

# IRON DEFICIENCY IN CYSTIC FIBROSIS-

## To treat or not to treat with Iron supplements?

### Pro

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The Annual Israeli CF Society Conference

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## Iron deficiency (ID) –

### Common in people with CF



- # Inadequate dietary intake
- # Malabsorption
- # Gastro-esophageal reflux
- # Short bowel syndrome
- # Liver and renal complications
- # Bleeding, Hemoptysis, GI bleeding
- # Inflammation & Chronic infection

# Iron deficiency (ID) - symptoms & complications



מרכז שניידר לרפואת ילדים בישראל  
مركز شتاينر لطب الأطفال في إسرائيل  
Schneider Children's Medical Center of Israel

# Anemia

# Tiredness ↑

# Lung function ↓ & overall health

Gifford. *Pediatr pulmonol*, 46 (2012) 160-65.

von Drygalski. *Nutr clin pract*, 23(2008) 557-56.

# Appetite ↓

# Growth problems

Borowitz. *J Pediatr Gastroenterol Nutr*, 35 (2002) 246-59.

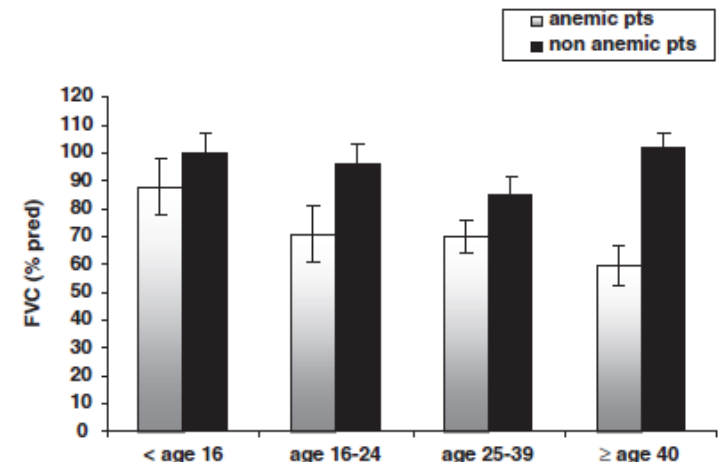
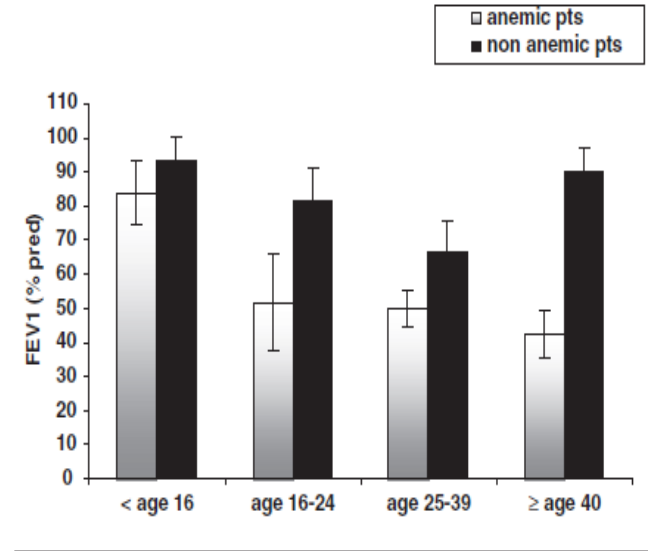
# risk of infections ↑

# Pregnancy complications

Pasricha. *Med J Aust*, 193 (2010) 525-32.

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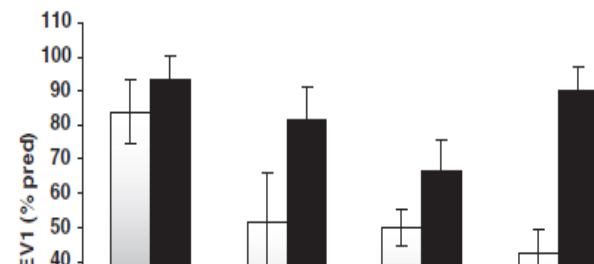
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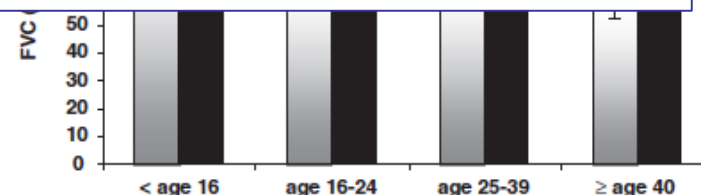
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□ anemic pts  
■ non anemic pts



**218 CF patients.**  
**Mean FEV1 -51.6%**  
**mean FVC – 69.7% in**  
**anemic and 82.5%**  
**and 95% in**  
**nonanemic patients.**





	Absolute ID	Functional ID (Chronic inflammation)	Absolute + Functional iron deficiency
Serum iron levels	LOW < 40 µg/dl	LOW < 40 µg/dl	LOW < 40 µg/dl
Transferrin saturation	LOW <20%	LOW <20%	LOW <20%
Serum ferritin level	LOW < 20 ng/ml	HIGH > 200 ng/ml	20-200 ng/ml
sTFR	HIGH > 1.76 mg/L	NORMAL < 1.76 mg/L	HIGH > 1.76 mg/L

# Pseudomonas Aeruginosa (PA)



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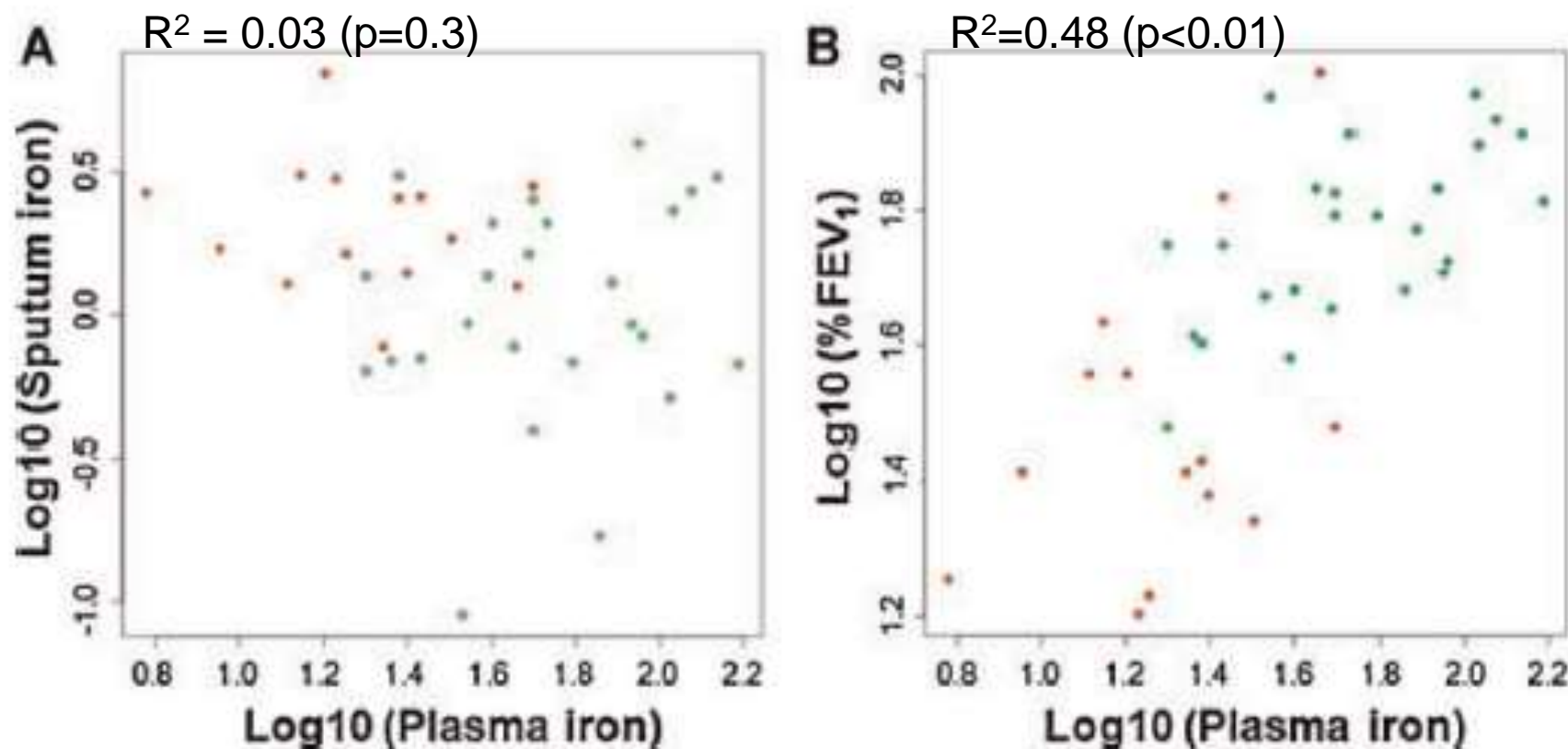




## Iron and CF-Related Anemia: Expanding Clinical and Biochemical Relationships

A.H. Gifford, MD<sup>1,\*</sup>, S.D. Miller, RN, MSN, MPH<sup>2</sup>, B.P. Jackson, PhD<sup>3</sup>, T.H. Hampton, MS<sup>4</sup>, G.A. O'Toole, PhD<sup>5</sup>, B.A. Stanton, PhD<sup>4,5,6,7</sup>, and H.W. Parker, MD<sup>1</sup>

### Cross-sectional study- 39 CF patients



Red= patients with worsened clinical features .

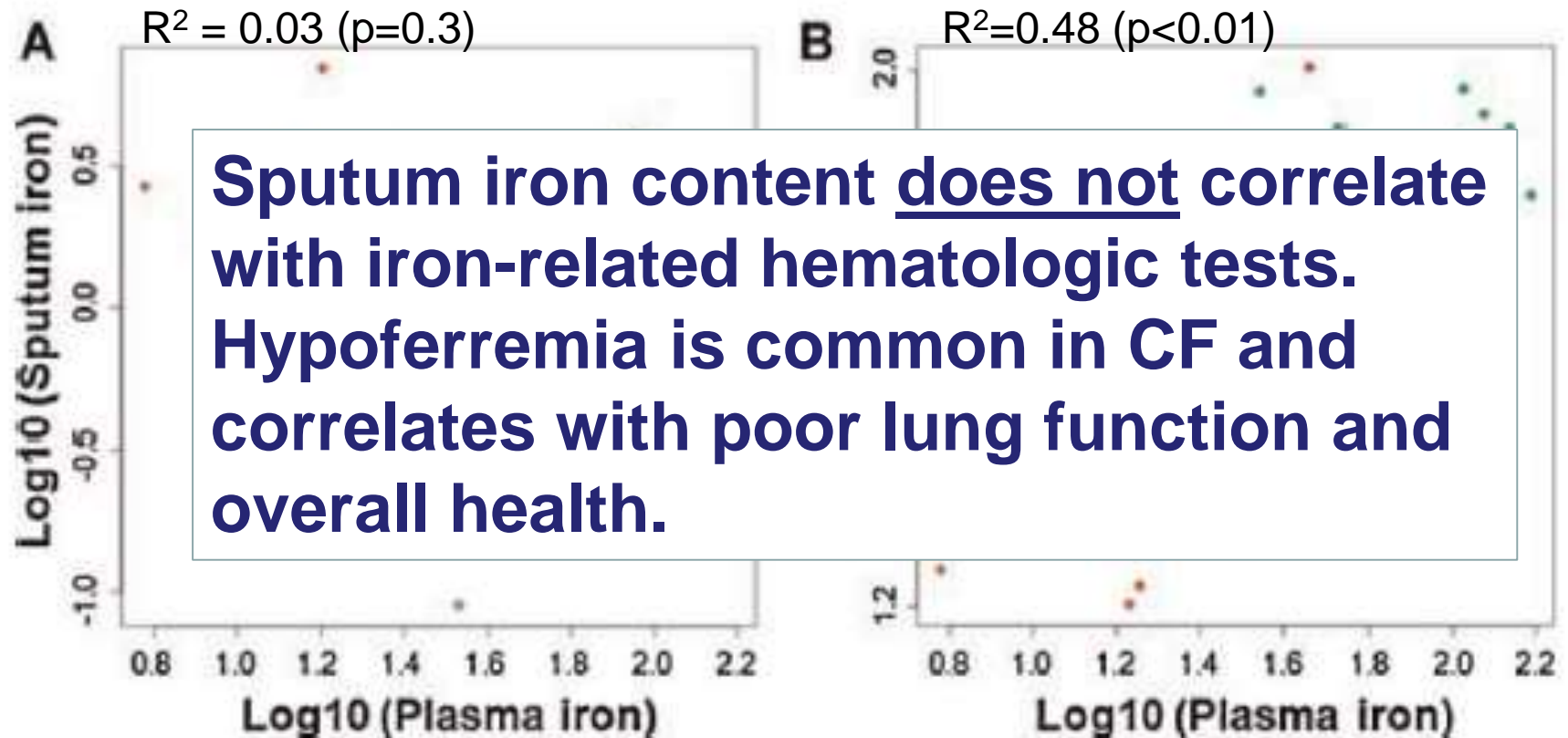
Green=stable patients.



## Iron and CF-Related Anemia: Expanding Clinical and Biochemical Relationships

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### Cross-sectional study- 39 CF patients



**Sputum iron content does not correlate with iron-related hematologic tests. Hypoferremia is common in CF and correlates with poor lung function and overall health.**

**Red**= patients with worsened clinical features .

**Green**=stable patients.



Original Article



# Iron supplementation does not worsen respiratory health or alter the sputum microbiome in cystic fibrosis

Alex H. Gifford <sup>a,\*</sup>, Diana M. Alexandru <sup>b</sup>, Zhigang Li <sup>c</sup>, Dana B. Dorman <sup>a</sup>, Lisa A. Moulton <sup>a</sup>, Katherine E. Price <sup>d</sup>, Thomas H. Hampton <sup>d</sup>, Mitchell L. Sogin <sup>e</sup>, Jonathan B. Zuckerman <sup>b</sup>, H. Worth Parker <sup>a</sup>, Bruce A. Stanton <sup>d</sup>, George A. O'Toole <sup>d</sup>

1) Does it increase sputum iron?

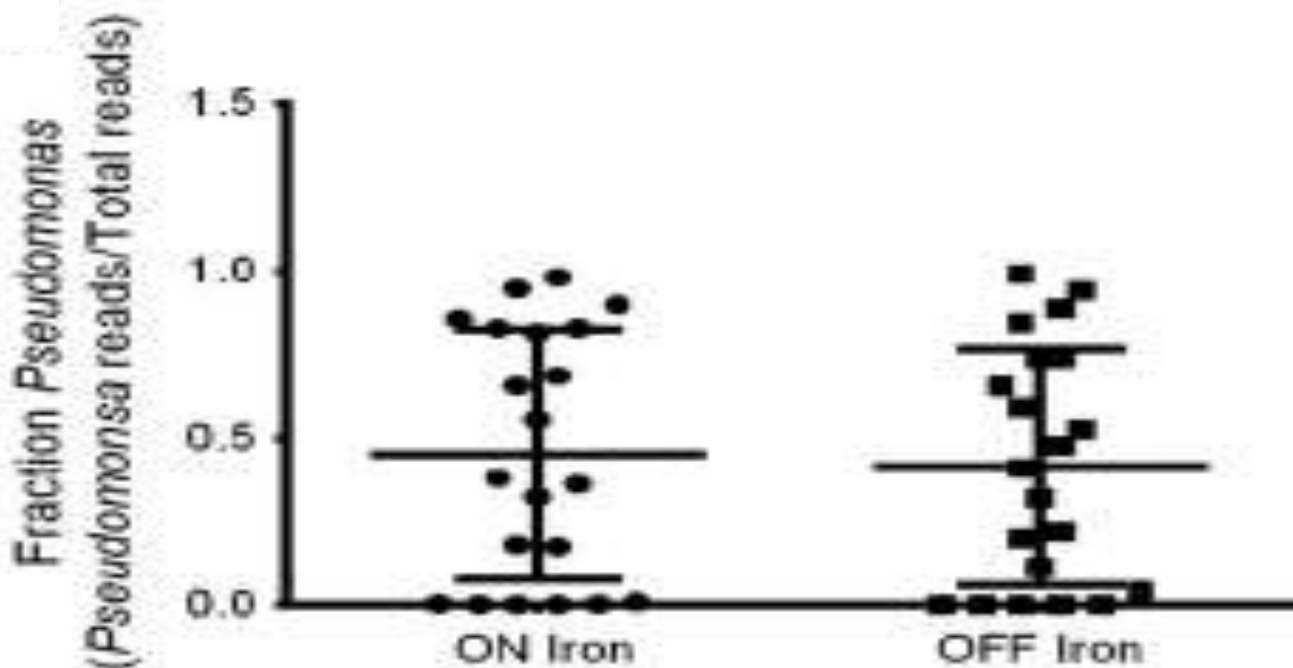
2) Does it alter bacterial communities?

3) Compared to placebo, does it increase the frequency of CF pulmonary exacerbation ?

# Randomized, double-blind, placebo-controlled, crossover trial



- ✚ 22 adults with CF + ID anemia.
- ✚ TSAT  $\leq 21\%$  and Hb  $< 15.5$  g/dl/13.6 g/dl.
- ✚  $\geq 1$  PA-positive sputum culture
- ✚ Ferrous sulfate 325 mg daily for 6 weeks

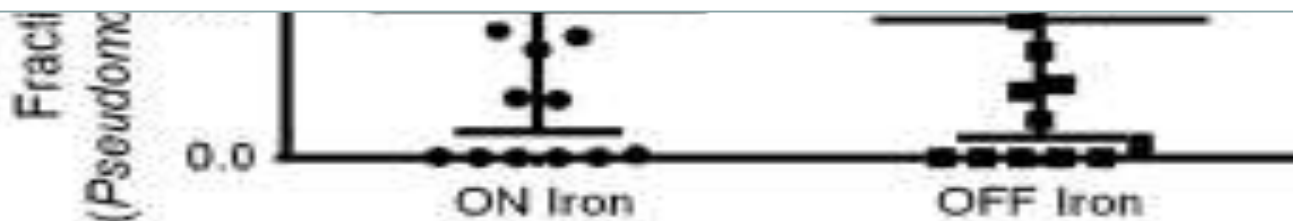


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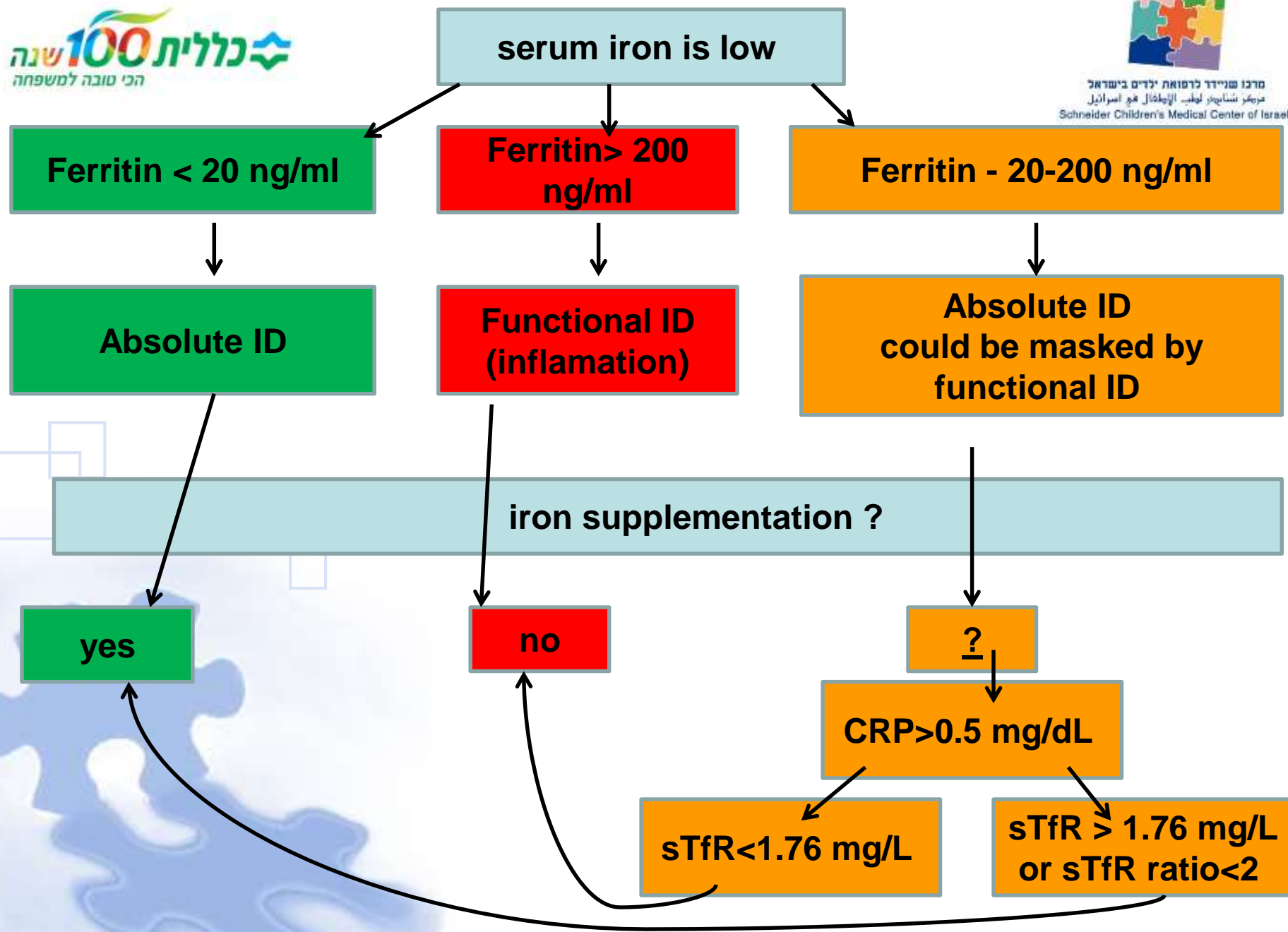
There were no evidence that 325 mg of ferrous sulfate taken daily increased sputum iron, increased the relative abundance of *PA* or other CF pathogens, or hastened CFPE onset.



Letter to the Editor

Accurate assessment of systemic iron status in cystic fibrosis will avoid the hazards of inappropriate iron supplementation

- ✚ Traditional measures of iron status in CF -high false positive rates (up to 75%) and misses some cases of ID.
- ✚ The best test is sTfR (soluble transferrin receptor) to log ferritin ratio (sTfR ratio).
- ✚ In “true” iron deficiency (ferritin<12 mg/l or sTfR ratio<2), we have not observed increased systemic inflammation.
- ✚ Iron infusions should be administered towards the end of an antibiotic course and with continued antibiotic cover and close patient monitoring.



# To treat or not to treat with Iron supplements?



## CF nutrition guidelines

- ✚ “In cases of ID: resolve inflammation & treat with iron if ID persists.”

Turck . ESPEN-ESPGHAN-ECFS guidelines on nutrition care for infants, children, and adults with CF. Clin Nutr, 35 (2016) 557-77.

- ✚ “Until further evidence is available, iron status in CF should be assessed as per guidelines for the general population.

**When indicated, an iron supplement should be prescribed for adults and children chronically colonized with *PA*”**

Van der Haak. Nutrition guidelines for CF in Australia and New Zealand (2017).



## Summary



- ✚ **Anemia & ID in CF is associated with low FEV1, and may affect lifestyle.**
- ✚ **Iron supplementation is not contraindicated for people with CF chronically colonized with *PA*.**
- ✚ **Proper diagnosis and testing appropriate measures will lead to proper care and improve life quality.**

# גורמה רבה על ההקשר!!!

