Il riscontro di anemia in Pronto Soccorso: l'importanza di una diagnosi e di un intervento precoce

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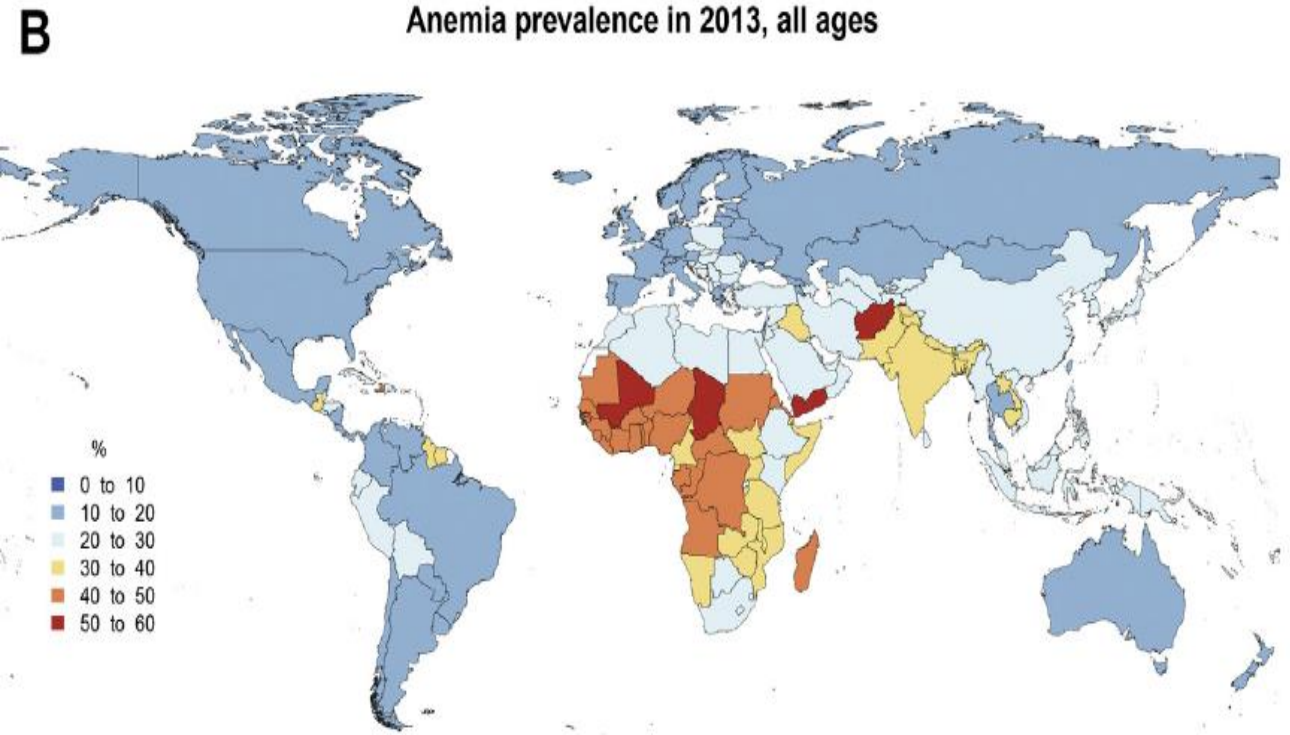
Prevalenza dell'anemia



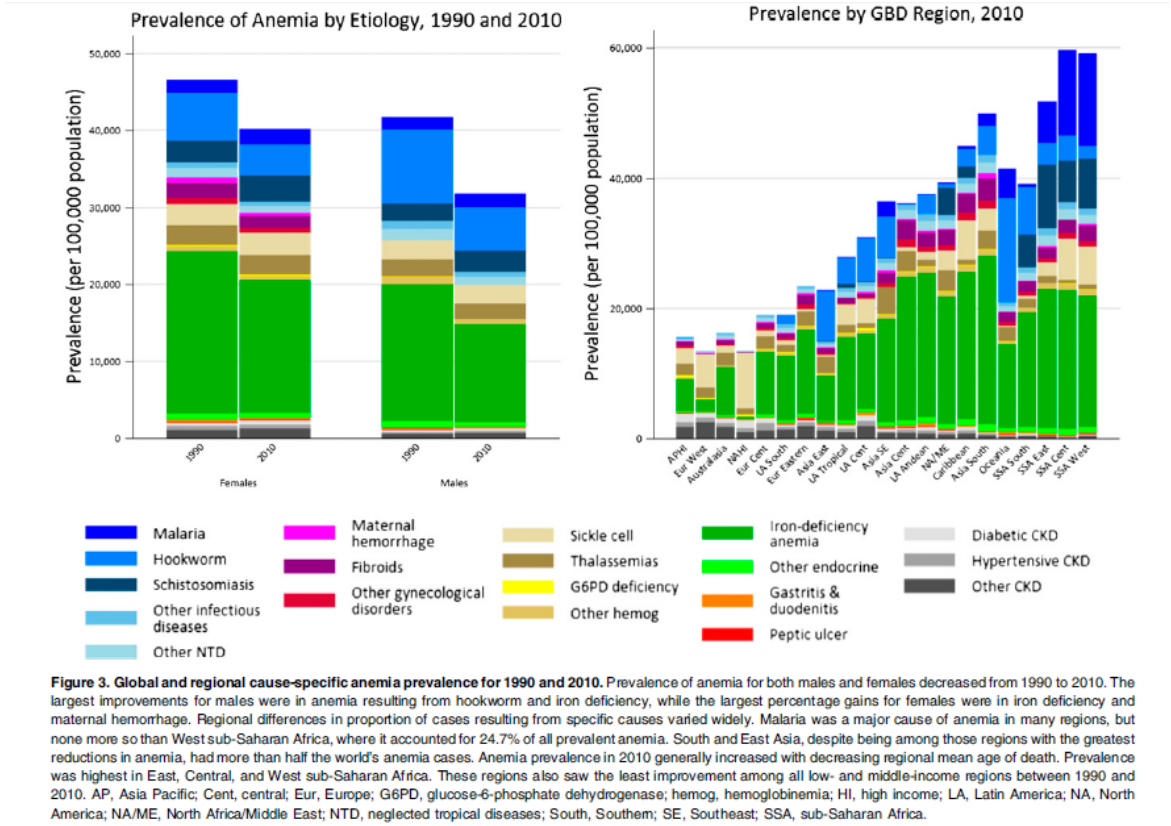


Figure 3. Global and regional cause-specific anemia prevalence for 1990 and 2010. Prevalence of anemia for both males and females decreased from 1990 to 2010. The largest improvements for males were in anemia resulting from hookworm and iron deficiency, while the largest percentage gains for females were in iron deficiency and maternal hemorrhage. Regional differences in proportion of cases resulting from specific causes varied widely. Malaria was a major cause of anemia in many regions, but none more so than West sub-Saharan Africa, where it accounted for 24.7% of all prevalent anemia. South and East Asia, despite being among those regions with the greatest reductions in anemia, had more than half the world's anemia cases. Anemia prevalence in 2010 generally increased with decreasing regional mean age of death. Prevalence was highest in East, Central, and West sub-Saharan Africa. These regions also saw the least improvement among all low- and middle-income regions between 1990 and 2010. AP, Asia Pacific; Cent, central; Eur, Europe; G6PD, glucose-6-phosphate dehydrogenase; hemog, hemoglobinemia; HI, high income; LA, Latin America; NA, North America; NA/ME, North Africa/Middle East; NTD, neglected tropical diseases; South, Southern; SE, Southeast; SSA, sub-Saharan Africa.

1/3 della popolazione mondiale

50% dei casi sono dovuti a sideropenia

Kassebaum N, Hematol Oncol Clin N Am 2016
Kassebaum NJ, *Blood* 2014

Prevalenza dell'anemia in PS

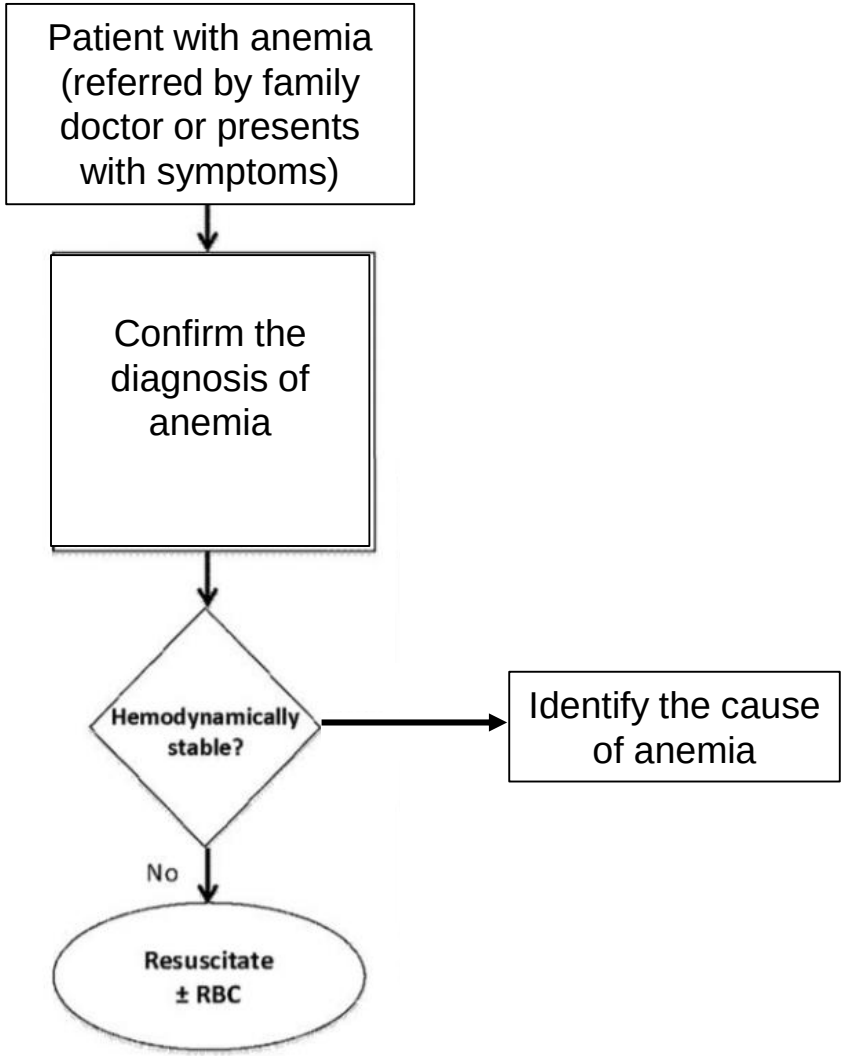
Table 1
Prevalence of anemia.

	All patients n. 22,329	M n. 11,127	F n. 11,202
NON ANEMIC			
Patients n. (%)	16,185 (72.5)	8067 (72.5)	8118 (72.5)
Hb (g/dL) – (± SD)	14.0 (1.2)	14.5 (1.6)	13.4 (1.0)
Mean age (± SD)	52 (25)	51 (24)	53 (26)
ANEMIC			
Patients (n)	6144 (27.5)	3060 (27.5)	3084 (27.5)
Hb (g/dL)	10.8 (1.5)	11.0 (1.2)	10.5 (1.4)
Mean age (± SD)	67 (22)	69 (19)	64 (25)
Anemia severity			
Mild – n. (%)	3409 (15.3)	1906 (17.1)**	1504 (13.4)
Moderate – n. (%)	2376 (10.6)	994 (8.9)	1382 (12.3)**
Severe – n. (%)	359 (1.6)	160 (1.4)	199 (1.8)*

* $p = 0.044$.
** $p < 0.000$.

Beverina I, *Transfus Apher Sci* 2019

Management dell'anemia in PS



- Emocromo con formula (Hb, MCV, RDW, PLT, GB)
- LDH
- Bilirubina reflex
- Funzione renale
- PCR

Adapted from Khadadah, *Transfusion* 2018

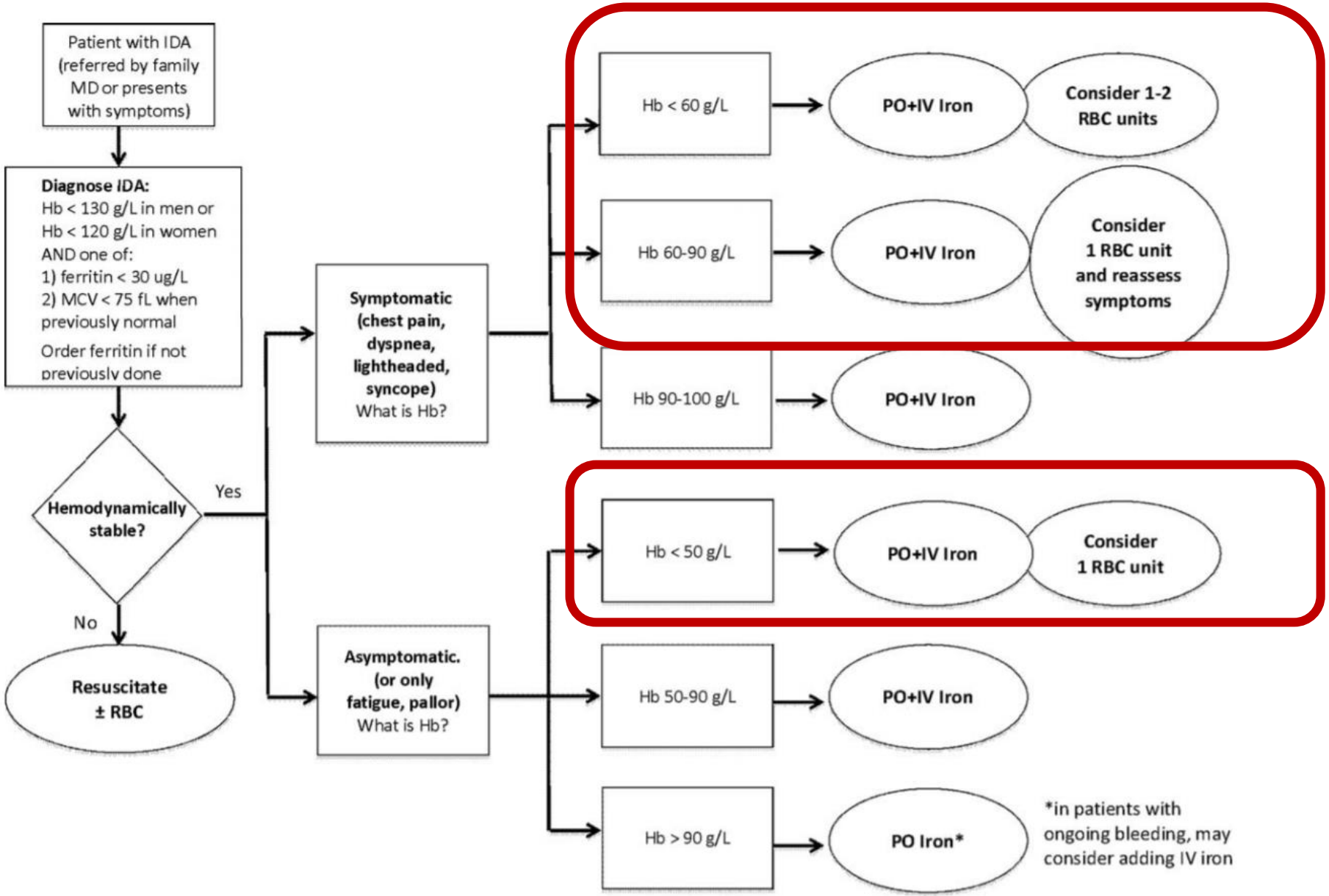


Fig. 1. Algorithm for management of IDA in the ED.

Khadadah, *Transfusion* 2018

Management dell'anemia

Maggio 2019

♀, 40 anni
Menorragie
Nota per anemia sideropenica

Accede in PS di grande ospedale milanese per riscontro agli EE eseguti per astenia di Hb 5.7 g/dl

TRASFUSA CON 4 U EC
DIMESSA SENZA TERAPIA

Era necessario ????

JAMA | Special Communication

Clinical Practice Guidelines From the AABB
Red Blood Cell Transfusion Thresholds and Storage

Jeffrey L. Carson, MD; Gordon Guyatt, MD; Nancy M. Heddle, MSc; Brenda J. Grossman, MD, MPH; Claudia S. Cohn, MD, PhD; Mark K. Fung, MD, PhD; Terry Gernsheimer, MD; John B. Holcomb, MD; Lewis J. Kaplan, MD; Louis M. Katz, MD; Nikki Peterson, BA; Glenn Ramsey, MD; Sunil V. Rao, MD; John D. Roback, MD, PhD; Aryeh Shander, MD; Aaron A. R. Tobian, MD, PhD

JAMA November 15, 2016 Volume 316, Number 19

First Recommendation

The AABB recommends a restrictive RBC transfusion threshold in which the transfusion is not indicated until the hemoglobin level is 7 g/dL for hospitalized adult patients who are hemodynamically stable, including critically ill patients, rather than a liberal threshold when the hemoglobin level is 10 g/dL (strong recommendation, moderate quality evidence). For patients undergoing orthopedic surgery or cardiac surgery and those with preexisting cardiovascular disease, the AABB recommends a restrictive RBC transfusion threshold (hemoglobin level of 8 g/dL; strong recommendation, moderate quality evidence). The restrictive hemoglobin transfusion threshold of 7 g/dL is likely comparable with 8 g/dL, but RCT evidence is not available for all patient categories. These recommendations apply to all but the following conditions for which the evidence is insufficient for any recommendation: acute coronary syndrome, severe thrombocytopenia (patients treated for hematological or oncological disorders who at risk of bleeding), and chronic transfusion–dependent anemia.

(In)appropratezza delle trasfusioni

Appropriate use of red blood cell transfusion in emergency departments: a study in five emergency departments

Manuel Quintana Díaz[1,2], Alberto M. Borobia[3], José A. García Erce[4], Charbel Maroun-Eid[1], Sara Fabra[1], Antonio Carcas[3], Jesus Frías[3], Manuel Muñoz[5], on behalf of the USEES-URG Research Group

- Multicentrico osservazionale
- Appropriatezza della prescrizione (eventi) e del numero di sacche
- 908 eventi, età media 72.6±15.7
- Mediana 2 U per pz

Prescrizioni inappropriate 21.4%

Il 45% delle prescrizioni appropriate ha ricevuto un numero di unità di EC inappropriato

IL 60% degli eventi erano OVER-TRANSFUSION

Table II - Patients' demographic and clinical characteristics.

Patients (n)	**202**
Gender (female/male)	150/52
Age (years)	64±22
Weight (kg)	69±15
Provenance (%)	
Emergency Department	55
Primary health care	36
Other	9
Underlying pathology (%)	
Gynaecological	26
Digestive tract	44
Anaemia with ID	12
Haematological	5
Other	13
Referral to (%)	
Gynaecological care	7
Digestive tract care	9
Internal Medicine	6
Primary health care	12
Others	5
IV iron dose (mg)	1,500 [1,000-2,000]
Transfusion, n (%)	35 (17)
RBC concentrates (unit/patient)	2 [1-3]
FTAC visits (n)	3 [2-4]

Data are expressed as incidence (n) and percentage (%), mean±standard deviation, or median [interquartile range].
FTAC: fast-track anaemia clinic; ID: iron deficiency; RBC: red blood cell.

A fast-track anaemia clinic in the Emergency Department: feasibility and efficacy of intravenous iron administration for treating sub-acute iron deficiency anaemia

Manuel Quintana-Díaz[1,2,3], Sara Fabra-Cadenas[1,3], Susana Gómez-Ramírez[4], Ana Martínez-Virto[1,3], José A. García-Erce[3,5], Manuel Muñoz[4]

Parameter	**N***	**Baseline**	**4 week follow-up visit**	**p**
Haemoglobin (g/dL)	183	8.3±1.4	12.2±1.8	0.001
Haematocrit (L/L)	183	28±2	39±6	0.001
MCV (fL)	183	76±11	89±8	0.001

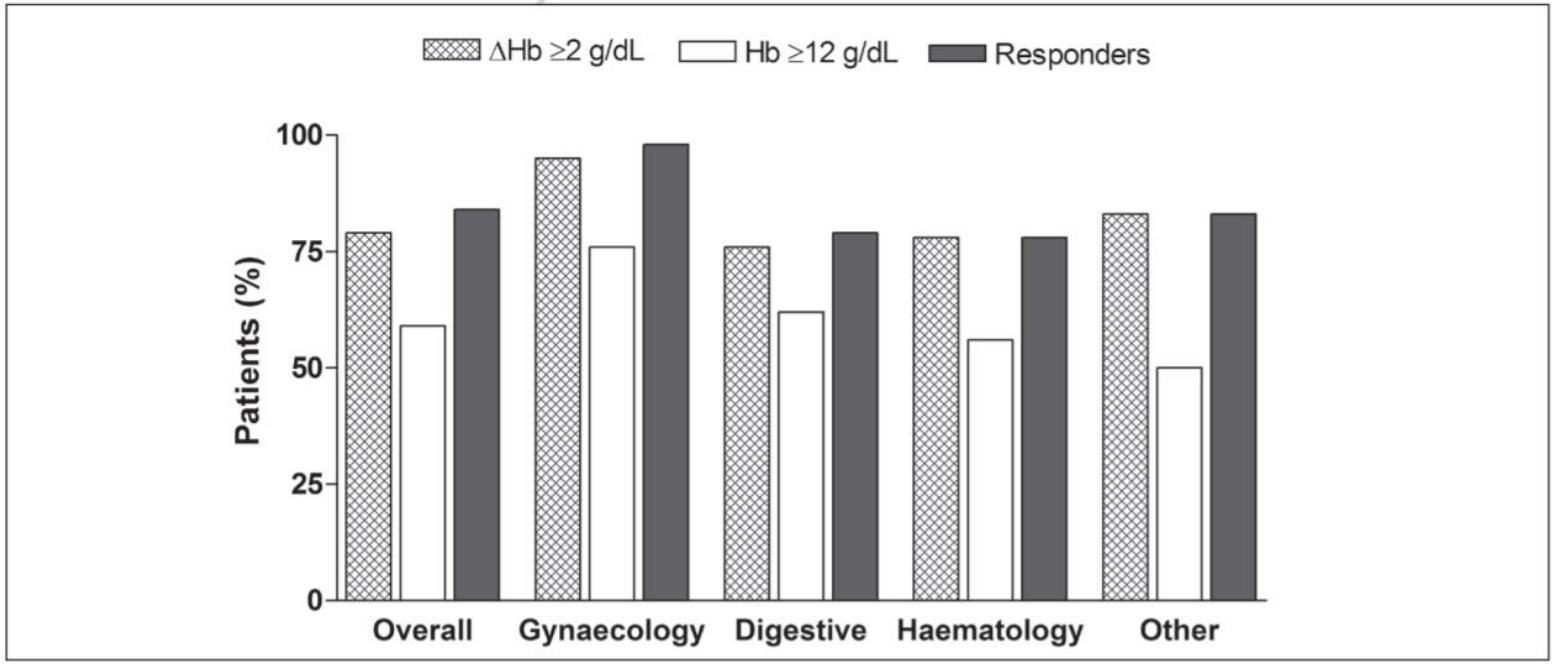


Figure 2 - Percentage of patients showing a haematological response (responders), as defined by a haemoglobin increment (ΔHb) ≥2 g/dL and/or a haemoglobin level ≥12 g/dL, at 4 weeks after administration of the total dose of iron.

not-assessed.

Quintana-Diaz M, *Blood Transfus* 2016

Choosing Wisely®

An initiative of the ABIM Foundation

AABB®

Five Things Physicians and Patients Should Question

1 Don't transfuse more units of blood than absolutely necessary.

Each unit of blood carries risks. A restrictive threshold (7.0-8.0g/dL) should be used for the vast majority of hospitalized, stable patients without evidence of inadequate tissue oxygenation (evidence supports a threshold of 8.0g/dL in patients with pre-existing cardiovascular disease). Transfusion decisions should be influenced by symptoms and hemoglobin concentration. Single unit red cell transfusions should be the standard for non-bleeding, hospitalized patients. Additional units should only be prescribed after re-assessment of the patient and their hemoglobin value.

2 Don't transfuse red blood cells for iron deficiency without hemodynamic instability.

Blood transfusion has become a routine medical response despite cheaper and safer alternatives in some settings. Pre-operative patients with iron deficiency and patients with chronic iron deficiency without hemodynamic instability (even with low hemoglobin levels) should be given oral and/or intravenous iron.

3 Don't routinely use blood products to reverse warfarin.

Patients requiring reversal of warfarin can often be reversed with vitamin K alone. Prothrombin complex concentrates or plasma should only be used for patients with serious bleeding or requiring emergency surgery.

4 Don't perform serial blood counts on clinically stable patients.

Transfusion of red blood cells or platelets should be based on the first laboratory value of the day unless the patient is bleeding or otherwise unstable. Multiple blood draws to recheck whether a patient's parameter has fallen below the transfusion threshold (or unnecessary blood draws for other laboratory tests) can lead to excessive phlebotomy and unnecessary transfusions.

5 Don't transfuse O negative blood except to O negative patients and in emergencies for women of child bearing potential with unknown blood group.

O negative blood units are in chronic short supply due in part to overutilization for patients who are not O negative. O negative red blood cells should be restricted to: (1) O negative patients; or (2) women of childbearing potential with unknown blood group who require emergency transfusion before blood group testing can be performed.

Preparati ferro EV

Table 3 Currently used IV iron preparations

Drug	Brand name	Stability	Maximum single dose	Total replacement dose in single infusion (1–1.5 g)	Minimun administration time (min)
Fe-gluconate	Ferlixit®	Low	125 mg	No (repeated access needed)	30–60
Fe-sucrose	Venofer®	Low-moderate	200 mg	No (repeated access needed)	30
Fe-carboxymaltose	Ferinject®	High	1000 mg	Yes	15
Fe-isomaltoside	Monofer®	High	20 mg Fe/Kg	Yes	15
Ferumoxytol	Feraheme®	High	510 mg	Yes/no	15

Body weight	Body weight 35 kg to <70 kg		Body weight ≥70 kg	
Hb level (g/dL)	≥10	<10	≥10	<10
Total iron dose	1000 mg	1500 mg	1500 mg	2000 mg
Administration in week 1	1000 mg	1000 mg	1000 mg	1000 mg
Administration in week 2	–	500 mg	500 mg	1000 mg

- **1000 mg as an I.V. injection or infusion should be administered over 15 min.**

- Up to a maximum of 20mg iron/kg body weight. Do not administer more than 1000 mg iron per week.
- A cumulative iron dose of 500 mg should not be exceeded for patients with body weight <35 kg.
- For patients with an Hb value ≥14 g/dL, an initial dose of 500 mg iron should be given and iron parameters should be checked prior to repeat dosing.

Girelli D, *Int J Hematol* 2018

Indicazioni al ferro EV

Table 4 Indications for IV iron

Established	Examples/comments
Failure of oral iron	Non-adherence, AEs
Malabsorption	Celiac disease, gastritis (atrophic, autoimmune, Hp +), bariatric surgery, genetic IRIDA
Severe IDA	Generally accepted threshold: Hb < 8 g/dl
End-stage chronic kidney disease (CKD)	(+ Erythropoiesis Stimulating Agents-ESAs)
Inflammatory bowel diseases	IDA in active disease
Pregnancy	Severe IDA in II–III trimester
Heart failure (HF)[a]	Systolic HF (LVEF[b] ≤ 45%)
Potential (extended)	**Examples/comments**
ID/IDA in elderly	If comorbidities/polypharmacy (including PPI) prevent adherence to (or effectiveness of) long-term oral iron
Perioperative anemia	Patient blood management strategies to prevent RBCs transfusions
IDA in cancer	± ESAs
Restless leg syndrome	
Mountain sickness	(Prevention)
Heavy uterine bleeding	

[a]Iron deficiency (even without anemia): serum ferritin < 100 or < 300 µg/L, if transferrin saturation ≤ 20%

[b]Left Ventricular Ejection Fraction

Girelli D, *Int J Hematol* 2018

La nostra esperienza

Analisi retrospettiva database PS da gennaio 2014 - luglio 2018
Dal 2016 FCM in PS

CRITERI DI INCLUSIONE

- **anemia sideropenica grave cronica o sub-acuta** (<8 g/dl) da perdita cronica nota o presunta (sideropenia assoluta: ferritina<30 ng/ml e TSAT <20%)
- Età **18-55 anni**
- **Stabilità emodinamica**

CRITERI DI ESCLUSIONE

- **Macro-sanguinamento attivo** (escluse mestruazioni)
- Ipotensione ortostatica
- Tachicardia a riposo
- Alterazioni ECG di tipo ischemico
- Dolore toracico, dispnea a riposo
- Infezione in atto
- Gravidanza

ero

CONFRONTO TRA CHI E' STATO TRATTATO CON FCM IN PS (FCM1) E CHI NON HA RICEVUTO FCM IN PS (FCM0)

Motta I, *Intern Emerg Med* 2019

Caratteristiche dei pazienti all'ingresso

	FCM1 n=23	FCM0 n=48	p-value
Sex F, n (%)	20 (87)	40 (83)	0.69
Age, years*	43 ± 8	41 ± 9	0.46
History of IDA, n (%)	15 (65)	31 (65)	0.96
Symptoms, n (%)	17 (74)	29 (60)	0.27
Syncope or pre-syncope, n, (%)	3 (13)	5 (10)	0.71
Hematological parameters			
Hb, g/dL*	6.3 ± 0.9	6.7 ± 0.8	0.06
MCV, fL*	61 ± 8	62 ± 5	0.57
RDW, %	20 ± 3	20 ± 2	0.70
RBC, 10^{12}/µL*	3.8 ± 0.5	3.9 ± 0.5	0.25
PLT, 10^{3}/µL*	340 ± 83	378 ± 105	0.12
Ferritin, ng/mL*	3 ± 2	5 ± 4	0.17
TSAT, %	3 ± 1	4 ± 3	0.18

* media±DS

Motta I, *Intern Emerg Med* 2019

Gestione dei pazienti in PS

	FCM1 (n=23)	FCM0 (n=48)	P-value
Pz trasfusi, n (%)	3 (13%)	19 (40%)	p=0.02
Unità trasfuse per pz, n*	0.2±0.5	0.7±0.9	p=0.02
Unità per paziente trasfuso, n*	1.3±0.6	1.8±0.5	P=0.17
Ricoveri, n (%)	0 (0)	10 (21%)	p=0.02

* media±DS

Motta I, *Intern Emerg Med* 2019

Digestive and Liver Disease 51 (2019) 471–483

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journal homepage: www.elsevier.com/locate/dld

Guidelines

Diagnosis of chronic anaemia in gastrointestinal disorders: A guideline by the Italian Association of Hospital Gastroenterologist and Endoscopists (AIGO) and the Italian Society of Paediatric Gastroenterology Hepatology and Nutrition (SIGENP)

Luca Elli[a,*], Lorenzo Norsa[b], Angelo Zullo[c], Antonio Carroccio[d,e], Carlo Girelli[f], Salvatore Oliva[g], Claudio Romano[h], Gioacchino Leandro[i], Massimo Bellini[j], Riccardo Marmo[k], Marco Soncini[l], Fabio Monica[m], Vincenzo De Francesco[n], Emma Paulon[m], Maria Domenica Cappellini[o,p], Irene Motta[o,p], Francesca Ferretti[a], Stefania Orlando[a], Pasquale Mansueto[e], Elisabetta Buscarini[q], Guido Manfredi[q], Carlo Agostoni[r,p], Carolina Tomba[s], Renato Cannizzaro[t]

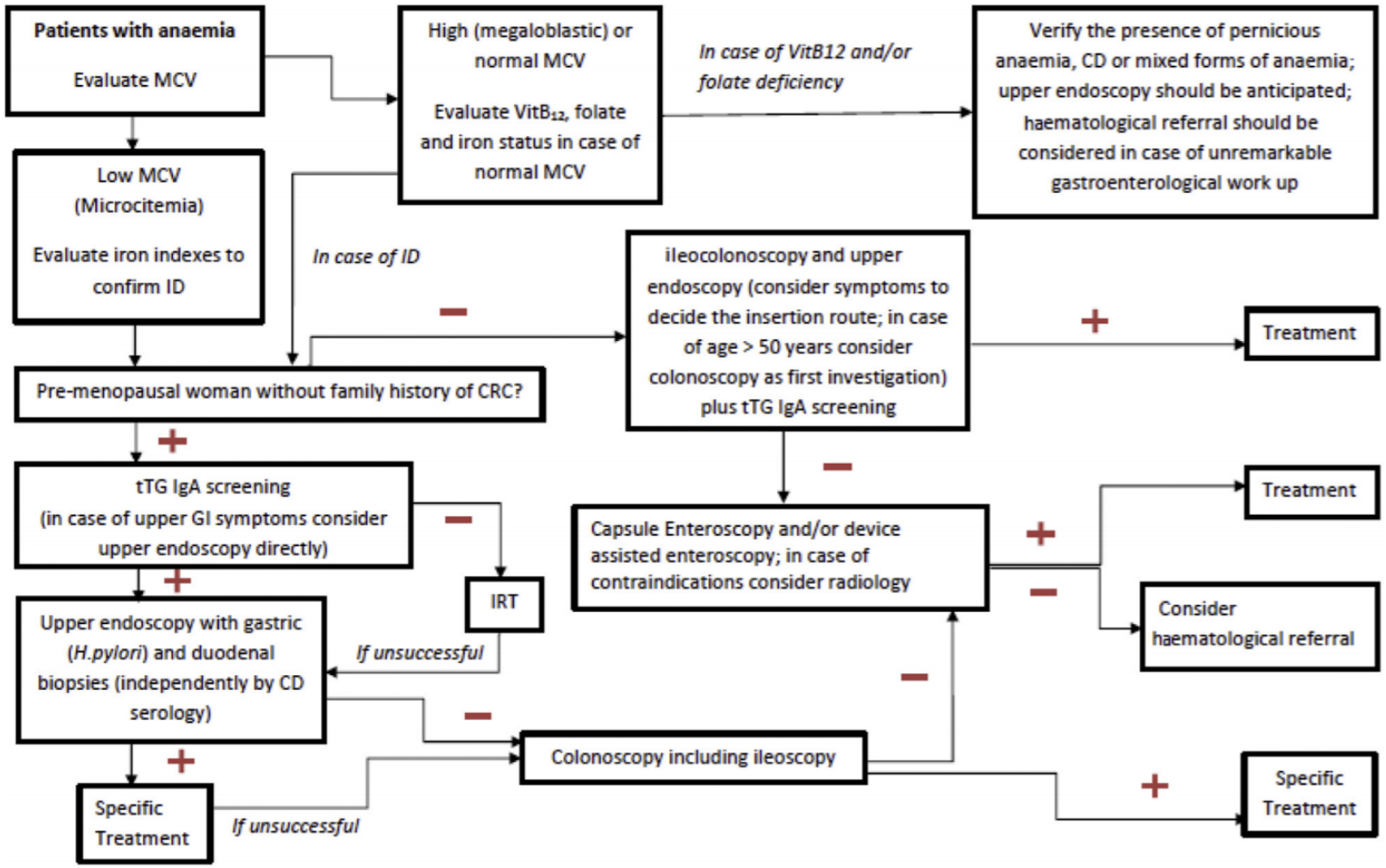


Fig. 1. Diagnostic gastroenterological flowchart for adult patients with anaemia.

Follow-up gruppo FCM1

		11 ± 3 gg	52 ± 28 gg
	T0 n=23	**T2 n=20**	**T3 n=16**
Hb, g/dL*	6.3 ± 0.9	9.3 ± 1.1	11.8 ± 1.1
MCV, fL*	61 ± 8	72 ± 7	80 ± 7
RDW, %	20 ± 3	28 ± 5	18 ± 6
RBC, x10^{12}/µL*	3.8 ± 0.5	4.5 ± 0.4	4.6 ± 0.4
PLT, x10^{3}/µL*	340 ± 83	311 ± 88	256 ± 90
Reticulocytes, x10^{3}/µL*	-	162 ± 86	-
Hb change from ED discharge, g/dL*	-	2.8±1	5.3 ± 1.4

* media±DS

Motta I, *Intern Emerg Med* 2019

Caso clinico

	FCM 1000 mg	FCM 500 mg	
	11/07	**23/07**	**23/08**
Hb (g/dl)	**4.7**	**8.7**	**12.1**
MCV (fl)	**61**	**74.3**	81
GR (n/mm3)	**2710000**	4210000	4600000

INCREMENTO DI 7.4 g/dl DI Hb IN 42 GIORNI

Ret (n/mm3)		103000	80000
GB (n/mm3)	5040	4040	4530
PLT (n/mm3)	181000	171000	178000

Selezione dei pazienti

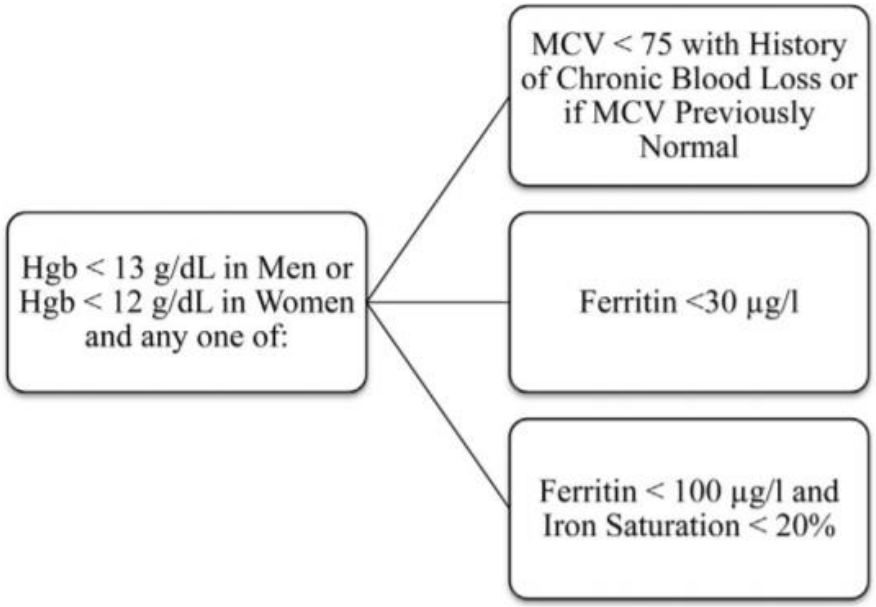


Figure 1. Identification of iron deficiency in the emergency department. Hgb = hemoglobin; MCV = mean corpuscular volume. Adapted from Khadadah et al., with permission (11). Copyright 2016 by Cambridge University Press.

IDA grave (Hb < 8 g/dL) cronica o subacuta da perdita cronica o ridotto intake/malassorbimento

- Ferritina < 30 µg/L (stato del ferro eseguito negli ultimi 3 mesi)
- Anemia microcitica in anamnesi positiva per IDA o storia di perdita cronica e/o malassorbimento
- Stato del ferro in PS

Boone S, J Emerg Med 2019
Motta I, *Intern Emerg Med* 2019

Selezione dei pazienti

♀, 32 anni
Si presenta in PS per astenia
Mestruazioni abbondanti

	Paziente 1
Hb (g/dl)	**7.3**
MCV (fl)	**69**
GR (n/mm3)	**3530000**
RDW (%)	**29.3**
GB (n/mm3)	9800
PLT (n/mm3)	400000

Ferritina 400 mcg/L
TSAT 50%

TALASSEMIA NON TRASFUSIONE DIPENDENTE

♀, 34 anni
Si presenta in PS per astenia
Mestruazioni abbondanti

	Paziente 1
Hb (g/dl)	**7.7**
MCV (fl)	**67**
GR (n/mm3)	**3200000**
RDW (%)	**22**
GB (n/mm3)	7200
PLT (n/mm3)	350000

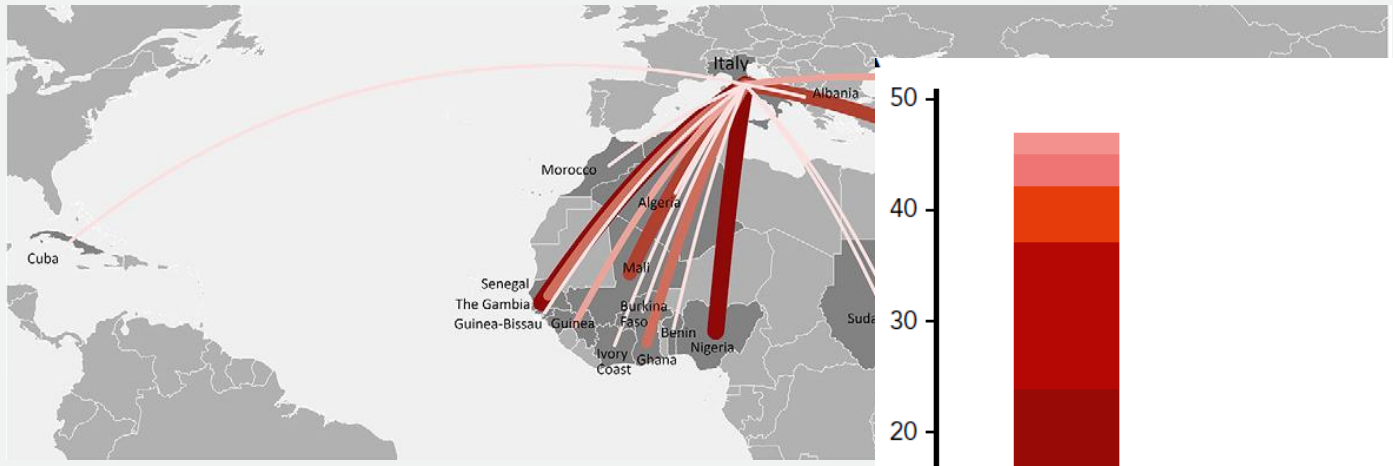
Ferritina 2 mcg/L
TSAT 3 %

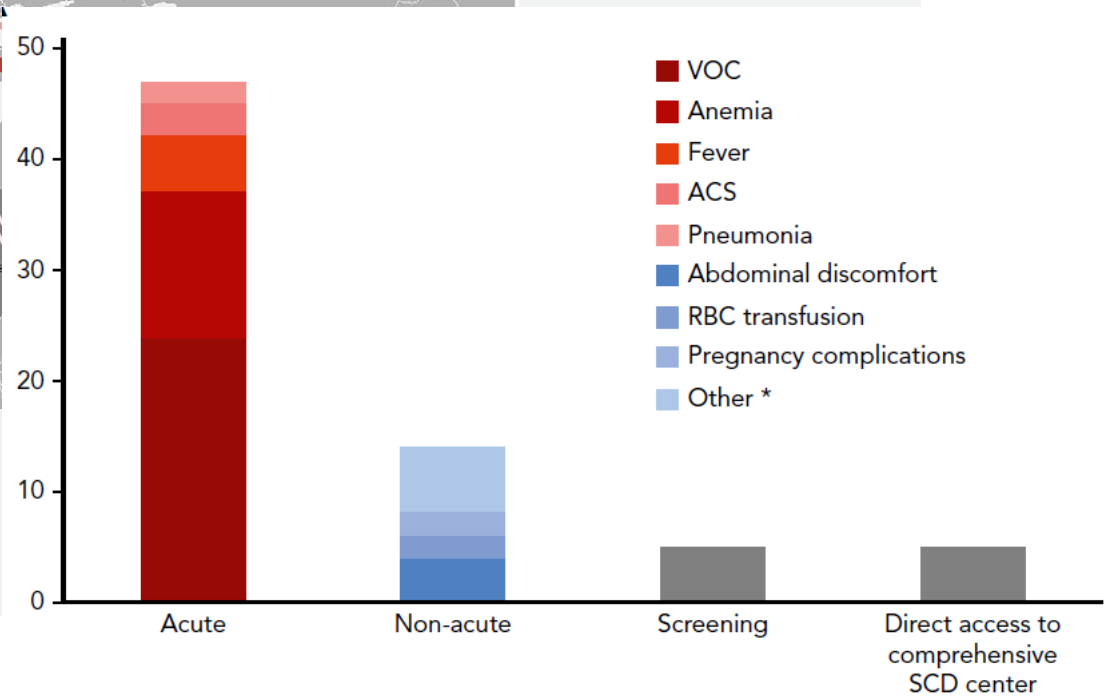
ANEMIA SIDEROPENICA

blood®
Letters to *Blood*

TO THE EDITOR:

Access to emergency departments for acute events and identification of sickle cell disease in refugees





De Franceschi, *Blood* 2019

Take home messages

- La nostra scelta di trasfondere deve basarsi sulla clinica e non solo sul valore di Hb
- FCM è sicuro ed efficace nell'incrementare rapidamente i valori di Hb
- FCM in pazienti selezionati è un'alternativa alla trasfusione
- Lo stato del ferro in PS può favorire l'utilizzo del ferro ev e ridurre le trasfusioni inappropriate
- MCV da solo non può guidare la nostra scelta terapeutica
- Percorsi dedicati con un follow-up ambulatoriale

GRAZIE!