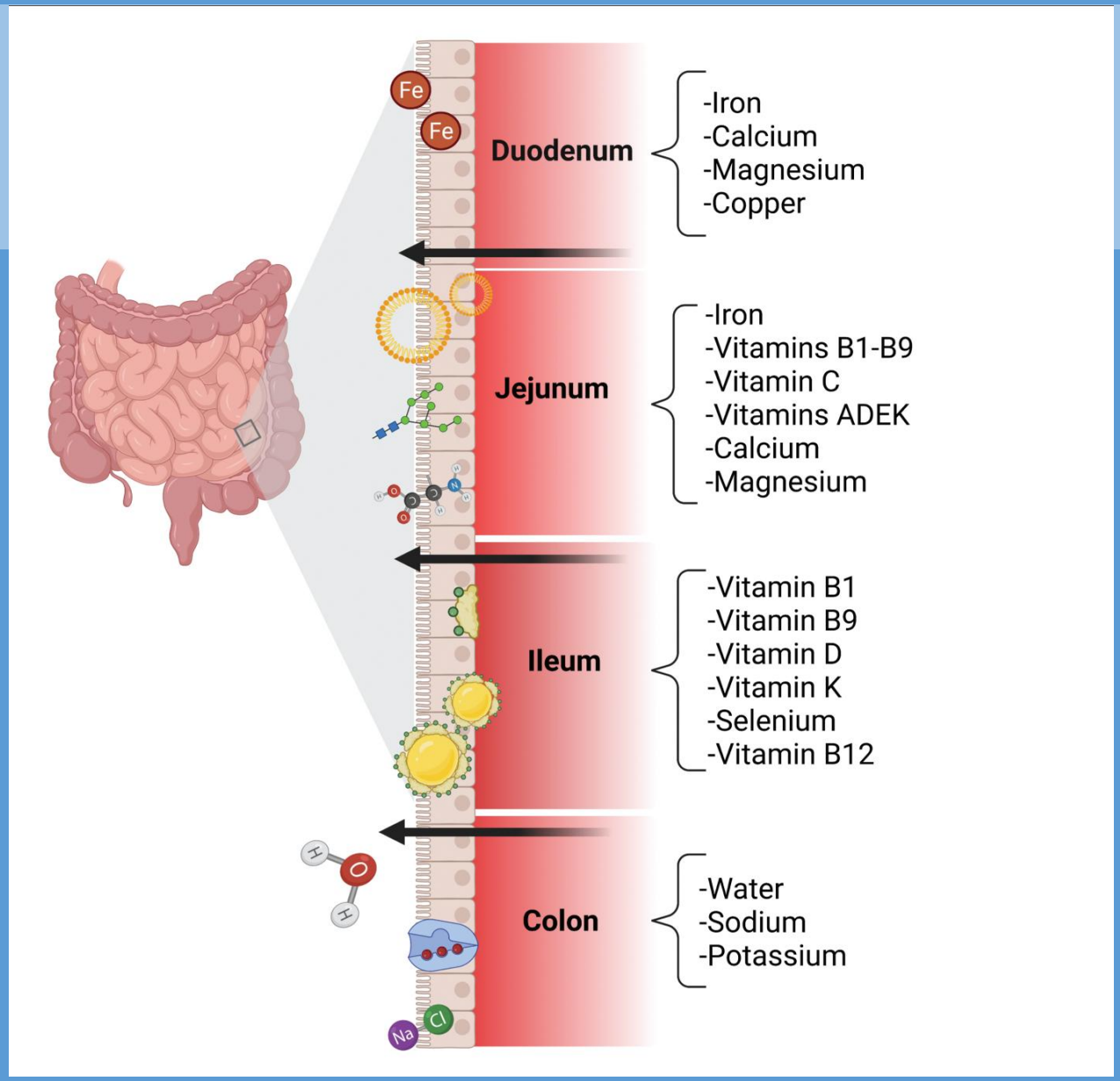
Practical Recommendations on Micronutrient Deficiencies in Gastrointestinal Diseases

- Almost all micronutrients being absorbed in gastrointestinal tract
- Gastrointestinal disorders are at highest risk of having multiple nutritional deficiencies including micronutrient deficiencies
- can be prevented or treated by optimal medical nutrition therapy,
- limited specific knowledge about micronutrients remains among clinicians


Fe
Fe
Duodenum
-Iron
-Calcium
-Magnesium
-Copper
Jejunum
-Iron
-Vitamins B1-B9
-Vitamin C
-Vitamins ADEK
-Calcium
-Magnesium
Ileum
-Vitamin B1
-Vitamin B9
-Vitamin D
-Vitamin K
-Selenium
-Vitamin B12
H
O
H
Colon
-Water
-Sodium
-Potassium
Na
Cl

Physiologic and Pathophysiologic Factors Affecting Micronutrient Requirements

dietary requirements of micronutrients are affected by number of physiological and pathological factors

- bioavailability of given micronutrient
- Amount
- Age and gender
- disease or drug that may interfere metabolism of the given micronutrient

Elderly

- Aging have specific impact on requirements of micronutrients :
- Reduced energy requirements, food intake, absorption, metabolism and utilization and that can cause deficiency of certain micronutrients.
- Atrophic gastritis, is highly prevalent in elderly population and this can lead to impaired absorption of protein bound vitamin B12.
- greater requirements are set for Vitamin B6, Calcium and Vitamin D3
- decreased absorption of calcium, osteoporosis in elderly.
- Deficiency of Vitamin D3 has been found to have association with multiple diseases like hypertension, dyslipidaemia, insulin resistance, obesity, diabetes, metabolic syndrome Alzheime certain cancers

All patients with GI diseases should be identified with potential micronutrient deficiencies and screen

- Assessment of malnutrition and treatment is important for positive clinical outcome and to reduce costs.
- Patients may have preexisting malnutrition
- Anemia and micronutrient deficiencies should be checked by blood tests in patients with GI disorder

Clinical Scenario		Micronutrients Potentially Affected	Supplementation
Disease characteristics	Active diarrhea or high-output ileostomy or jejunostomy	Zinc Magnesium Electrolytes	Close monitoring of electrolytes (sodium, potassium) and supplementation as needed. Can consider empiric zinc and magnesium supplementation for a short course (unclear safe duration). If ongoing symptoms, check urine magnesium level.
	Draining fistula	Vitamin A Vitamin C Zinc Magnesium	Can consider empiric supplementation (unclear safe duration). Zinc: need to be cautious about resultant copper/iron deficiency. Consider empiric supplementation with ongoing symptoms.
	Recent surgery or impaired wound healing	Vitamin A Vitamin C Zinc	Can consider empiric supplementation for a short course (<10 d).
	Steatorrhea/malabsorption	Vitamins ADEK	Multivitamin; reversing etiology of steatorrhea.
	History of an ileal resection	Vitamin B1 Vitamin B9 Vitamin B12	B complex vitamin + vitamin B12 (IM or sublingual) lifelong.
	Low-residue diet	Vitamin C	Vitamin C: 250-500 mg/d until diet improves.
	Gluten-free diet	B vitamins Vitamin D Zinc Iron Folate	B complex vitamin or multivitamin.
	TPN use	Selenium Chromium Copper Manganese	Supplementation with TPN.
Medication use	Methotrexate	Vitamin B9 (folate)	Folate 1 mg/d.
	Sulfasalazine	Vitamin B9 (folate)	Folate 1 mg/d.
	Corticosteroids	Vitamins A	Can consider supplementation with prolonged corticosteroid use based on nutri-

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	Sulfasalazine	Vitamin B9 (folate)	Folate 1 mg/d.
	Corticosteroids	Vitamins A Vitamin D Vitamin B6 Calcium	Can consider supplementation with prolonged corticosteroid use based on nutrient levels.
	Isoniazid	Vitamin B6	B complex vitamin or pyridoxine 50-100 mg/d.
	Cholestyramine	Vitamins ADEK	Avoiding cholestyramine dosing with food and multivitamin.
Comorbidities	Anemia	Iron Vitamin B12 Vitamin B9	Determination of cause of anemia. Iron-deficiency anemia guidelines with specific iron supplementation recommendations.
	Osteoporosis	Vitamin D Calcium Vitamin K Magnesium	Calcium: 1000-1500 mg/d with: Vitamin D: 1000 IU/d[73] Regular interval DEXA scans
	Neurologic symptoms	Vitamin B12 Vitamin E	Supplementation based on micronutrient testing.
	Cardiovascular disease	Selenium	Supplementation based on micronutrient testing.
General well-being in IBD		Calcium Vitamin D Iron	Calcium: <1000 mg/d (in addition to a calcium-rich diet) with 1000-IU/d vitamin D. Routine iron screening? (controversial)

All Micronutrients will be included in adequate amounts as soon as medical nutrition therapy is initiated in the patient. Additional supplementation of specific micronutrient will be provided only in the settings of documented deficiencies

- Micronutrient deficiencies may lead to serious nutritional consequences.
- Inadequate intake of micronutrients may initially be compensated by increased absorption from gut, decreased renal excretion or by decreased growth velocity in case of zinc.
- Short term effects like cognitive effects fatigue and impaired immune functions, whereas long term effects such as free radical damage to DNA/cell membrane may occur as non-specific functional effects leading to clinical disease or even death.
- Therefore adequate intake of micronutrients is crucial for public as well as individual health

If possible, provision of micronutrient supplements should be done orally or enterally considering the safety and effectiveness of same

- Clinician should not forget some patients especially out patients may be benefited from specific single or multiple oral micronutrient supplements.
- Ideal way to provide micronutrients is through gut as absorption of micronutrients by the gut can be adapted to the requirements
- During critical illness nutrient absorption can be compromised due to bowel ischemia, edema or ileus, yet even in haemodynamically unstable patients hypo caloric enteral feeding have been found to be unaffected
- levels can be achieved more confidently with the intravenous administration of micronutrient supplementation

If patient is on standard, balanced and complete formula feeds, with provision of formula as a soul source of nutrition providing 2000kcal/day, there is no requirement of additional micronutrient supplementation

- if it is providing 1500 kcal, therefore those who are on complete nutritionally balanced formula feeds may not require supplementation of micronutrients.
- Minimum intake suggested for an individual with complete formula feeding is kept 2000kcal/day, which is higher than the energy requirements of normal population to address increase requirements of an individual on enteral feeding.

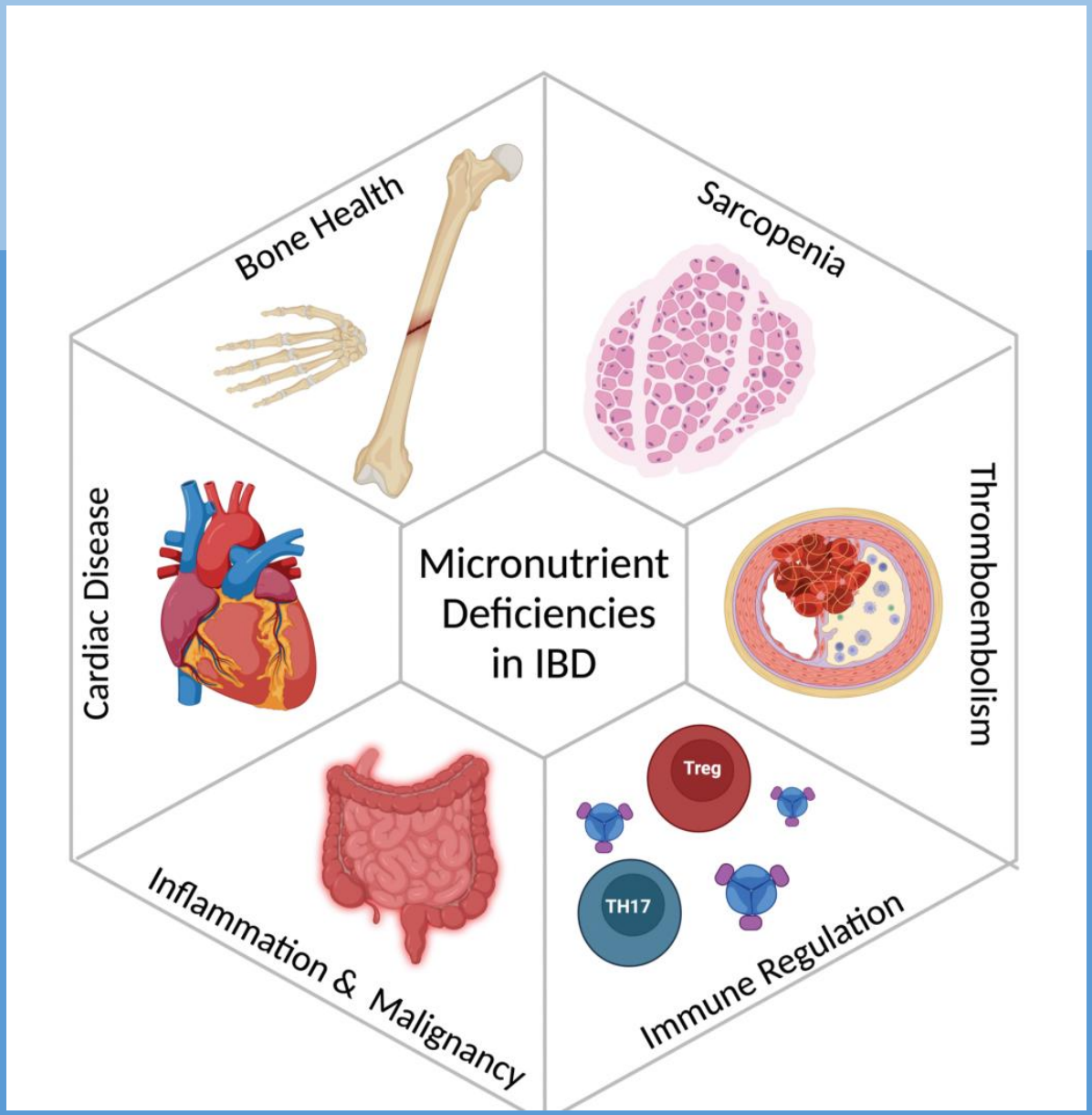
Disease specific recommendations for major Gastrointestinal Diseases

Monitoring nutritional status

- Screen! Up to 30% of ambulatory patients are malnourished
- Refer to RD → eatright.org, iffgd.org, local hospital
- Anthropometric assessment:
  - height, weight, %wt loss, BMI, growth curves
- Diet history-Food and symptom diary
- Activity level (involvement in sports)
- Medications- including vitamins, minerals and herbal supplements
- Nutritional Labs:
  - Annually: Iron, B6, vitamin D, B12, zinc, CBC, Albumin
  - Small bowel resection/disease: vitamin A/E, copper, selenium, folic acid, 24 hour urinary oxalate

Inflammatory Bowel diseases

- Being at higher risk of malnutrition including micronutrient deficiency, regular assessment and optimal correction of micronutrient deficiencies in IBD patients should be done.
- Routine monitoring (at least annually) is advised in well-nourished IBD patients too, even during remission period


Bone Health
Sarcopenia
Cardiac Disease
Micronutrient Deficiencies in IBD
Thromboembolism
Inflammation & Malignancy
Treg
TH17
Immune Regulation

- Malnutrition is highly prevalent in IBD patients and CD patients have higher occurrences (25%-69%) of deficiencies as compared to UC patients (1%-32%) as

- The mechanism of malnutrition in IBD patients are multifactorial significantly reduced intake ,increased requirements, malabsorption, increased losses ,consequences of medical and surgical treatment modalities

- A Daily multivitamin supplement may be helpful
- Iron, Zinc and Vitamin D deficiencies should be anticipated over longer period requiring specific correction therapy

- All IBD patients require iron supplements if found anemic.
- Oral iron should be considered first in mild anemia,inactive IBD and patient has no oral iron intolerance, but in those who are intolerant to oral iron supplements
- Active disease, serum hemoglobin level< 10gm/dl and who require erythropoiesis stimulating agents Intravenous iron should be considered as a first line of treatment.
- Pregnant IBD patients should be regularly monitored for iron and folate deficiency and supplemented accordingly

- Patients most frequently have anemia as manifestation of IBD other than intestinal symptoms.
- Anemia is prevalent in 6%-74% patients due to both iron deficiency as well as GI blood loss.
- B12 and folate deficiency and certain medications in IBD can also cause anemia, especially in UC as compared to CD

- Patients with active IBD, on treatment with Steroids should be monitored for calcium and Vitamin D deficiency and adequate supplementations to correct deficiency should be offered to prevent bone loss.

- E Resection of More than 20 cm with or without ileo cecal valve, distal ileum in CD patients, warrants vitamin B12 administration

Liver disease

Statement	Quality of Evidence/Strength of recommendation	Key Supporting Evidence
1. Suggest initiating early oral or enteral nutrition in hospitalized patients with cirrhosis	Low/Conditional	Three RCTs and 2 cohort studies[2-6] showed that starting oral/enteral feeds within 48 h increased calorie/protein delivery, shortened hospital/ICU stay, and reduced in-hospital mortality by ≈30%
2. Suggest implementation of nutritional supplementation therapy in patients with cirrhosis or alcohol-associated hepatitis	Very Low/Conditional	In AH, daily 1-month adequate caloric intake in VA trials correlated with 6-month survival; EN improved bilirubin, antipyrine clearance, and reduced 1-year mortality vs prednisone; intake <21.5 kcal/kg/day or <77.6 g protein/day predicted worse outcomes[7-9]
3. Suggest use of natural vitamin E (800 IU/day) in patients with MASH without cirrhosis	Low/Conditional	PIVENS (adults) and TONIC (children) RCTs showed 800 IU/day d-α-tocopherol for 96 wk improved steatosis, ballooning, and inflammation in 43%-58 % vs 19%-28% on placebo, with ALT normalization in >50%[10-12]
4. Suggest intake of ≥2 cups of coffee/day in chronic liver	Low/Conditional	Large prospective cohorts (>200,000 subjects) demonstrated dose-responsive 25%-40% reductions

4. Suggest intake of ≥2 cups of coffee/day in chronic liver disease to reduce fibrosis risk progression and HCC development	Low/Conditional	Large prospective cohorts (>200,000 subjects) demonstrated dose-responsive 25%-40% reductions in advanced fibrosis and 50% lower HCC incidence among drinkers of ≥2 cups/day, independent of alcohol and obesity[13-15]
5. No recommendation for or against strict sodium restriction in patients with cirrhosis and ascites managed with diuretic therapies	Insufficient	Two small RCTs (≤60 patients) comparing 2g vs unrestricted sodium showed inconsistent effects on ascites control, hyponatremia, and QoL; both with high bias risk[16, 17]
6. Recommend against protein restriction in decompensated cirrhosis with HE	Very Low/Conditional	Four crossover studies showed ≤0.6 g/kg protein worsened nitrogen balance and muscle loss without HE improvement; reintroduction of 1.2 g/kg improved cognition[18,19]
7. Suggest vegetarian protein sources in cirrhosis with HE when supplementation is needed	Very Low/Conditional	Plant-based protein lowers ammonia via higher arginine/fiber content. Four studies have shown clinical improvement with vegetarian protein. A RCT (120 patients) found vegetable protein improved minimal HE (71% vs 23%) and reduced HE risk (10%

		vs 22%)[20,21]
8. Recommend adding branched-chain amino acids to standard therapy in patients with cirrhosis and HE </td?	Moderate/Strong	BCAA deficiency impairs ammonia detoxification via muscle. BCAA supplementation improves muscle mass, reduces ammonia, and enhances glutamine synthesis. A Cochrane meta-analysis of 16 RCTs (n=827) found oral BCAAs improved HE (RR 0.67); after excluding lactulose/neomycin controls, reduced mortality (RR 0.76); IV BCAAs showed no benefit[22,23]
9. Recommend incorporating a late-evening snack in cirrhosis to improve BMI, lean mass, and reduce ascites/HE	Moderate/Strong	Outpatient nutrition therapy improves survival and reduces hospitalizations in cirrhosis. Late evening snacks (≈710 kcal) reduce protein catabolism and improve nitrogen balance, with meta-analyses showing improved liver function and fewer complications (ascites, HE); effects on muscle mass and survival remain inconsistent[24, 25] >

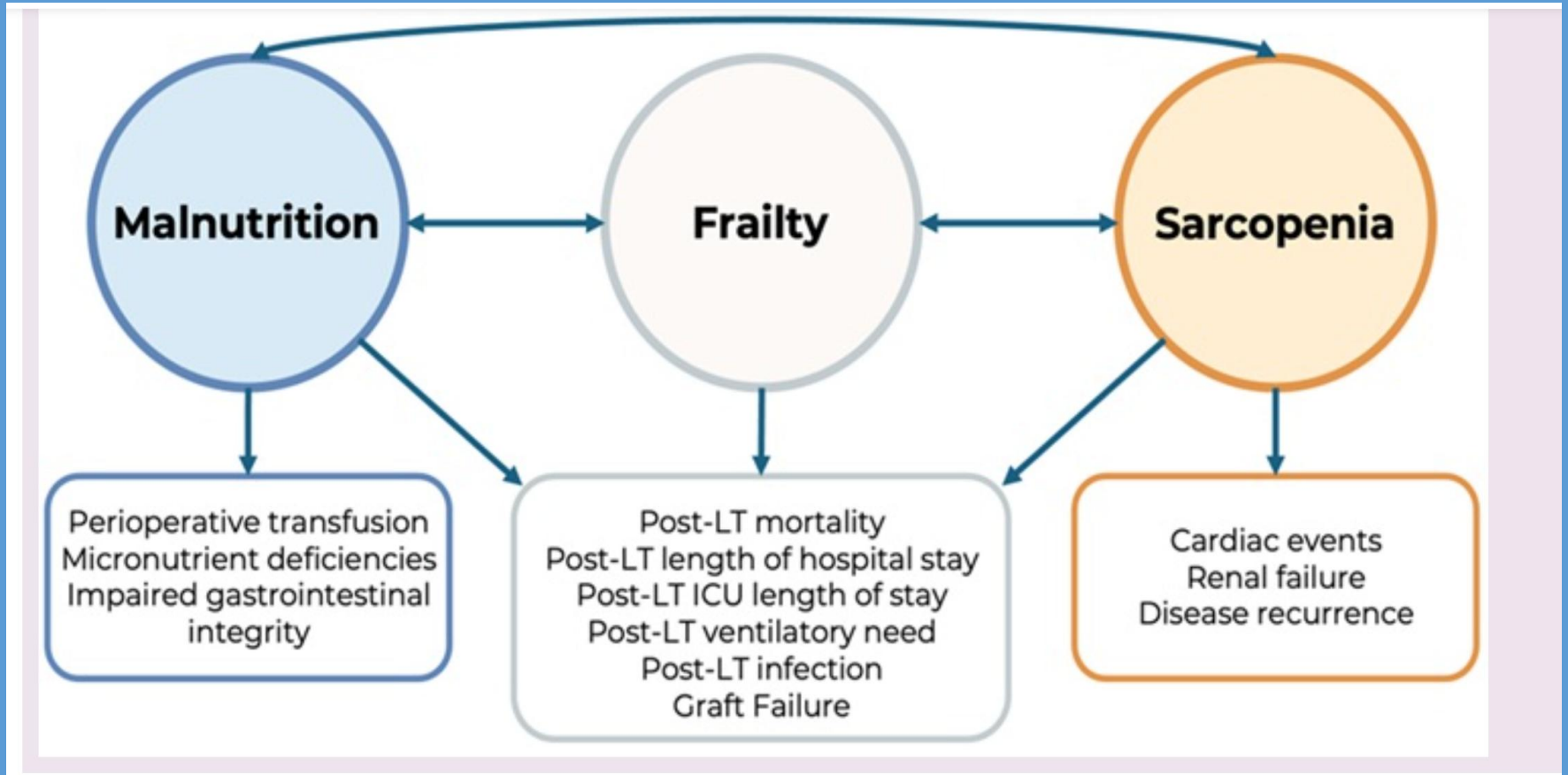


Figure 1. The impact of malnutrition, frailty, and sarcopenia in end-stage liver disease.

Liver disease

- In patients with severe Alcoholic Steatohepatitis micronutrient deficiencies should be foreseen and replaced, especially vitamin B, zinc and Vitamin D.
- In the absence of expensive laboratory measurements for deficiencies,empirical oral micronutrient supplementation of multivitamin and Zinc may be reasonable.
- Routine supplementation of Thiamin is advised to avoid Wernicke's encephalopathy and korsakoff psychosis

- Vitamin E supplementation with 800 IU/day in an adult non diabetic histopathologically confirmed NASH patient is beneficial to improve liver enzymes levels as well as liver histology.

- Vitamin C deficiency has been linked with NASH/NAFALD, yet supplementation with vitamin C lack adequate data to be recommended for its antioxidant properties to treat NASH/NAFALD.

- In obese NASH patients undergoing bariatric surgeries, preoperative vitamin and mineral testing as well as post operatively at regular interval as surgical weight loss patients are at high risk of micronutrient deficiencies either due to primary or secondary malabsorption or inadequate dietary intake

- A In patients with chronic Cholestatic liver diseases, deficiencies of fat soluble vitamins are expected.

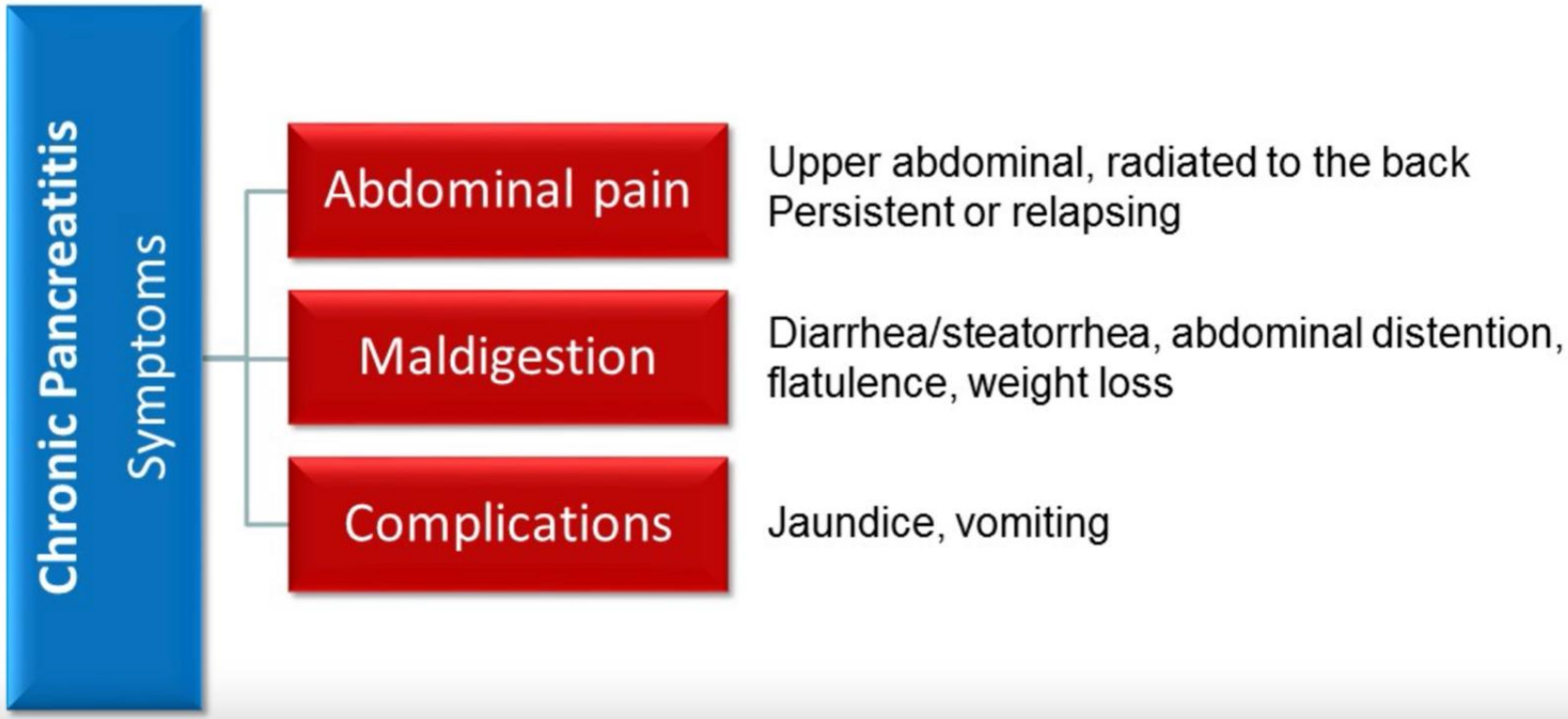
- Vitamin D, at least 800 IU/day should be considered to prevent bone loss.

- Patient with PBC should have their vitamin A levels checked, but in patients having vitamin A deficiency only those who have impaired dark adaptation should be advised vitamin A supplements in water soluble form along with zinc to increase absorption.

- In patients with cirrhosis micronutrient supplementations e. g. Water soluble vitamins particularly thiamine, fat soluble vitamins especially vitamin D and Trace elements mainly Zinc and Selenium should be treated in case of documented deficiency or when suspected clinically

- Among patients on wait list for liver transplant, with decompensated cirrhosis, micronutrient deficiencies particularly vitamin D deficiency is highly prevalent.
- Pre-transplant minimum 800 IU /day vitamin D should be advised to improve post-transplant outcome, while post-transplant at least 400 IU/day vitamin D is recommended.(

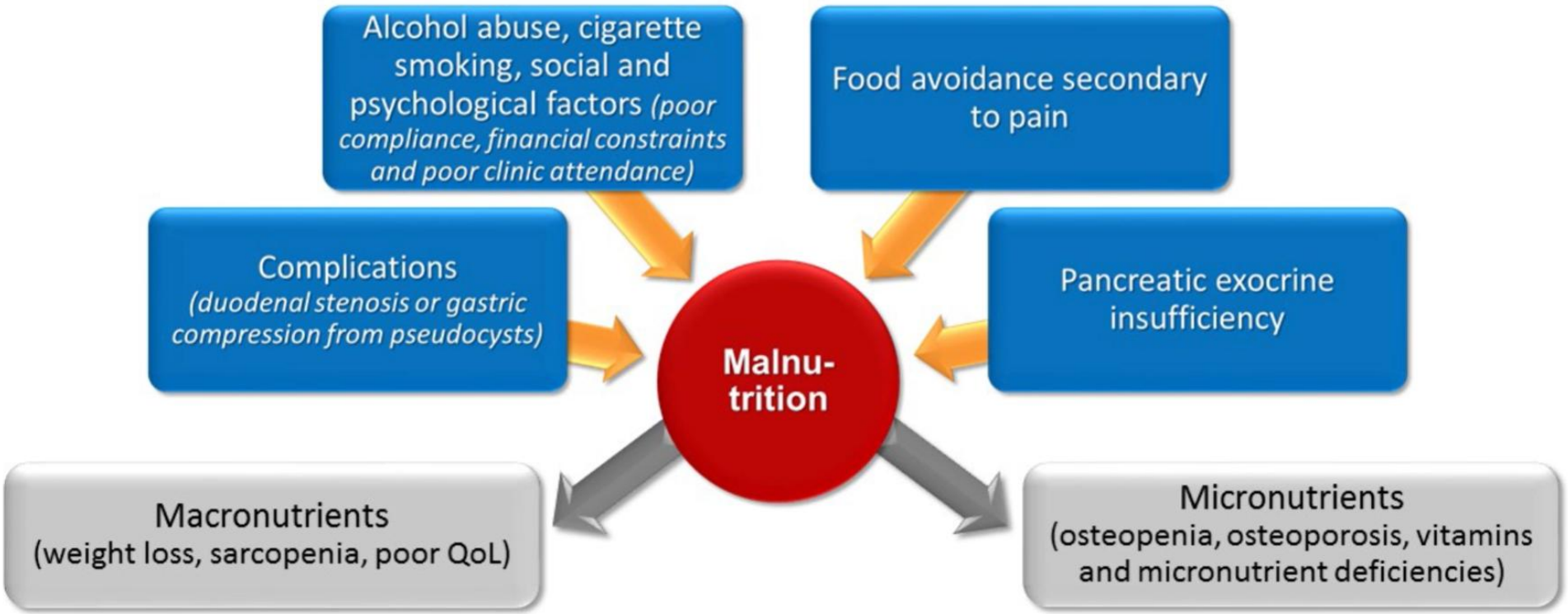
Chronic Pancreatitis Symptoms



Malnutrition in chronic pancreatitis

Author	Year	Abnormal nutritional parameters
Kalvaria	1986	Fat soluble vitamins
Twersky	1989	Fat soluble vitamins Calcium, zinc, selenium
Marotta	1994	Fat soluble vitamins Retinol binding protein
Montalto	1994	Apolipoproteins
Hartmann	2007	Apolipoproteins
Schnitzler	2010	Magnesium
Sobral-Oliveira	2011	Total cholesterol, magnesium
Lindkvist, Dominguez-Munoz	2012	Hemoglobin, albumin, prealbumin, retinol binding protein, magnesium
Sikkens	2013	Fat-soluble vitamins

Malnutrition in chronic pancreatitis is multifactorial



Pancreatic Exocrine Insufficiency

Clinical consequences

- Malnutrition
  - Low circulating levels of esential aminoacids, fatty acids, micronutrients and fat soluble vitamins
  - Low levels of HD-lipoprotein C, apolipoprotein A-I and lipoprotein A

↓

High morbi-mortality

Malnutrition-related complications

Pancreatic enzyme supplements
What is the correct dose?



Oral pancreatic enzymes should be given at a dose able to avoid symptoms and to **normalize digestion** !!

Minimum dose:
40-50,000 USP/meal
20-25,000 USP/snack

- Micronutrient deficiencies should be anticipated in chronic pancreatitis patients.
- Management and adequate correction of micronutrient deficiencies especially fat-soluble vitamins and minerals are advised to prevent problems arising due to these deficiencies.
- Appropriate diet recommendations and pancreatic enzyme supplementations are equally important.

Table 3. Common deficiencies of micronutrients found in CP. [49]

Micronutrient	Mechanism
VitaminA, D, E, K	Exocrine insufficiency in lipid malabsorption (E>A, D, K) Due to Alcohol Anorexia
Vitamin B1, B2, B6, B12	Due to alcohol R-binder inability impairing B12 absorption
Zinc	Due to alcohol, decreased pancreatic exocrine stores

Food containing minerals

Nutrient	Sources	RDA or AI (adults > 19 years)
Vitamin B1 (thiamine)	Whole grains, meat, fish	1.1-1.2 mg
Vitamin B2 (riboflavin)	Organ meats, eggs, milk	1.1-1.3 mg
Vitamin B3 (niacin)	Meat, salmon, leafy greens, beans	14-16 mg
Vitamin B5 (pantothenic acid)	Organ meats, mushrooms, tuna, avocado	5 mg
Vitamin B6 (pyroxidine)	Fish, milk, carrots, potatoes	1.3-1.7 mg
Vitamin B7 (biotin)	Eggs, almonds, spinach, sweet potatoes	30 mcg
Vitamin B9 (folate)	Beef, liver, black-eyed peas, spinach, asparagus	400 mcg
Vitamin B12 (cobalamin)	Clams, fish, meat	2.4 mcg
Vitamin C (ascorbic acid)	Citrus fruits, bell peppers, Brussels sprouts	75-90 mg

Nutrient	Sources	RDA or AI (adults > 19 years)
Vitamin A	Retinol (liver, dairy, fish), cartenoids (sweet potatoes, carrots, spinach)	700-900 mcg
Vitamin D	Sunlight, fish oil, milk	15-20 mcg
Vitamin E	Sunflower seeds, wheat germ, almonds	15 mg
Vitamin K	Leafy greens, soybeans, pumpkin	90-120 mcg