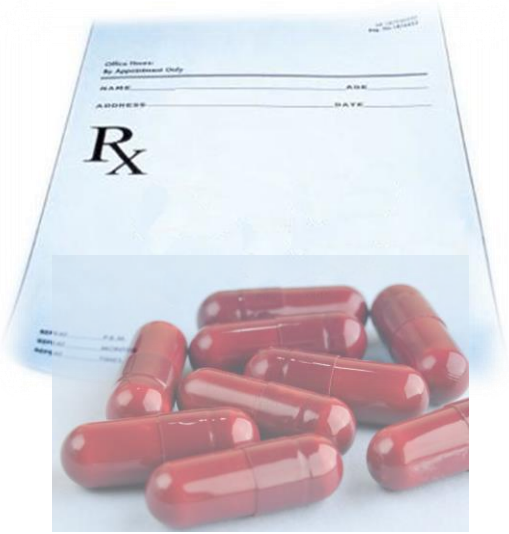
- Significant predictors
  - Low baseline hemoglobin ($P<0.001$)
  - Low hepcidin ($P=0.002$)
  - High TIBC ($P=0.003$)
  - Low ferritin ($P=0.027$)
- Neither TSAT nor iron levels predicted response

TIBC = Total Iron Binding Capacity
TSAT = Transferrin Saturation

Bregman DB, et al. *Am J Hematol*. 2013;88:97-101.

Practical Considerations for Oral Iron Therapy

- Once daily dosing can improve compliance[1]
- Delayed-release or enteric-coated iron formulations may bypass key absorption sites[1,2]
- Instruct patients to take on empty stomach with vitamin C[1]
- Monitor for response, tolerance, adherence[3,4]
- Concomitant medications may limit oral iron absorption[5]
  - Medications that raise gastric pH (antacids, H_2-blockers, PPIs)[5]
  - Quinolone antibiotics should be avoided[6]
  - Phytates from bran[5,7]
  - Tannates from tea[5,8]



PPIs=Proton Pump Inhibitors

1. Tom W-C. *Pharmacist's Letter / Physician's Letter.* 2008;44:No. 240811; 2. McDiarmid T, et al. *J Fam Pract.* 2002;51:576; 3. Gasche C, et al. *Inflamm Bowel Dis.* 2007;13:1545-1553; 4. Stein J, Dignass AU. *Ann Gastroenterol*. 2012;26:1-10; 5. Goldberg N. *Clin Exp Gastroenterol*. 2013; 6:61-70; 6. Kara M, et al. *Br J Clin Pharmacol*. 1991;31:257-261; 7. Disler PB, et al. *Gut.* 1975;16:193-200; 8. Hallberg L, et al. *Am J Clin Nutr*. 1987;45:988-996.

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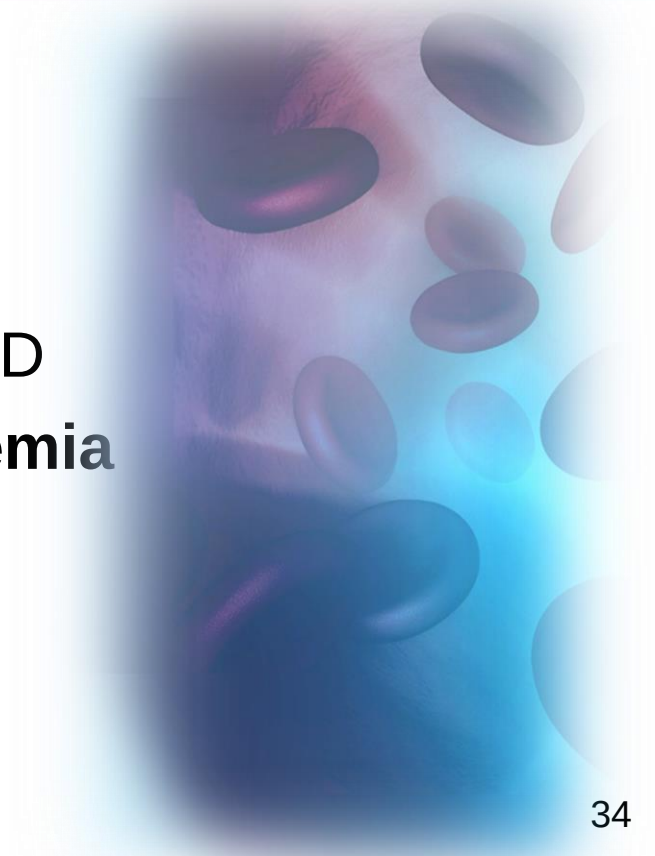


Why IV Iron in IBD?

- Active disease results in **malabsorption** of iron
- **GI intolerance** may be magnified in patients with IBD
- **Significant anemia** may require more potent treatment

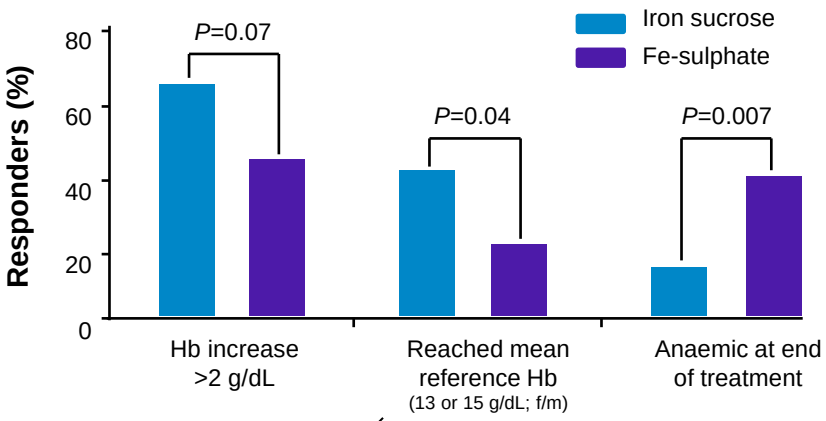
Intravenous Iron Products: Approved Indications in the United States

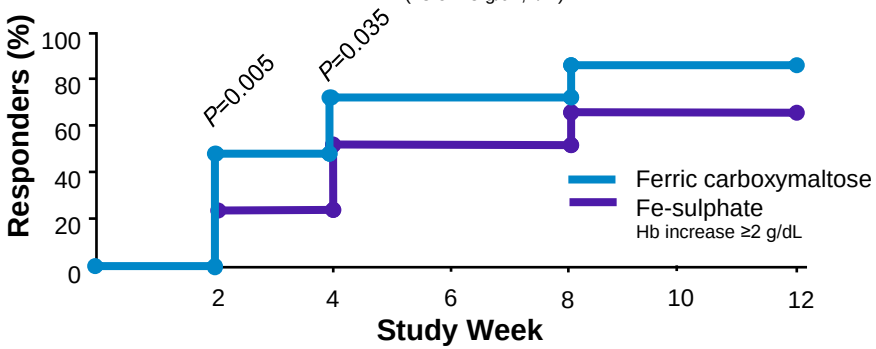
IV Iron Agent	FDA-Approved Indication
Iron dextran	Treatment of patients with iron deficiency when oral administration is unsatisfactory or impossible
Sodium ferric gluconate	Treatment of iron deficiency anemia in adults and in pediatrics (≥6 years of age) with CKD receiving hemodialysis who are receiving supplemental epoetin therapy
Iron sucrose	Treatment of iron deficiency anemia in adult and pediatric patients ≥2 years of age with CKD
Ferumoxytol	Treatment of iron deficiency anemia in adult patients with CKD
Ferric carboxymaltose	Treatment of iron deficiency anemia (IDA) in adult patients: • Who have intolerance to oral iron or have had unsatisfactory response to oral iron • Who have non-dialysis dependent chronic kidney disease

Blue Highlights = FDA Approved Outside of Renal Disease
Data Derived From Respective Package Inserts

Venofer® (iron sucrose injection). Full Prescribing Information. American Regent, Inc., Shirley, NY 11967;2000.
Dexferrum® (iron dextran injection). Full Prescribing Information. American Regent, Inc., Shirley, NY 11967;2008.
Injectafer® (ferric carboxymaltose injection). Full Prescribing Information. American Regent, Inc., Shirley, NY 11967;2013.
Feraheme® (ferumoxytol injection). Full Prescribing Information. AMAG Pharmaceuticals, Inc., Waltham, MA 02451;2015.

Intravenous vs Oral Iron: Response





Lindgren et al[1]

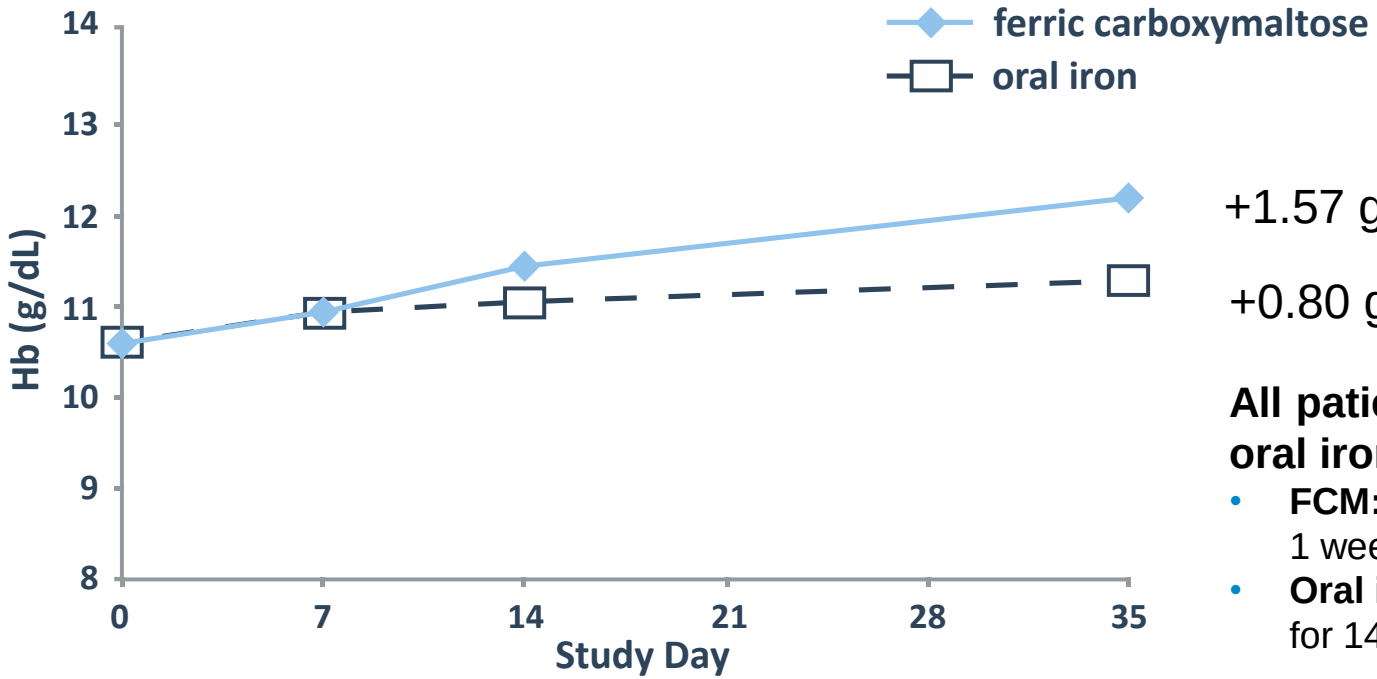
- Improved response
- 0% vs 24% AE-related discontinuation

Kulnigg et al[2]

- Faster response
- 1.5% vs 7.9% AE-related discontinuation

1. Lindgren S, et al. *Scand J Gastroenterol.* 2009;44:838-845; 2. Kulnigg S, et al. *Am J Gastroenterol* 2008;103:1182-1192.

Efficacy of IV Iron (FCM) vs Oral Iron ($FeSO_4$) in IDA



+1.57 g/dL

+0.80 g/dL

***P*=0.001**

All patients received 14 day oral iron run-in, followed by:

- **FCM:** 2 doses x 750 mg 1 week apart
- **Oral iron:** 325 mg, TID for 14 additional days

Onken JE, et al. *Transfusion.* 2014;54:306-315.

Safety of IV Iron (FCM) vs Oral Iron ($FeSO_4$) in Iron Deficiency Anemia

	Oral iron	IV iron
Treatment-emergent Adverse Events (%)	6.3	22.8
Serious Adverse Events (%)	4.0	3.3
Adverse Events Resulting in Discontinuation (%)	0.8	1.1
Hypersensitivity Events (%)	0.8	0.0

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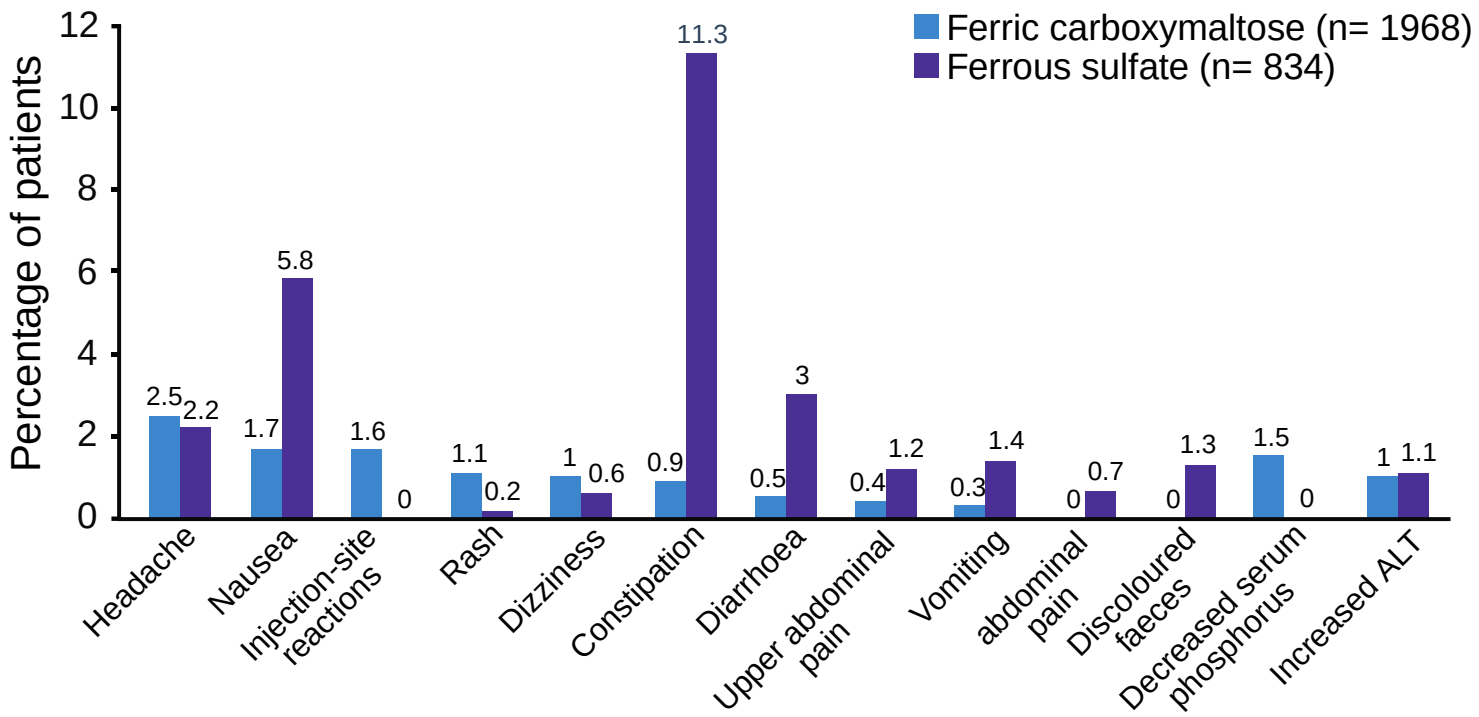
Adverse Events: IV Versus Oral Iron



Lyseng-Williamson KA, et al. *Drugs*. 2009;69:739-756.

IV Iron: Dosage and Administration

	Iron Sucrose	Iron Dextran	Ferric Carboxymaltose
Test dose required	No	Yes (**Initial Test Dose of 0.5 mL**)	No

†Adult Patients With CKD Not On Dialysis

Hb = Hemoglobin
LBW = Lean Body Weight
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Dexferrum® (iron dextran injection). Full Prescribing Information. American Regent, Inc., Shirley, NY 11967;2008
Injectafer® (ferric carboxymaltose injection). Full Prescribing Information. American Regent, Inc., Shirley, NY 11967;2013
Feraheme® (ferumoxytol injection). Full Prescribing Information. AMAG Pharmaceuticals, Inc., Waltham, MA 02451;2015

IV Iron: Dosage and Administration

	Iron Sucrose	Iron Dextran	Ferric Carboxymaltose
Test Dose Required	No	Yes (**Initial Test Dose of 0.5 mL**)	No
Other Dosing Recommendation	Observe for signs and symptoms of hypersensitivity during and after administration for ≥30 minutes and until clinically stable	Observe patient for ≥1 hour after test dose for signs and symptoms of anaphylaxis	Observe for signs and symptoms of hypersensitivity during and after administration for ≥30 minutes and until clinically stable

NDD-CKD: Adult Patients With CKD Not On Dialysis
Hb: Hemoglobin
LBW: Lean Body Weight

Venofer® (iron sucrose injection). Full Prescribing Information. American Regent, Inc., Shirley, NY 11967;2000
Dexferrum® (iron dextran injection). Full Prescribing Information. American Regent, Inc., Shirley, NY 11967;2008
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Adult Recommended Dose	200 mg on 5 different occasions for a total dose of 1000 mg	According to LBW (kg) and observed hemoglobin concentration (g/dL): Dose (mL) = 0.0442 (Desired Hb − Observed Hb) × LBW+ (0.26 × LBW)	**Weight ≥50 kg:** 2 doses separated by ≥7 days; 750 mg/dose; total 1500mg/course **Weight <50 kg:** 2 doses separated by ≥7 days at 15 mg/kg

†NDD-CKD: Adult Patients With CKD Not On Dialysis
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IV Iron: Adverse Events and Management

Anaphylaxis/ Hypersensitivity	• Treatment: – Steroids, antihistamines, epinephrine • Premedication with diphenhydramine and acetaminophen prior to iron dextran administration may help
Hypotension	• Caused by free iron reactions or anaphylaxis • May resolve spontaneously
Extravasation	• Choose large vein with adequate blood flow and monitor for extravasation, manifested as pain, discomfort, tightness at infusion site • Discontinue administration of the drug and apply cold compress

Goldberg N. *Clin Exp Gastroenterol*. 2013;6:61-70.

Iron Dextran Boxed Warning

WARNING: RISK FOR ANAPHYLACTIC-TYPE REACTIONS

- Anaphylactic-type reactions, including fatalities, have followed the parenteral administration of iron dextran injection.
- Have resuscitation equipment and personnel trained in the detection and treatment of anaphylactic-type reactions readily available during iron dextran administration.
- Administer a test iron dextran dose prior to the first therapeutic dose. If no signs or symptoms of anaphylactic-type reactions follow the test dose, administer the full therapeutic iron dextran dose.
- During all iron dextran administrations, observe for signs or symptoms of anaphylactic- type reactions.
- Fatal reactions have followed the test dose of iron dextran injection. Fatal reactions have also occurred in situations where the test dose was tolerated.
- Use iron dextran only in patients in whom clinical and laboratory investigations have established an iron deficient state not amenable to oral iron therapy.
- Patients with a history of drug allergy or multiple drug allergies may be at increased risk of anaphylactic-type reactions to iron dextran.

Dexferrum® (iron dextran injection, USP) [package insert]. American Regent, Inc., Shirley, NY;2012.

Ferumoxytol Boxed Warning

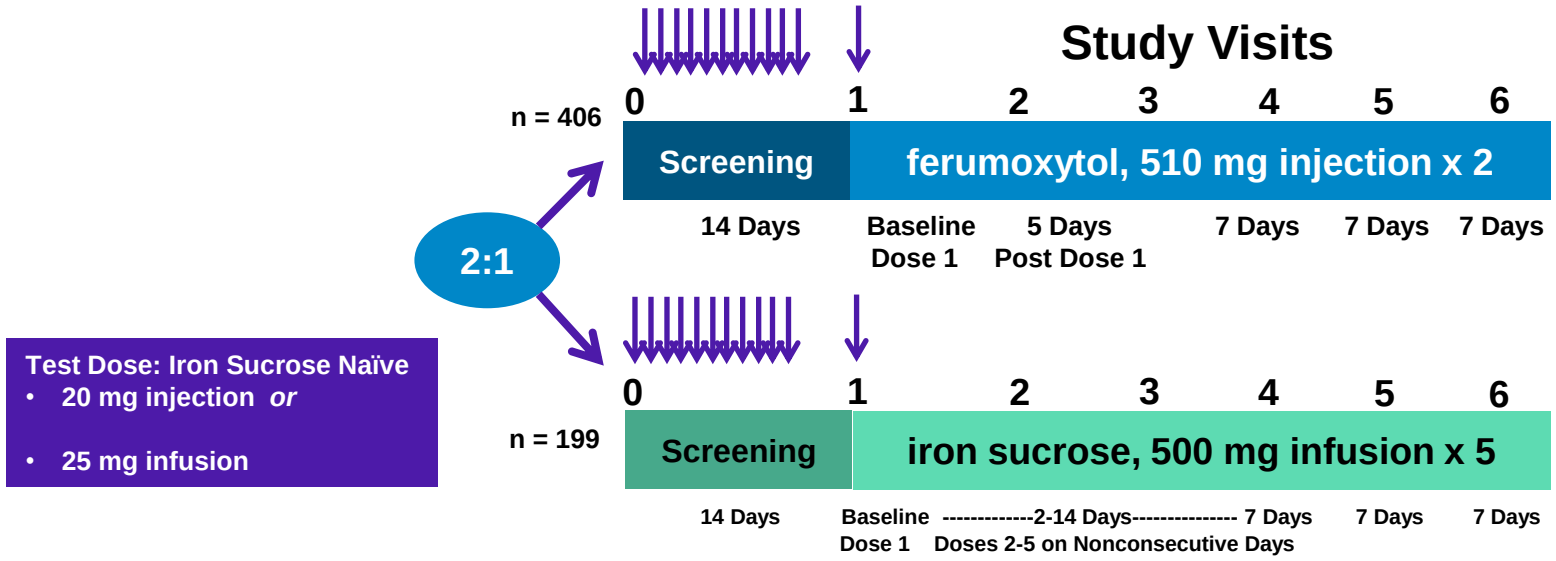
WARNING: RISK FOR ANAPHYLACTIC-TYPE REACTIONS

- Fatal and serious hypersensitivity reactions, including anaphylaxis have occurred in patients receiving ferumoxytol.
- Initial symptoms may include hypotension, syncope, unresponsiveness, cardiac/cardiorespiratory arrest.
- Only administer ferumoxytol when personnel and therapies are immediately available for the treatment of anaphylaxis and other hypersensitivity reactions.
- Observe for signs and symptoms of hypersensitivity reactions during and for at least 30 minutes following ferumoxytol infusion including monitoring of blood pressure and pulse during and after ferumoxytol administration.
- Hypersensitivity reactions have occurred in patients in whom a previous ferumoxytol dose was tolerated.

Feraheme® (ferumoxytol injection). Full Prescribing Information. AMAG Pharmaceuticals, Inc., Waltham, MA 02451;2015.

Ferumoxytol Compared with Iron Sucrose in Patients with IDA Unresponsive to Oral Iron

- Open label, active-controlled, multicenter, global, Phase 3 clinical trial of 605 patients with iron deficiency anemia (IDA)



Hetzel D, et al. *Am J Hematol*. 2014;89:646-650.

Eligibility Criteria

Inclusion Criteria:

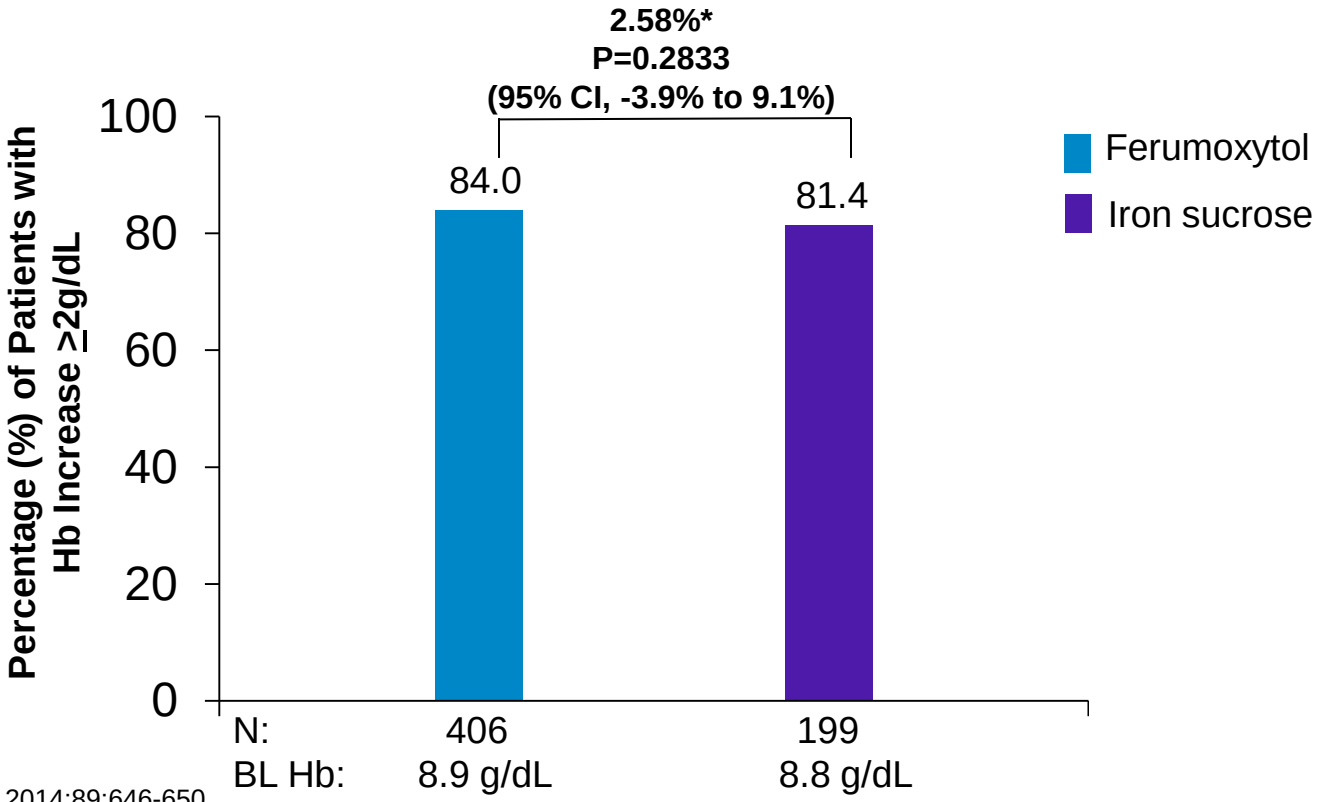
- > 18 years of age
- Diagnosis of iron deficiency anemia (IDA)
  - Hemoglobin: <10.0 g/dL
  - Transferrin Saturation: <20%
- History of unsatisfactory oral iron therapy or in whom oral iron could not be used

Exclusion Criteria:

- History of allergy to IV iron
- Serum ferritin >600 ng/mL
- Active infection
- Pregnant / Intend to become pregnant
- Dialysis
- IV iron within 4 weeks of screening
- Hemoglobin <7.0 g/dL
- Known causes of anemia other than IDA
- Hematologic Malignancies
- Breastfeeding
- GFR <30 mL/min/1.73m^2
- Oral iron or blood transfusion within 2 weeks prior to screening

Hetzel D, et al. *Am J Hematol*. 2014;89:646-650.

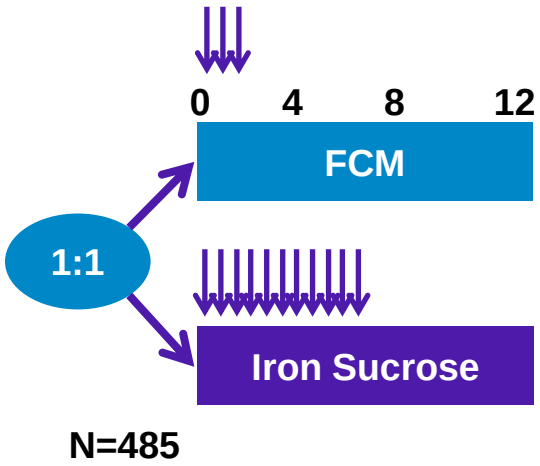
Ferumoxytol Achieves Non-inferiority vs Iron Sucrose for Hb Increase ≥ 2.0 g/dL Over Baseline



*Treatment Difference

Hetzel D, et al. *Am J Hematol*. 2014;89:646-650.

Iron Sucrose vs FCM in IBD Patients with IDA

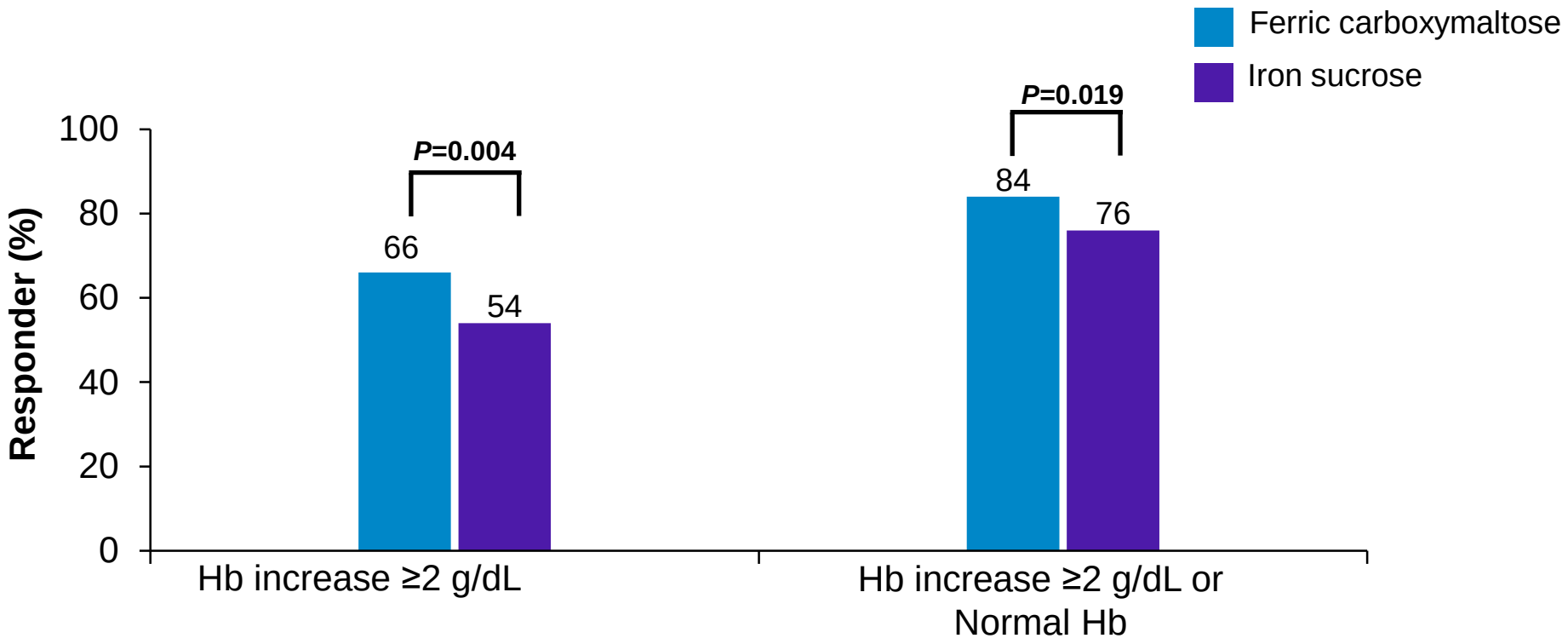


- **Induction (FERGIcor)**
  - Inclusion: Ferritin <100 ng/mL
  - Hb 7-12 g/dL (female)
    Hb 7-13 g/dL (male)
  - FCM (fixed-dose) versus iron sucrose (Ganzoni Formula)*
  - Primary endpoint: Hb increase ≥2g/dl

*Ganzoni Formula:
Total Iron Dose = [Body Weight (Target Hb- Actual Hb)] x 2.4 + Iron Storage Depot
FCM = ferric carboxymaltose

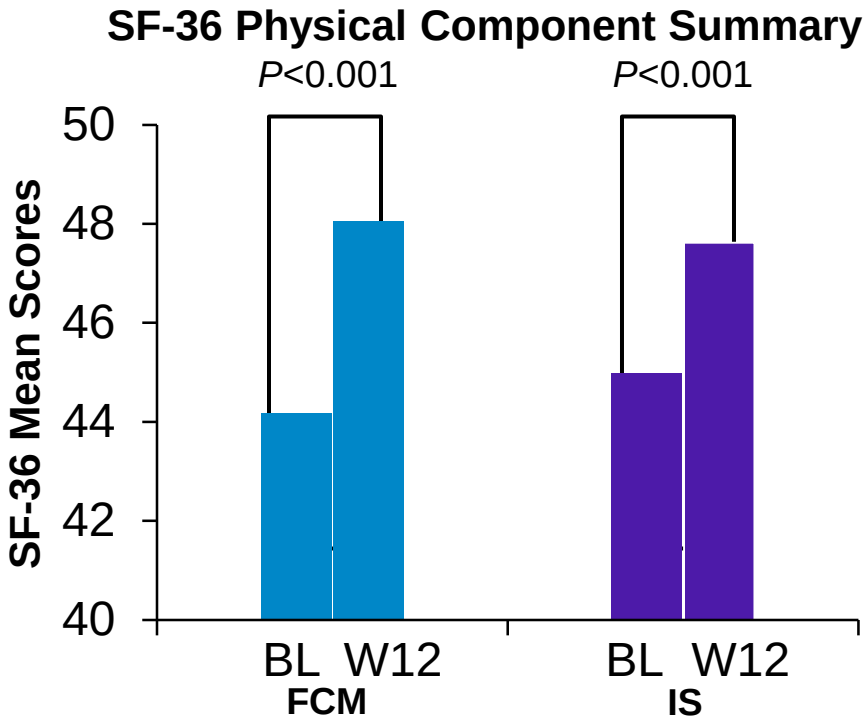
Evstatiev R, et al. *Gastroenterology*. 2011;141:846-85.
Evstatiev R, et al. *Clin Gastroenterol Hepatol*. 2013;11:269-277.

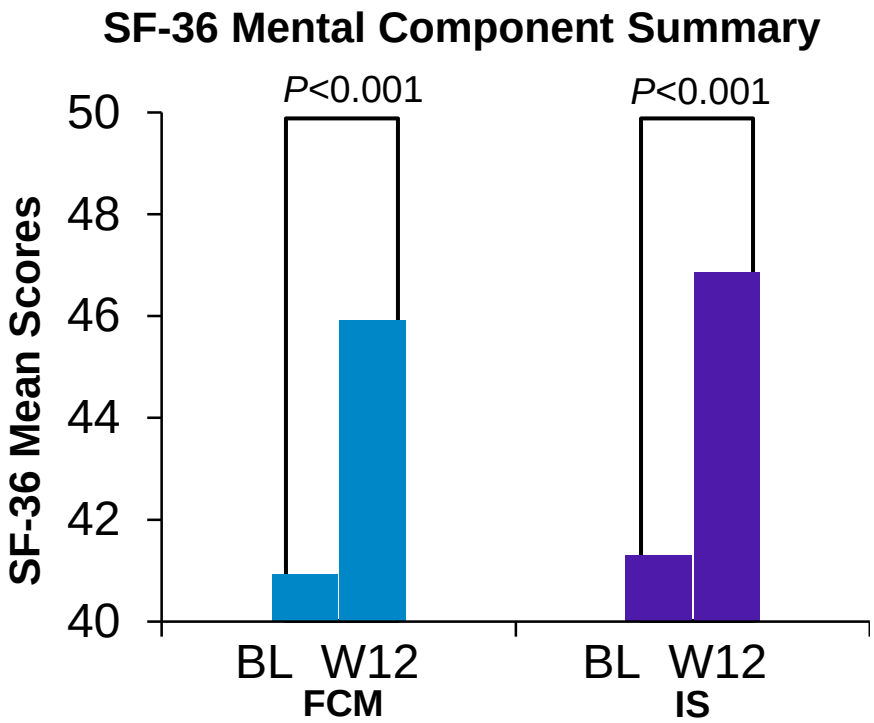
FCM vs Iron Sucrose: Response Rates at Week 12



Evstatiev R, et al. *Gastroenterology*. 2011;141:846-853.

Impact of IV Iron on Quality of Life

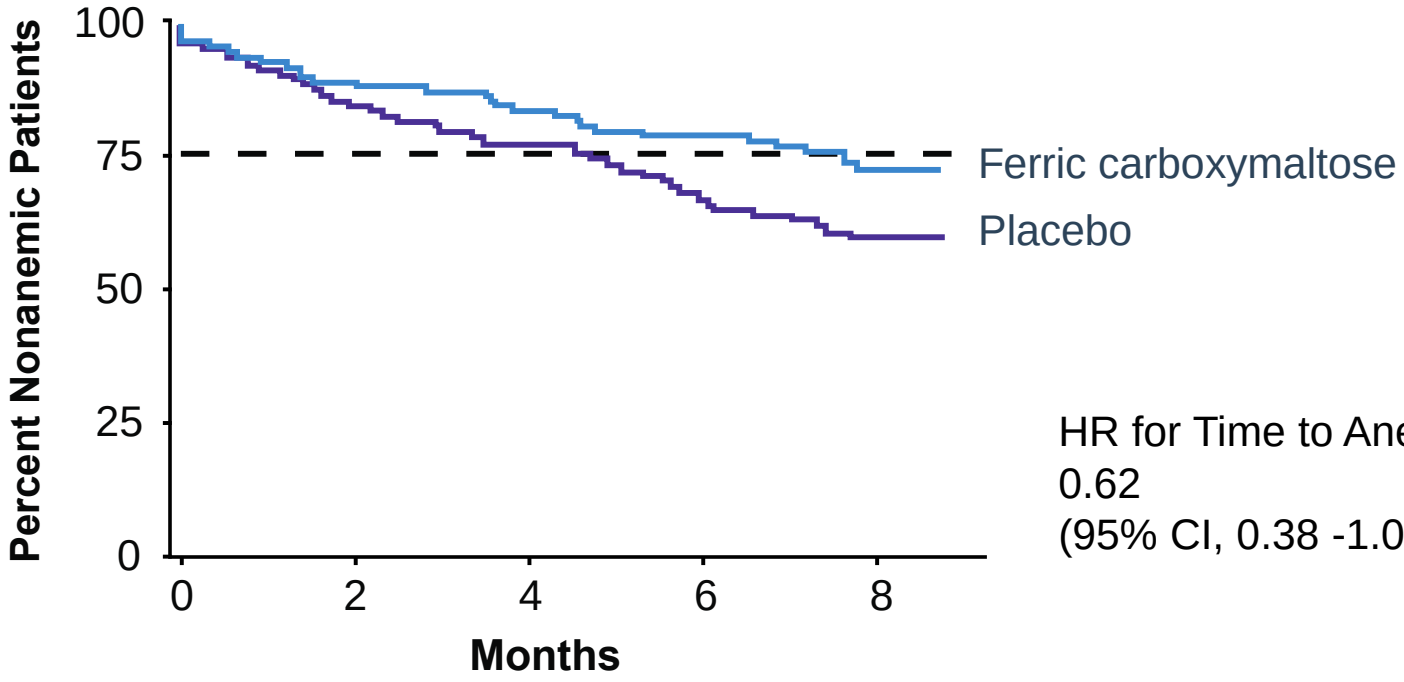




BL = Baseline; FCM = Ferric Carboxymaltose; IS = Iron Sucrose; W12 = Week 12

Evstatiev R, et al. *Gastroenterology*. 2011;141:846-853.

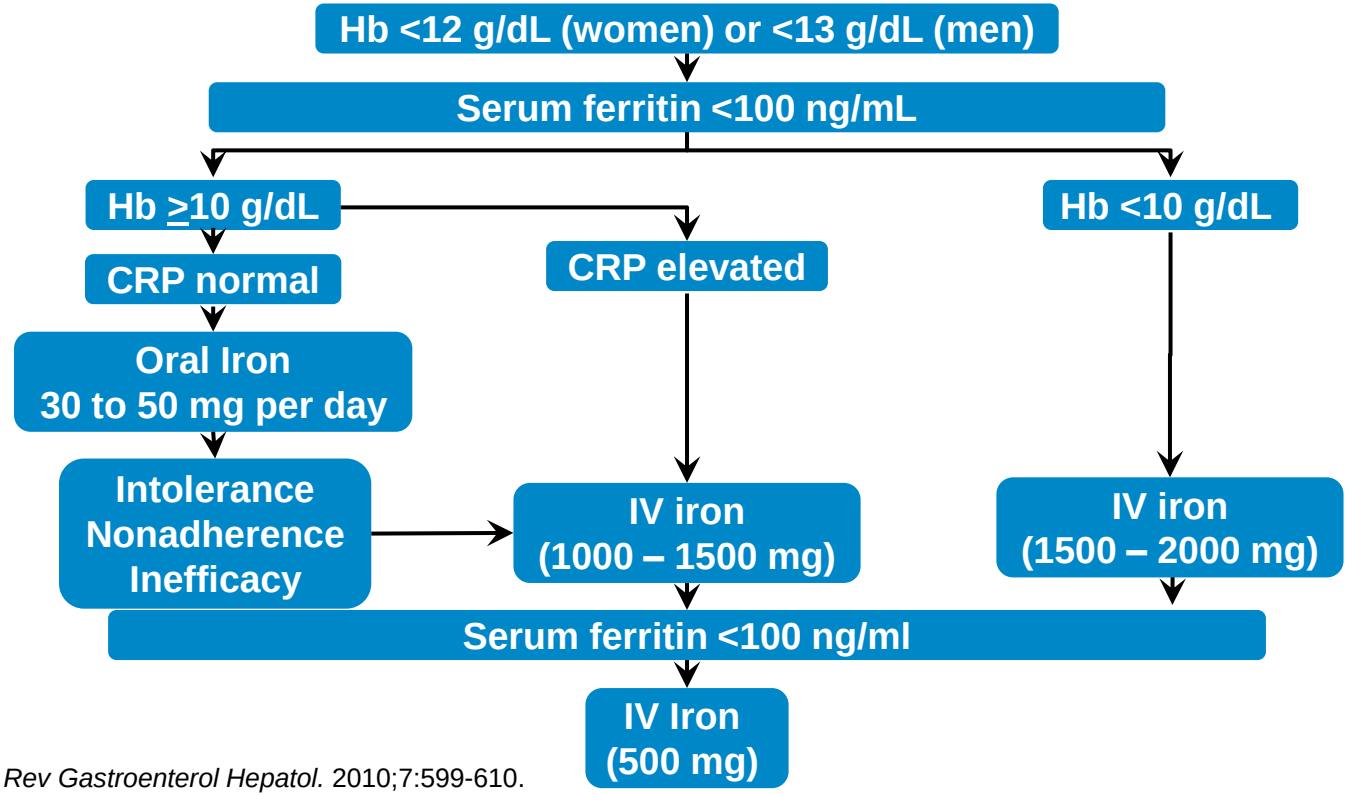
FCM Delays Recurrence of Anemia in Patients With IBD



HR for Time to Anemia Recurrence: 0.62
(95% CI, 0.38 -1.00; *P=0*.049)

Evstatiev R, et al. *Clin Gastroenterol Hepatol*. 2013;11:269-277.

One Potential Algorithm for the Diagnosis and Management of IDA in IBD



Adapted from:
Stein J, et al. *Nat Rev Gastroenterol Hepatol.* 2010;7:599-610.

Summary: IV Iron

- IV iron may be an appropriate first-line therapy in many patients with GI disease, including those with IBD
  - More rapid and complete repletion of iron stores
  - Avoids gastrointestinal side effects of oral iron supplementation
- Two IV iron formulations are approved for general treatment of IDA in the United States
  - Iron dextran
  - Ferric carboxymaltose
- Adverse events with IV iron can be managed

Case Studies in Iron Deficiency Anemia: Martin W.

Case Study #1: Martin W.
Medical and Social History

- Computer programmer by profession
- Non-smoker
- Occasional use of alcohol
- Denies use of ASA or NSAIDs

BMI: 24.7 kg/m2

Concomitant medications: lansoprazole, 15 mg, qd for non-erosive GERD

Fecal occult blood test (FOBT): Negative

Case Question #1: Martin W. Differential Work-Up of Anemia

Which of the following laboratory assessments ***most appropriately*** defines iron deficiency anemia in this patient?

A. Vitamin B12 level
B. Mean corpuscular volume (MCV)
C. Serum erythropoietin
D. Serum ferritin concentration

Martin: Baseline Laboratory Values

8,000 cells/mm^3

11 g/dL

33%

450 x10^3/µL

MCV	**70 fl**
MCHC	**30 g/dL**
Reticulocyte Count	**0.5%**

Serum Ferritin: 18 ng/mL	**TSat%: 12**	**Serum Iron: 45 mg/dL**
Serum Transferrin : 180 mg/dL	**TIBC: 375 µg/dL**	**CRP: 1.5 mg/L (Normal: <8 mg/L)**

Laboratory Workup of Anemia

Initial Evaluation:

- CBC with differential
- *Serum ferritin*
- *Transferrin saturation*
- CRP
- Creatinine
- Reticulocyte count

If Cause of Anemia Not Identified:

- Vitamin B12
  - Methylmalonic acid
- Folic acid
- Haptoglobin
- Lactate dehydrogenase
- Bone marrow aspirate

CBC = Complete Blood Count
Hb = Hemoglobin
MCH = Mean Corpuscular Hemoglobin
MCV = Mean Corpuscular Volume

Gasche C, et al. *Inflamm Bowel Dis.* 2007;13:1545-1553.

Laboratory Tests for IDA

Degree of iron deficiency evaluated by serum ferritin or transferrin saturation in adults

Level	Serum Ferritin (µg/L)	Transferrin Saturation (%)
Adequate iron stores	>100	16-50
Depleted iron stores in healthy adults or in patients with quiescent IBD	<30	<16
Depleted iron stores during active IBD	<100	<16

Gasche C, et al. *Inflamm Bowel Dis.* 2007;13:1545-1553.

Summary

- Initial evaluation of patients with anemia suspected to be iron deficient:
  - CBC with differential
  - Serum ferritin
  - Transferrin saturation
  - C-reactive Protein (CRP)
  - Creatinine
  - Reticulocyte count

Case Question #2: Martin W. Initial Treatment of IDA in IBD

How would you treat this young, male patient with a hemoglobin of 11 g/dL, hematocrit of 30%, and correspondingly low serum ferritin?

A. Oral iron with a ferrous sulfate or gluconate formulation
B. Blood transfusion
C. Iron infusion
D. Erythropoietin (rHuEPO)

Case Study #1: Martin W. Follow-Up Office Visit

- Martin presents to his PCP after 4 weeks on-treatment with ferrous sulfate, 325 mg, po, TID (total elemental iron: 195 mg) taken before meals
- He complains of frequent episodes of nausea after taking iron, as directed
- The patient admits that he has not fully adhered to his prescribed dosing regimen
- His latest CBC and iron studies suggest a slow resolution of IDA

Case Study #1: Martin W.
On-Treatment Laboratory Values

8,000 cells/mm^3

12.5 g/dL

37.5%

380 x10^3/µL

MCV	**76 fl**
MCHC	**31 g/dL**
Reticulocyte Count	**0.8%**

Serum Ferritin: 29 ng/mL	TSat%: 15	Serum Iron: 60 mg/dL
Serum Transferrin: 200 mg/dL	TIBC: 400 µg/dL	CRP: 0.9 mg/L (Normal: <8 mg/L)

Case Question #3: Martin W. Treatment-Related Issues

Which of the following is ***most likely*** to explain the slow resolution of IDA in this patient?

A. Non-adherence
B. Elevated hepcidin
C. Mesalamine therapy
D. Concomitant azathioprine

Case Question #4: Martin W. What Would You Do Now?

Given Martin's history of IBD and GERD, what might your next steps be in the management of his iron deficiency anemia?

A. Change oral iron formulation
B. Reduce total daily dose of oral iron
C. Discontinue PPI
D. Replace orally delivered iron with IV infusion

Case Studies in Iron Deficiency Anemia: Sandra B.

Case Study #2: Sandra B. Medical and Social History

- Three-year history of moderately severe luminal Crohn's disease
- Nonresponsive to prior corticosteroids and aminosalicylates
- CD has stabilized on current maintenance therapy of:
  - IV infliximab, 5 mg/kg (250 mg), q8 weeks
  - 6-mercaptopurine, 2.5 mg/kg (125 mg), po, qd
- Concomitant medications: OTC analgesic prn headache

Case Study #2: Sandra B. Medical and Social History (Con't)

- (+) Family history for CD (Mother)
- Elementary school teacher
- BMI: 18.5 kg/m^2
- Smoker: ½ PPD x 5 years
- Denies use of alcohol
- You order a CBC with differential + iron studies

Case Study #2: Sandra B. Baseline Laboratory Values

5,000 cells/mm^3

9 g/dL

27%

380 x10^3/µL

MCV	74 fl
MCHC	28 g/dL
Reticulocyte Count	0.3%

Serum Ferritin: 22 ng/mL	TSat%: 10	Serum Iron: 52 mg/dL
Serum Transferrin: 160 mg/dL	TIBC: 520 µg/dL	CRP: 10 mg/L (Normal: <8 mg/L)

Case Question #1: Sandra B.
Initial Steps in Case Management

Which of the following parameters suggests the diagnosis of IDA?

A. Serum Transferrin
B. Serum Ferritin
C. C-reactive Protein
D. All of the above

Case Study #2: Sandra B. Optimizing Management of IDA in IBD

- Your treatment goal for Sandra is to minimize potential GI adverse effects by passing the metabolism of oral iron supplementation
- You consider iron replacement therapy with an intravenous formulation

Case Question #2: Sandra B.
Selection of IV Iron Replacement Therapy

Which of the following agents requires a test dose?

A. Iron dextran
B. Ferumoxytol
C. Iron sucrose
D. Ferric carboxymaltose

Case Study #2: Sandra B. Induction Therapy with IV Iron

- Based on her current weight of 50.3 kg, ferric carboxymaltose (FCM) is administered at a dose of 750 mg in two, separate infusions, delivered 7 days apart
- Upon completing her course of therapy, Sandra will have received a total FCM dose of 1500 mg
- Symptom resolution and on-treatment laboratory values will guide further therapeutic intervention

Case Study #2: Sandra B.
Tracking Response to Induction Therapy

- At her 4-week follow-up visit, Sandra reports significant symptomatic improvement
- The patient denies abdominal pain, hematochezia, or melena
- Current weight: 52.6 kg (116 Lbs.) / [BMI: 19.3 kg/m^2]
- The patient is regaining her appetite, gradually increasing food intake, and has resumed her normal class schedule

Case Study #2: Sandra B.
On-Treatment Laboratory Values

6,500 cells/mm^3

12 g/dL

31%

378 x10^3/µL

MCV	80 fl
MCHC	30 g/dL
Reticulocyte Count	0.5%

Serum Ferritin: 100 ng/mL	TSat%: 23	Serum Iron: 64 mg/dL
Serum Transferrin: 180 mg/dL	TIBC: 460 µg/dL	CRP: 1.0 mg/L (Normal: <8 mg/L)

Case Question #3: Sandra B. What Would You Do Now?

Next steps in managing this patient:

A. Reload parenteral iron
B. Transition to oral ferrous sulfate and monitor
C. Schedule maintenance ferric carboxymaltose
D. Monitor and repeat CBC and iron studies in 4 weeks' time