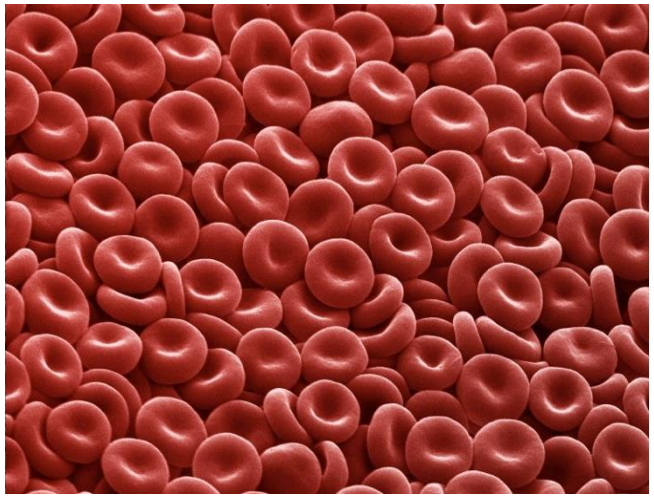

Von Flare bis Fatigue-

Was IBD-Nurses im Alltag wirklich Wissen müssen

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“Das neue Normal” für Patienten mit IBD

Viele Patienen mit IBD sehen ihre aktuelle Gesundheit als das **“neue normal”** aber sie fühlen sich häufig frustriert mit ihren Herausforderungen wie…[1-3]

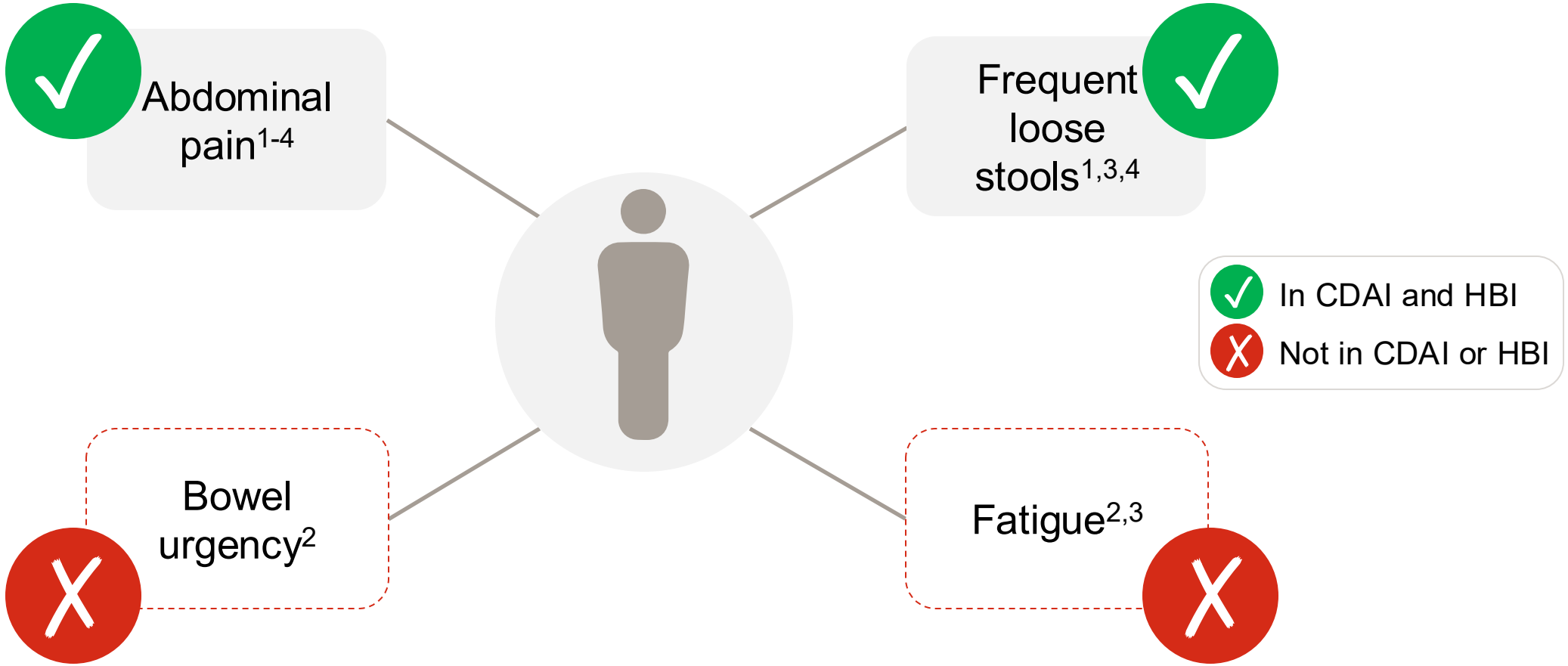
GI SYMPTOME	NICHT-GI SYMPTOME
• **Stuhldrang**	• **Fatigue**
• Bauchschmerzen	• Depression
• Durchfall	• Ängste
• …	

ABER: Patienten empfinden dass die HÄz **nicht interessiert** sind, diese Symptome anzugehen[2]

CD=Crohn’s Disease; HCP=Healthcare Professional; GI=Gastrointestinal.

1. Norton B, et al. *Patient Prefer Adherence*. 2012;6:509-520. 2. Keefer L, et al. *Gastroenterology*. 2022;162(5):1439-1451. 3. Kitchen H, et al. *Crohns Colitis 360*. 2020;2(2):otaa033.

Common Symptoms in Patients With IBD



CD=Crohn's Disease; CDAI=Crohn's Disease Activity Index; HBI=Harvey-Bradshaw Index.

1. Best R, et al. *Gastroenterology.* 1976;70(3):0:439-444. 2. Keefer L, et al. *Gastroenterology*. 2022;162(5):1439-1451. 3. Kemp K, et al. *J Crohns Colitis*. 2018;12(7):760-776. 4. Best WR. *Inflamm Bowel Dis*. 2006;12(4):304-310.

Up to 85% of Patients With CD Experience Fatigue

The proportion of patients with CD who experience fatigue ranges from…[1-8]

25%

to

85%

CD=Crohn's Disease.

1. D'Silva A, et al. *Clin Gastroenterol Hepatol*. 2022;20(5):995-1009.e7. 2. Chavarría C, et al. *J Crohns Colitis*. 2019;13(8):996-1002. 3. Frigstad SO, et al. *World J Gastroenterol*. 2018;24(29):3293-3301. 4. Hashash JG, et al. *J Clin Gastroenterol*. 2018;52(5):423-430. 5. Jelsness-Jørgensen LP, et al. *World J Gastroenterol*. 2012;18(5):445-452. 6. Villoria A, et al. *PLoS One*. 2017;12(7):e0181435. 7. Williet N, et al. *J Crohns Colitis*. 2017;11(2):165-174. 8. Bogale K, et al. *Sci Rep*. 2022;12(1):10577.

Pain and Fatigue are frequently observed at diagnosis of IBD

	CD (n=279)	UC (n=113)
Diarrhoea	89.5%	96.4%
Bloody stools	23.3%	89.3%
Pain	86.9%	81.3%
Fatigue	81.7%	40.2%
Weight loss	59.6%	38.4%
Arthralgia	29.2%	27.7%
Fever	24.7%	20.5%
Skin manifestations	14.2%	15.2%

Rath HC, et al. Med Klin (Munich) 1998;93:395-400

The Impact of Fatigue on Patients With CD[1-3]

Depression

Sexual impact

Hobbies

Socialising

FATIGUE

Work/ school

Anxiety

Family life

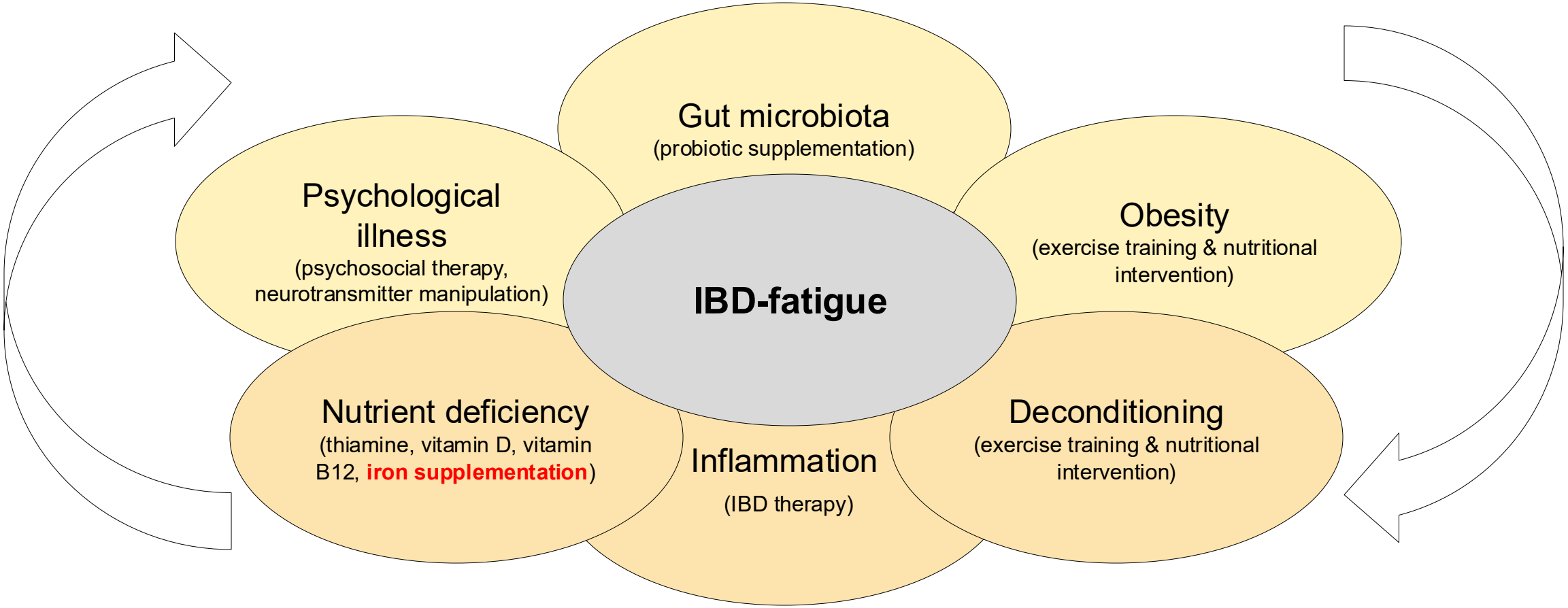
Housework

Stress

CD=Crohn's Disease.

1. Regueiro M, et al. *J Patient Rep Outcomes*. 2023;7(1):75. 2. Czuber-Dochan W, et al. *Aliment Pharmacol Ther.* 2013;37(5):505-516. 3. Rubin DT, et al. Presented at: *AIBD 2023.* Poster 03.

Modifiable factors associated with IBD-fatigue

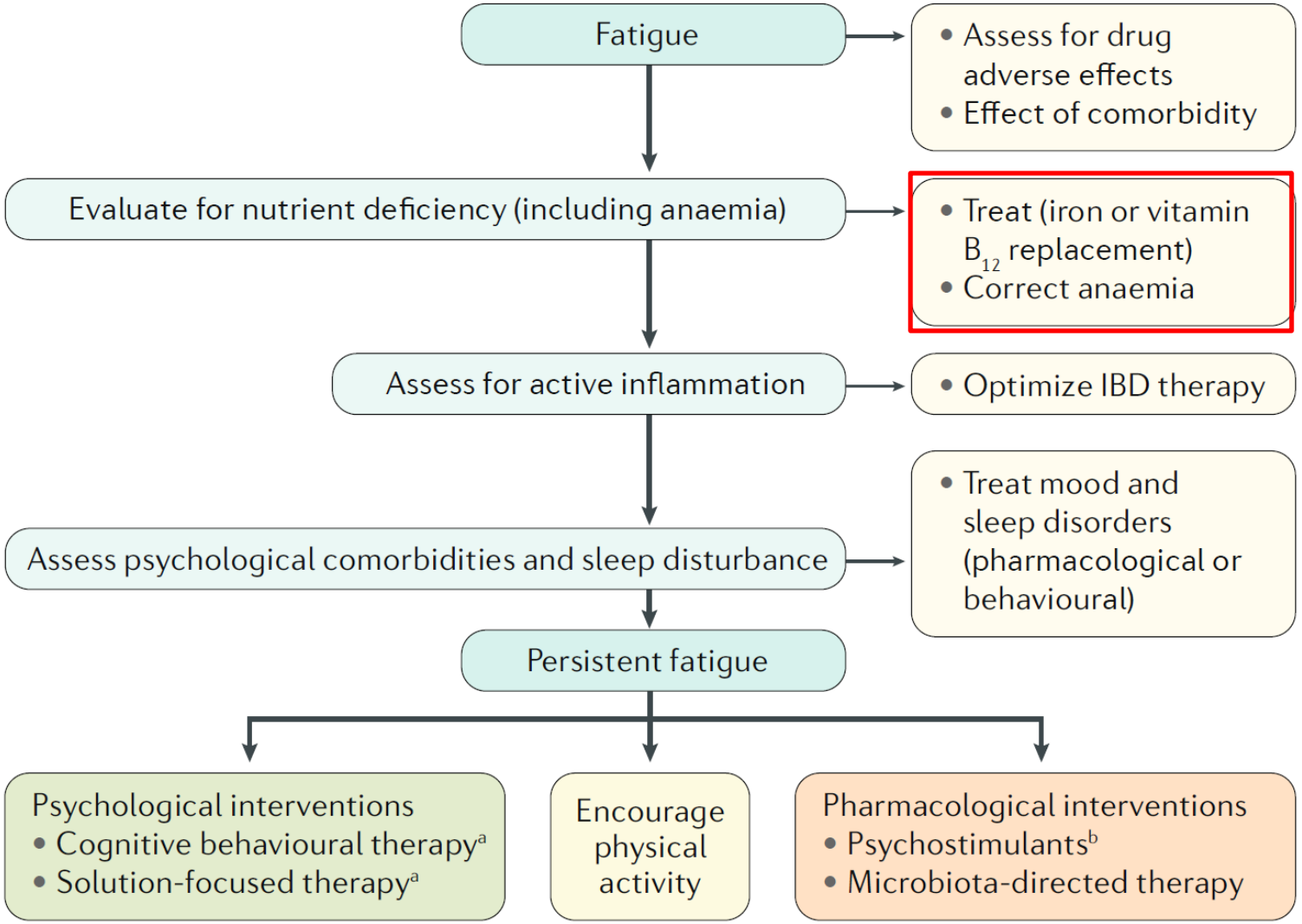


Adapted from McGing 2021 Figure 2

IBD=Inflammatory Bowel Disease

McGing et al. Aliment Pharmacol Ther 2021;54(4):368-387. doi: 10.1111/apt.16465.

Multidisciplinary management of IBD-fatigue



Proposed algorithm

- Owing to its complex, multifactorial pathophysiology, effective treatment of IBD-fatigue probably needs to be multidisciplinary
- Iron deficiency and anaemia should be evaluated at an early stage and corrected

[a]Greater than one study available in IBD
[b]No studies available in IBD

IBD=Inflammatory Bowel Disease

Figure 4 in Borren et al. Nat Rev Gastroenterol Hepatol 2019;16(4):247-259. doi: 10.1038/s41575-018-0091-9.

Assessment of Fatigue in CD

Validated questionnaires[1]

- Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue)[2,3]
- Fatigue Questionnaire (FQ)[4]
- Inflammatory Bowel Disease Fatigue (IBD-F)[5]
- Multidimensional Assessment Fatigue (MAF)[6]
- Multidimensional Fatigue Inventory (MFI)[7]

IBD=Inflammatory Bowel Disease.

1. Nocerino A, et al. *Adv Ther*. 2020;37(1):97-112. 2. Regueiro M, et al. *J Patient Rep Outcomes*. 2023;7(1):75. 3. Tinsley A, et al. *Aliment Pharmacol Ther*. 2011;34(11-12):1328-1336. 4. Chalder T, et al. *J Psychosom Res*. 1993;37(2):147-153. 5. Czuber-Dochan W, et al. *J Crohns Colitis*. 2014;8(11):1398-1406. 6. Belza BL, et al. *Nurs Res*. 1993;42(2):93-99. 7. Smets EM, et al. *J Psychosom Res*. 1995;39(3):315-325.

The Functional Assessment of Chronic Illness Therapy – Fatigue Scale (FACIT-Fatigue)

Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-Fatigue)

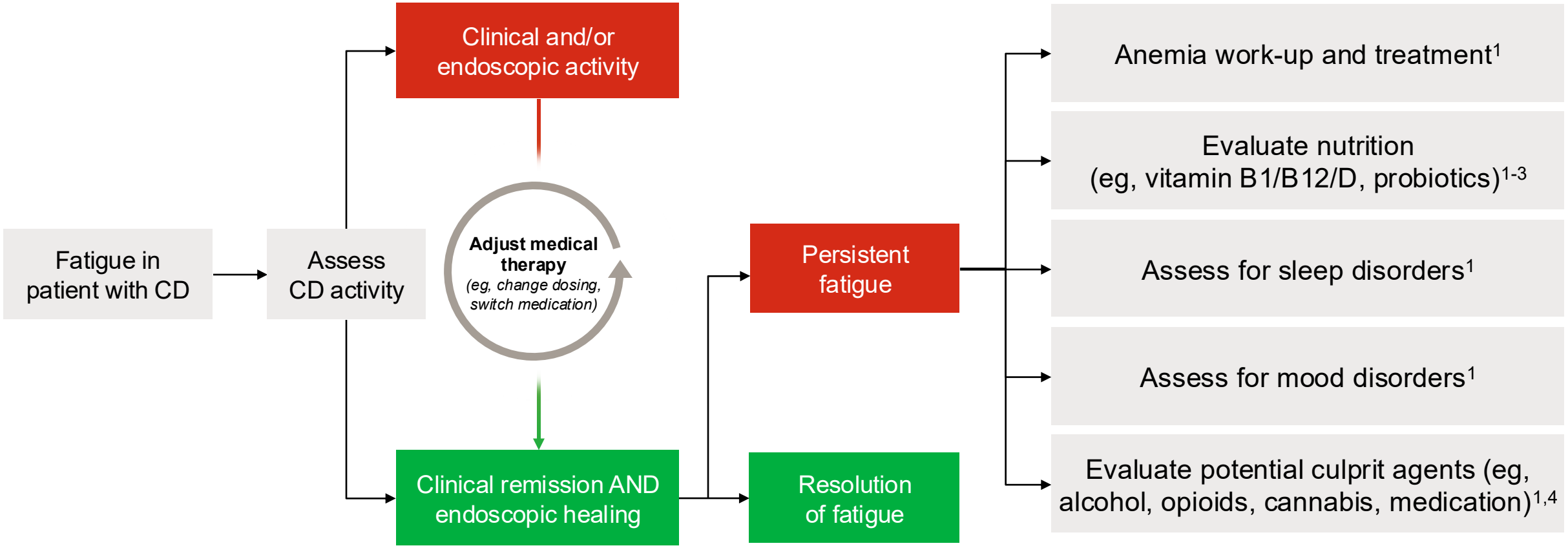
- FACIT-Fatigue is a reliable and validated tool, used in chronic illnesses, including CD[1]
- 13-items[1,2]
- Includes impact upon daily activities and function[1,2]

	Not at all	A little bit	Some-what	Quite a bit	Very much
I feel fatigued	0	1	2	3	4
I feel weak all over	0	1	2	3	4
I feel listless (“washed out”)	0	1	2	3	4
I feel tired	0	1	2	3	4
I have trouble starting things because I am tired	0	1	2	3	4
I have trouble finishing things because I am tired	0	1	2	3	4
I have energy	0	1	2	3	4
I am able to do my usual activities	0	1	2	3	4
I need to sleep during the day	0	1	2	3	4
I am too tired to eat	0	1	2	3	4
I need help doing my usual activities	0	1	2	3	4
I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
I have to limit my social activity because I am tired	0	1	2	3	4

CD=Crohn’s Disease.

1. https://www.facit.org/measures/FACIT-Fatigue (Accessed February 1, 2024).
2. https://www.facit.org/_files/ugd/626819_3f37469b87fc4f779aa9e31790c8c2f2.pdf (Accessed February 1, 2024).

Fatigue Management in CD[1]



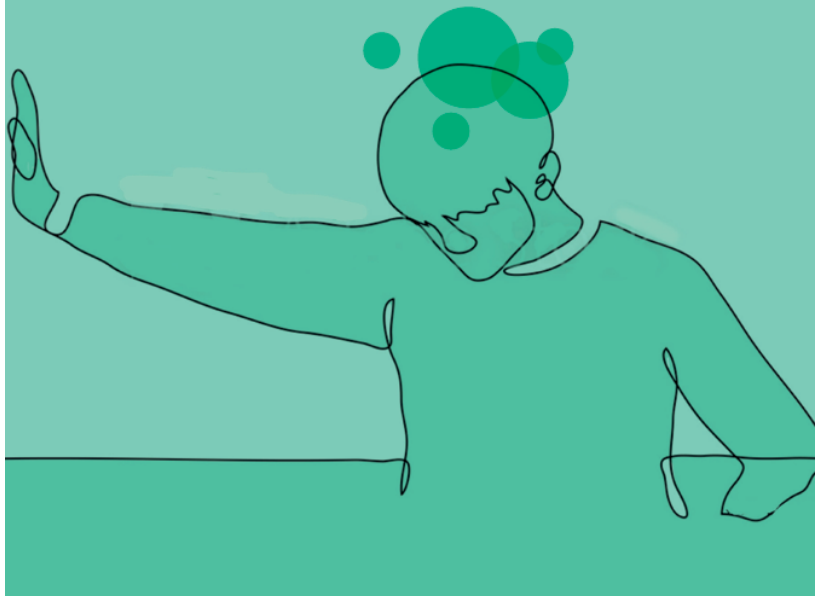
CD=Crohn's Disease.

1. Nocerino A, et al. *Adv Ther.* 2020;37(1):97-112. 2. Bager P, et al. A*liment Pharmacol Ther.* 2021;53(1):79-86. 3. Borren NZ, et al. *Clin Gastroenterol Hepatol.* 2021;19(3):519-527.e5.
4. Lamers CR, et al. *Inflamm Bowel Dis.* 2022;28(12):1791-1799.

Fatigue assessment Algorithm

In collaboration with:

PD Dr. med. Luc Biedermann
Dr. med. Sarah Lavina Florence Schiebler
Dr. med. Philipp Schreiner
Diana Studerus
Prof. Dr. med. Stephan Vavricka
PD Dr. med. Jonas Zeitz



Workaround possible by Gastroenterologists

1 Exclusion of other medical sources of fatigue

Among others, consider other inflammatory diseases as well as addison's disease, hyperthyreodism, sleep apnea, vasculitis, chronic infection, chronical heart and lung diseases, diabetes mellitus, tumor diseses multiple sclerosis, sarcoidosis, rheumatoid arthritis, collagenosis, psychiatric diseases etc.

2 Assess for disease activity

2.1 Assess Fatigue Activity: For Fatigue evaluation consider e.g. Fatigue Severity Scale (FSS)[38] cut off considered at 4 points.[38,40] Or a visual analog scale (VAS) known from pain assessment also, cut off considered at 4 points.[39,40]

2.2 Optimize IBD therapy: check e.g. for primary or secondary non-response and consider optimization and combination therapy.[42,43]

EIM: Chronic systemic inflammation has been linked to alterations in nervous system activity and initiation of distressing symptoms, such as fatigue.[53]

3 Drug Effect

Steroids: Long-term use can cause myopathy and fatigue.[34]

MTX: Folate deficiency is common in IBD patients and often linked to sulfasalazine and/or methotrexate (MTX) therapy.[55]

AZA and 6-MP: Anemia as a component of bone marrow suppression is associated with azathioprine (AZA) and 6-mercaptopurine (6-MP) use, especially in those with thiopurine S-methyltransferase (TPMT) deficiency or intermediate levels.[56]

anti-TNF: In CD Patients treated with Adalimumab for 56 weeks, increases in albumin, calcium, total protein, hemoglobin, hematocrit, and red blood cell counts were seen compared to placebo treated patients.[35]

Anti-Integrin: No data for effect of anti-integrin on fatigue. However, one study showed an improvement in sleep quality in IBD patients treated with Vedolizumab and anti-TNF.[59]

JAK: Although the mechanism is not fully understood, Upadacitinib, Tofacitinib and Baricitinib were able to reduce fatigue in patients with rheumatoid arthritis.[45,46]

IL12/23: Ustekinumab was associated to reduce fatigue in patients with psoriatic arthritis.[47]

Antidepressants and Narcotics: More commonly prescribed to patients with IBD than the general population, can be associated with lethargy and somnolence.[34]

Cannabis: No studies have evaluated the effect of cannabis or cannabis derivatives on fatigue among patients with IBD. Cannabis use, especially by young patients with IBD, is associated with depressive symptoms as well as a motivational syndrome, which may be interpreted as fatigue.[34]

Non-IBD Drugs, such as: neuroleptics, anxiolytics, (benzodiazepines), anti depressants (esp. betablockers), analgesics, muscle relaxants, antihistamines, alcohol, are known to have a negative effect on fatigue.[63,64,65]

4 Evaluation of Anemia

4.1 Hemoglobin and Hematocrit: Minimum hemoglobin and hematocrit levels used to define anemia in people living at sea level.[37]

Age or sex group	Hemoglobin		Hematocrit
	[g/dL]	[mmol/dL]	[%]
Children ½ to 5 years	11	6.83	33
Children 5-11 years	11.5	7.14	34
Children 12-13 years	12	7.45	36
Nonpregnant women	12	7.45	36
Pregnant women	11	6.83	33
Men	13	8.07	39

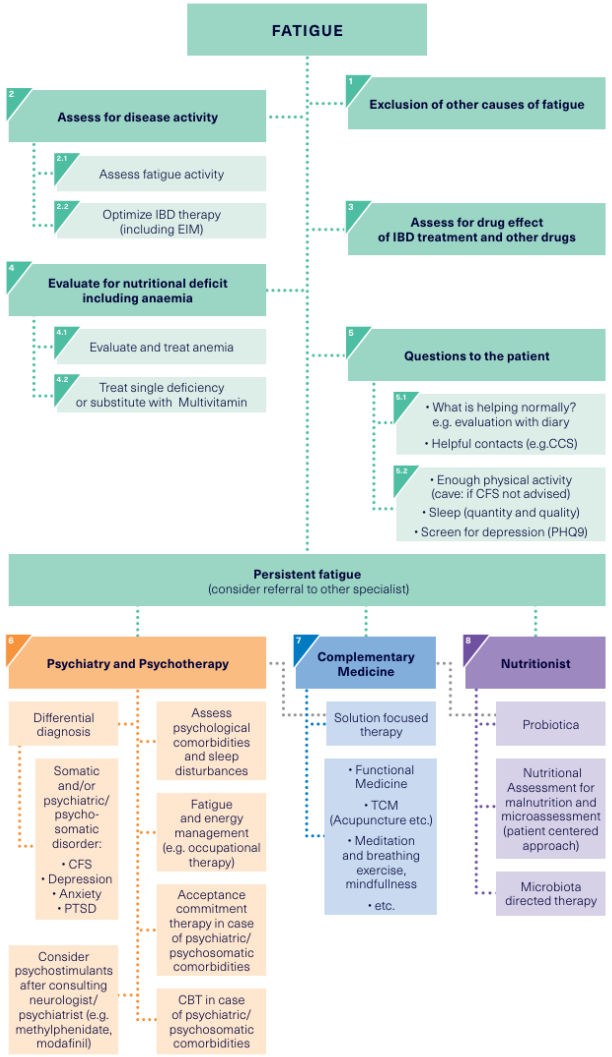
Ferritin: Normal value in nonanemic menstruating women with low ferritin assumed: Ferritin < 50 µg/l and Hemoglobin ≥12.0 g/dL.[48] However, whether iron deficiency without anemia improves fatigue and should be treated is debatable.[60,61,62] ECCO recommends treatment if ferritin <30 µg/liter in remission and if ferritin <100 µg/liter in active disease (elevated inflammatory values).[37]

Vitamin B12 and folate should be treated to avoid anemia:[37]
Vitamin B12: No effect on fatigue, normal value assumed at ≥ 150 pmol/l[12]
Folate (Vitamin B9). Normal value: >3 ng/mL[49] substitution considered: 1 mg/d.[34] However, no data on fatigue.

4.2 Evaluation of Nutritional Deficit

Vitamin B1 (Thiamine): No measurement required or suggested. Consider a 4 week empiric treatment with Thiamine: Scale adapted according to Bager et al.[44]

Body weight	Dosing female	Dosing male
<60 kg	600 mg	900 mg
60–70 kg	900 mg	1200 mg
71–80 kg	1200 mg	1500 mg
>81 kg	1500 mg	1800 mg



The follow-up study showed a greater improvement of fatigue in the SFT group (compared with control) after 3 and 6 months, but is not anymore present after 9 months. SFT has also a significant beneficial effect on the severity of fatigue and QoL, but is also diminishing during follow-up.[7]

Psychotherapy: A systematic research of studies of psychotherapy in IBD patients has shown, that it has a minimal effect on measures of anxiety, depression, QoL and disease progression but shows promise in reducing pain, fatigue, relapse rate and hospitalisation, and improving medication adherence.[85]

Review of management of fatigue in IBD patients: Non-pharmacological interventions, such as PST, SFT, CBT, psychoeducational intervention, exercise advise with omega-3 supplements, electro-acupuncture and AndoSan (a medicinal Agaricus blazei Murill mushroom extract) are helpful in managing IBD-fatigue.[81]

Approach for fatigue by Complementary Medicine / Functional Medicine:

This approach focuses not on individual symptoms but on holistic, personalized nad integrative medicine. Functional medicine complements the classic academic medicine. Anamnesis include (epi-) genetics, family history, triggering events and individual lifestyle and discussions on their emotional significance.

Treatment options that follow may include:

- Nutrition
- Gastrointestinal approaches incl. microbiome
- Meditation / breathing exercises
- Medical lab tests
- Acupuncture/massage
- Talking therapy
- Phyto-pharmacy and others

Acupuncture and moxibustion: Combined acupuncture and moxibustion as well as single acupuncture and single moxibustion have a better effect on fatigue compared to other Chinese treatments (compared treatments: Chinese herbal medicine, western medicine and sham-acupuncture). However, trials have relatively poor quality.[28]

Complementary and alternative medicines (CAM): Review of 26 RCTs included mind-body medicine, distant healing, massage, tuina and tai chi, homeopathy, ginseng, and dietary supplementation. Studies of qigong, massage and tuina have demonstrated positive effects on fatigue. Compared with placebo, homeopathy also had insufficient evidence of symptom improvement in CFS. Seventeen studies tested supplements for CFS. Most of the supplements failed to show beneficial effects for CFS, with the exception of NADH and magnesium.[27]

Approach for fatigue by Nutritionists:

With a detailed nutritional assessment, it is possible to take a differentiated look at the individual nutritional situation and to recognize a possible qualitative malnutrition (protein, vitamins, minerals, trace elements) and to assess the benefits of a possible therapy. An adaptation of the diet is not a "blanket diet", but complements the low-threshold, unspecific multivitamin supplementation with regards to other dietary factors in the genesis of fatigue. Nutritionists work with the hypothesis of mitochondrial dysfunction and try to optimize the intake in nutritional therapy in order to achieve a therapeutic benefit.

Microbiome: Prospective cohort study with 166 patients with IBD of which 91 with fatigue. Low diversity of the microbiome as well as Tryptophan in serum and butyrat-producing Phyla (as Faecalibacterium prausnitzii and Roseburia homins) are reduced with IBD patients with fatigue and in remission.[1]

CFS: Abundance of Actinobacteria and Firmicutes (similar to active IBD).[2,3]

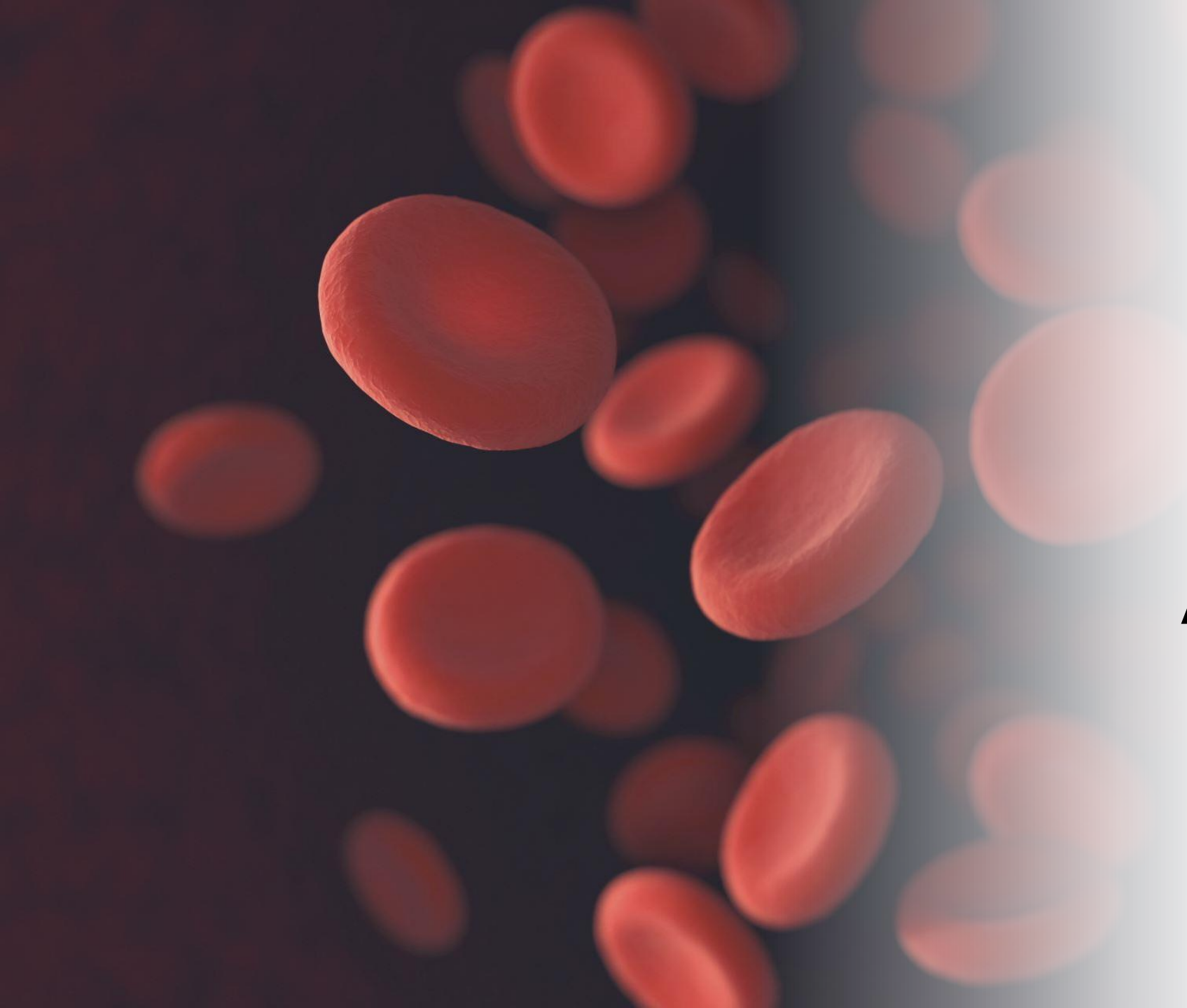
Probiotica: Insufficient evidence for use in CFS/ME. Limited study data and poor quality of these studies.[1]

Ginseng: Review of 10 studies showed a low risk of adverse events associated with ginseng use and modest evidence for efficacy on fatigue. Dosages used that showed effect: >400 mg daily (up to 2000 mg).[26]

Mitochondrial Dysfunction: Fatigue is a hallmark symptom of mitochondrial disease, making mitochondrial dysfunction a putative biological mechanism for fatigue. In clinical practice, vitamins such as riboflavin B2, niacin B3, vitamin E and other mitochondrial cofactors including levo-carnitine, lipoic acid, and acetyl-l-carnitine are used as supplemental treatment for mitochondrial disorders, in order to enhance electron transport complex enzyme activity as an antioxidant defense.[4,5]

Nutritional Assessment for malnutrion and microassessment: There is a strong biological and physiological rationale that indicates that the involvement of vitamins and minerals in cellular energy production translates into functional and physiological outcomes in humans, including perceived physical and mental fatigue as well as psychological and cognitive functions. With the evaluation of the supply and status of vitamins and minerals nutritional advice such as balanced food choices and secondly with the use of vitamin and mineral supplementation can be given.[82]

Workaround possible by other specialist



Anämie

Eisenmangel: man findet nur wonach man sucht…

Gaps in diagnosing and treating Iron deficiency in anemic IBD patients[1]

- **Mehr als ein Drittel der anemischen C. ulcerosa Patienten waren nicht für Eisenmangel getestet…**
- **… von denen, die getestet und mit Eisenmangel diagnostiziert wurden, erhielte ein Viertel keine Eisenersatztherapie**

1. Khan N, IBD. 2016

Anämie

Multi-faktoriell

- Eisenmangelanämie
- Anämie bei chronischer Krankheit
- Gemischt
- andere: Vit. B12, Folsäure, Medikamente

Epidemiologie

- 6–74%
- Hohe Prävalenz bei hospitalisierten und neu-diagnostizierten

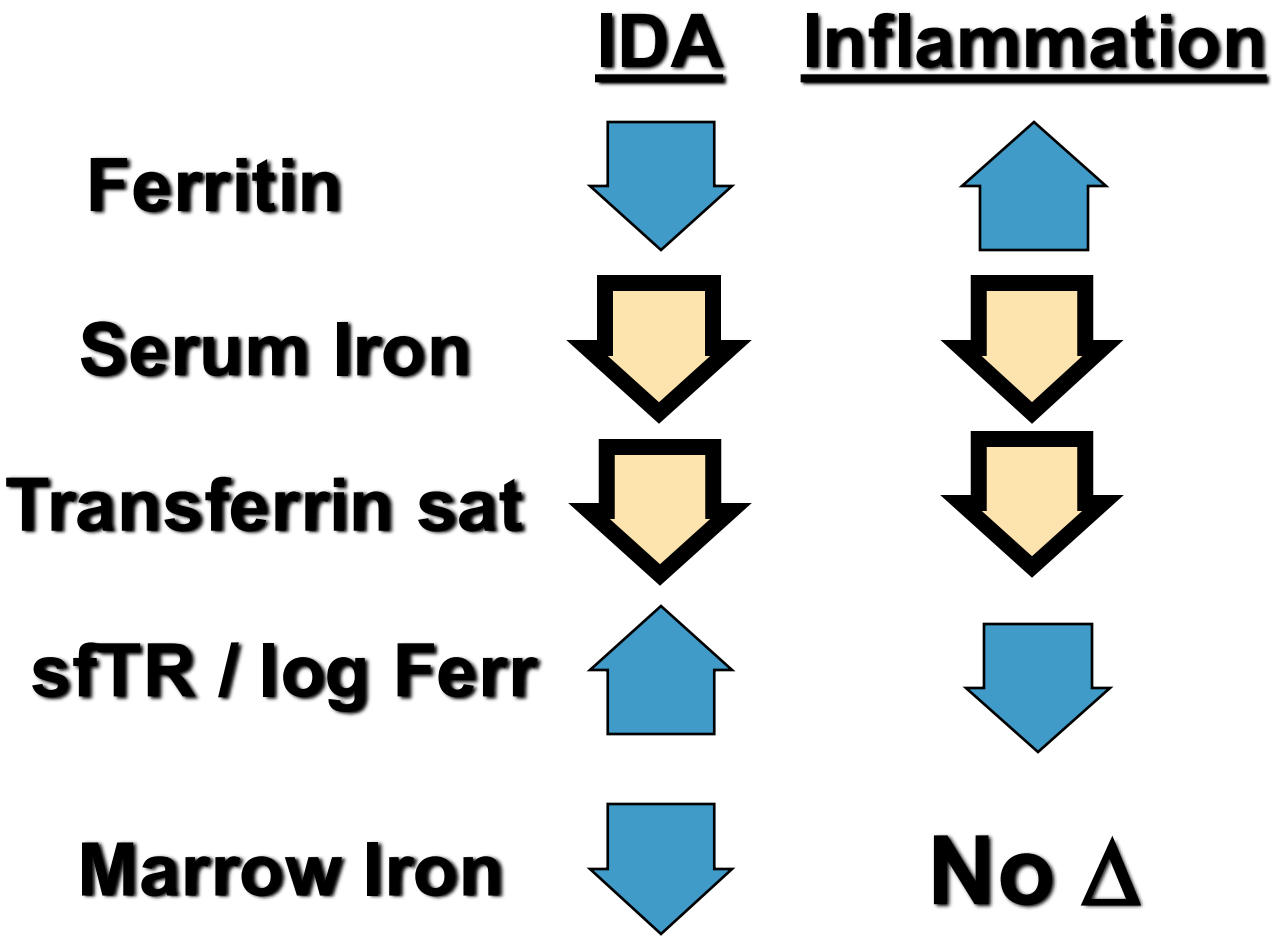
HÄMATOLOGIE

		Resultat		Ref.Wert		Vorwert
E	Hämoglobin	130	g/l	119-146	24/04/2025	120
E	Hämatokrit	0.39	l/l	0.37-0.44		0.37
E	Erythrozyten	4.11	tera/l	3.90-5.10		3.98
E	RDW (% Anisozytose)	13	%	12-15		12
E	MCH	32	pg	26-34		30
E	MCHC	331	g/l	320-360		328
E	MCV	96	fl	82-98		92
E ↑	Leukozyten	13.4	giga/l	4.0-10.0		9.3
E	Thrombozyten	273	giga/l	150-400		272
E	Mittleres Plättchenvolumen	9.5	fl	9.0-12.0		9.3

KLINISCHE CHEMIE

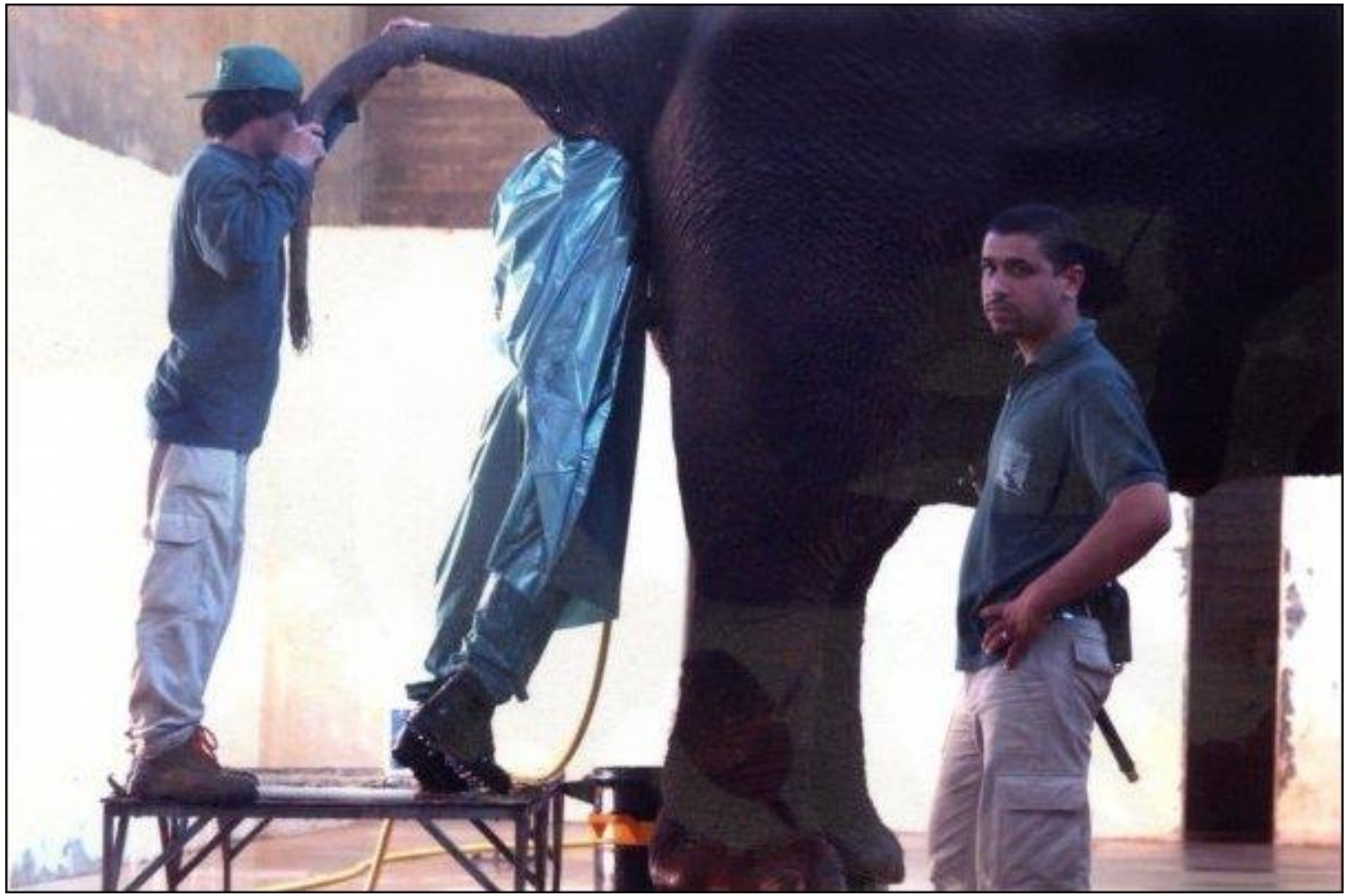
s ↑	CRP	8.8	mg/l	<5.0	24/04/2025	6.5
s	Ferritin	38	µg/l	15.0-175.0		29

Eisenmangel vs. chronische Entzündung



Die EINZIGE Ursache einer tiefen serum Ferritin Konzentration ist Eisenmangel. PUNKT.

Sometimes you need to look deeper as a gastroenterologist

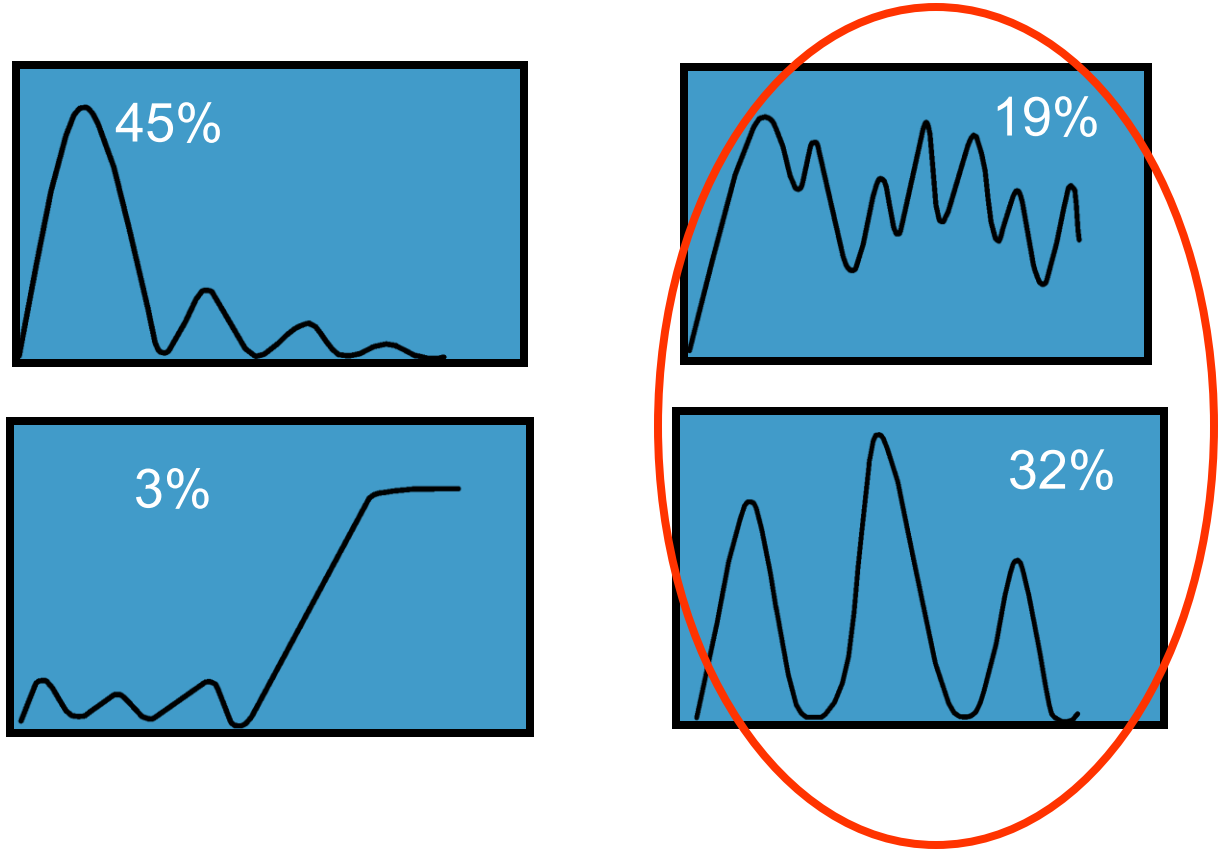


Take-home messages

- Eisenmangel ist häufig bei IBD und führt zu Fatigue und Beeinträchtigung der QoL
- Bestimmung der Tranferinsättigung

Der Schub bei IBD

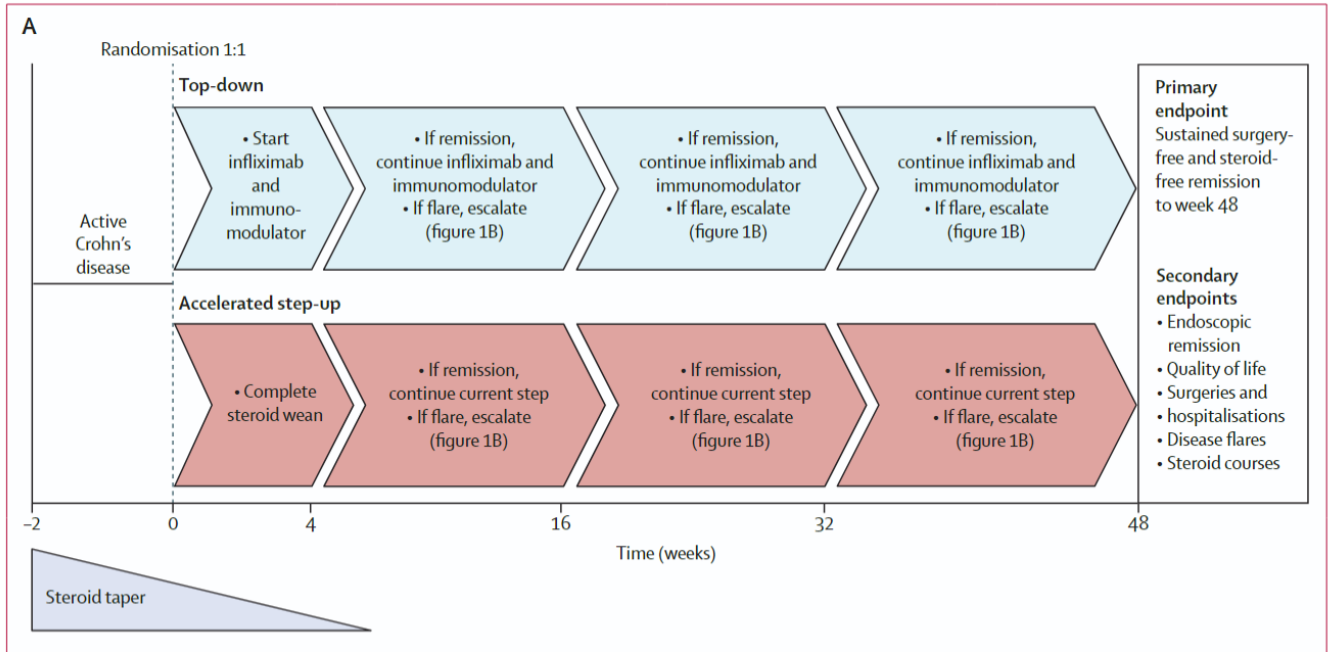
Verlauf des Morbus Crohn über die Zeit: nicht alle Patienten sind gleich

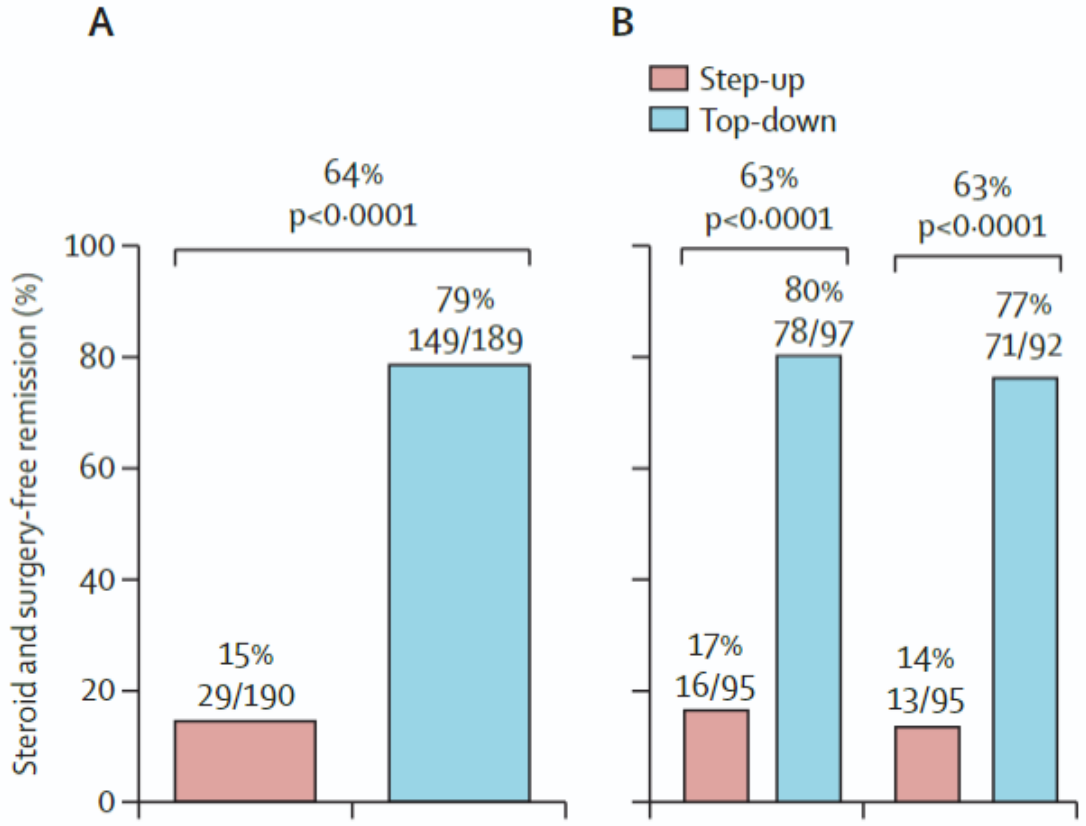


Verlauf der Erkrankung in einer norwegischen Kohorte mit 10 Jahren Beobachtungszeit zeigt, dass über 50% chronisch rezidivierende Symptome aufweisen

A biomarker-stratified comparison of top-down versus accelerated step-up treatment strategies for patients with newly diagnosed Crohn's disease (PROFILE): a multicentre, open-label randomised controlled trial

Nurulamin M Noor, James C Lee*, Simon Bond, Francis Dowling, Biljana Brezina, Kamal V Patel, Tariq Ahmad, Paul J Banim, James W Berrill, Rachel Cooney, Juan De La Revilla Negro, Shanika de Silva, Shahida Din, Dharmaraj Durai, John N Gordon, Peter M Irving, Matthew Johnson, Alexandra J Kent, Klaartje B Kok, Gordon W Moran, Craig Mowat, Pritash Patel, Chris S Probert, Tim Raine, Rebecca Saich, Abigail Seward, Dan Sharpstone, Melissa A Smith, Sreedhar Subramanian, Sara S Upponi, Alan Wiles, Horace R T Williams, Gijs R van den Brink, Séverine Vermeire, Vipul Jairath, Geert R D'Haens, Eoin F McKinney, Paul A Lyons, James O Lindsay, Nicholas A Kennedy, Kenneth G C Smith, Miles Parkes, on behalf of the PROFILE Study Group†*

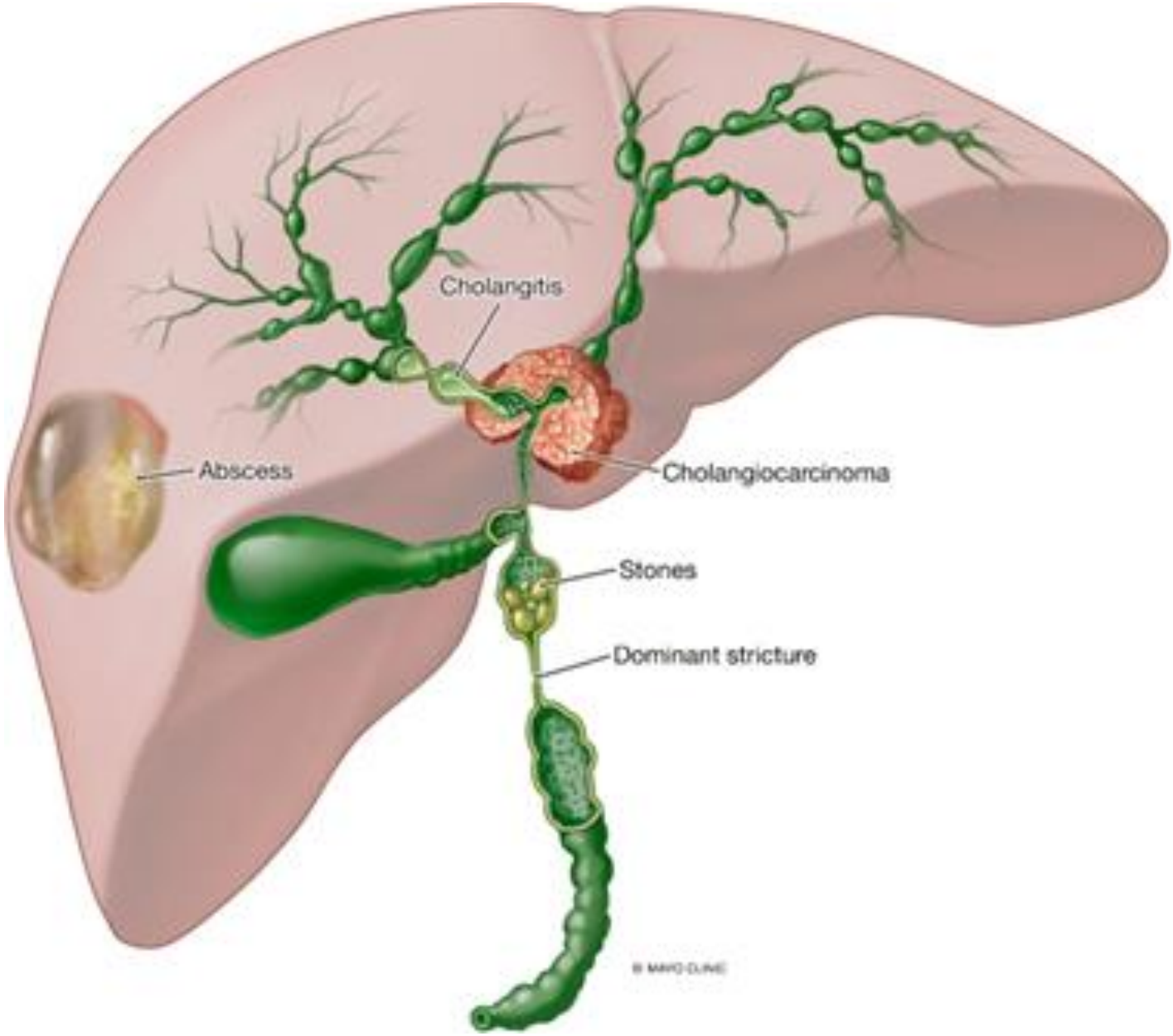




Sustained steroid free remission until week 48

Sustained steroid-free and surgery-free remission until week 48

PSC (Bedeutung von alk Phos)



Enzyme

Alkalische Phosphatase (AP)	!	113 U/l		35 - 105
		27.07.2023	111	
		06.12.2022	95	
GGT (Gamma-Glutamyltranspept.)		23 U/l		bis 36
		27.07.2023	22	
		06.12.2022	24	
ASAT (GOT)	!	44 U/l		bis 35
		27.07.2023	30	
		06.12.2022	27	
ALAT (GPT)	!	37 U/l		bis 35
		27.07.2023	31	
		06.12.2022	27	

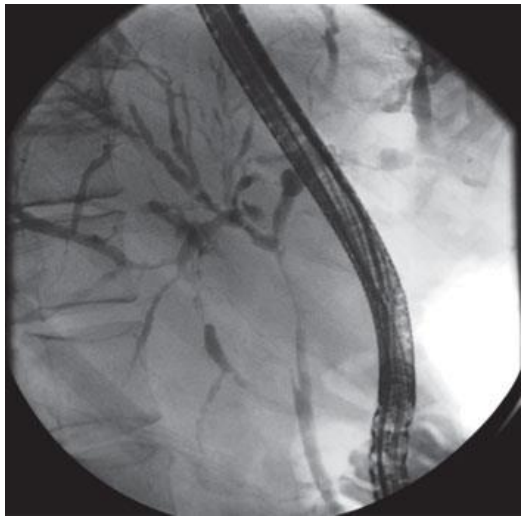
Klinik
Morbus Crohn (ED 8/2019)
- letzte Koloskopie 7/2021: Stenose der Ileozökalklappe, Ballondilatation auf 13mm, Engstelle auf 2cm Länge der Ileozökalklappe mit Ulzera, Divertikel im Sigma; Therapie mit Entocort
- Stn. Cholezystektomie.
Ausschluss einer PSC.

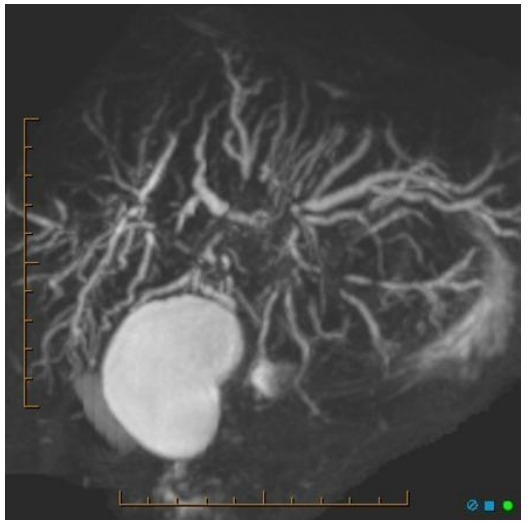
MRI Oberbauch nativ und mit i.v. KM, MRCP vom 22.11.2024

Beurteilung
- Geringe Dilatation und Unregelmässigkeiten der zentralen intrahepatischen Gallenwege, links etwas betonter als rechts, suspekt auf geringe Veränderungen im Rahmen einer PSC.
- Status nach Cholezystektomie mit lokal unauffälligen Verhältnissen.
- Geringe Lebersteatose.
- Mehrere kortikale Nierenzysten von einfachem Aspekt beidseits.

PSC

- UC > CD
- M > F
- Wichtiger Risikofaktor für: Cholangiokarzinom (10–15%), Dickdarmkarzinom
- Diagnose mit MRI (MRCP) – ERCP
- **CAVE dominante Striktur**
- 5% in UC und 3%–4% in CD
- 90% der PSC Patienten haben eine IBD
- Erhähte alk Phos bei 5% der UC Patienten (85% davon hatten eine PSC in einer ERCP, Schwedische Studie)
- Häufiger bei Männern mit Pancolitis
- Häufiges Symptom: Pruritus, Lethargie aber 40%–50% asymtpmatisch zum Zeitpunkt der Diagnose (mittleres Alter 40–45)





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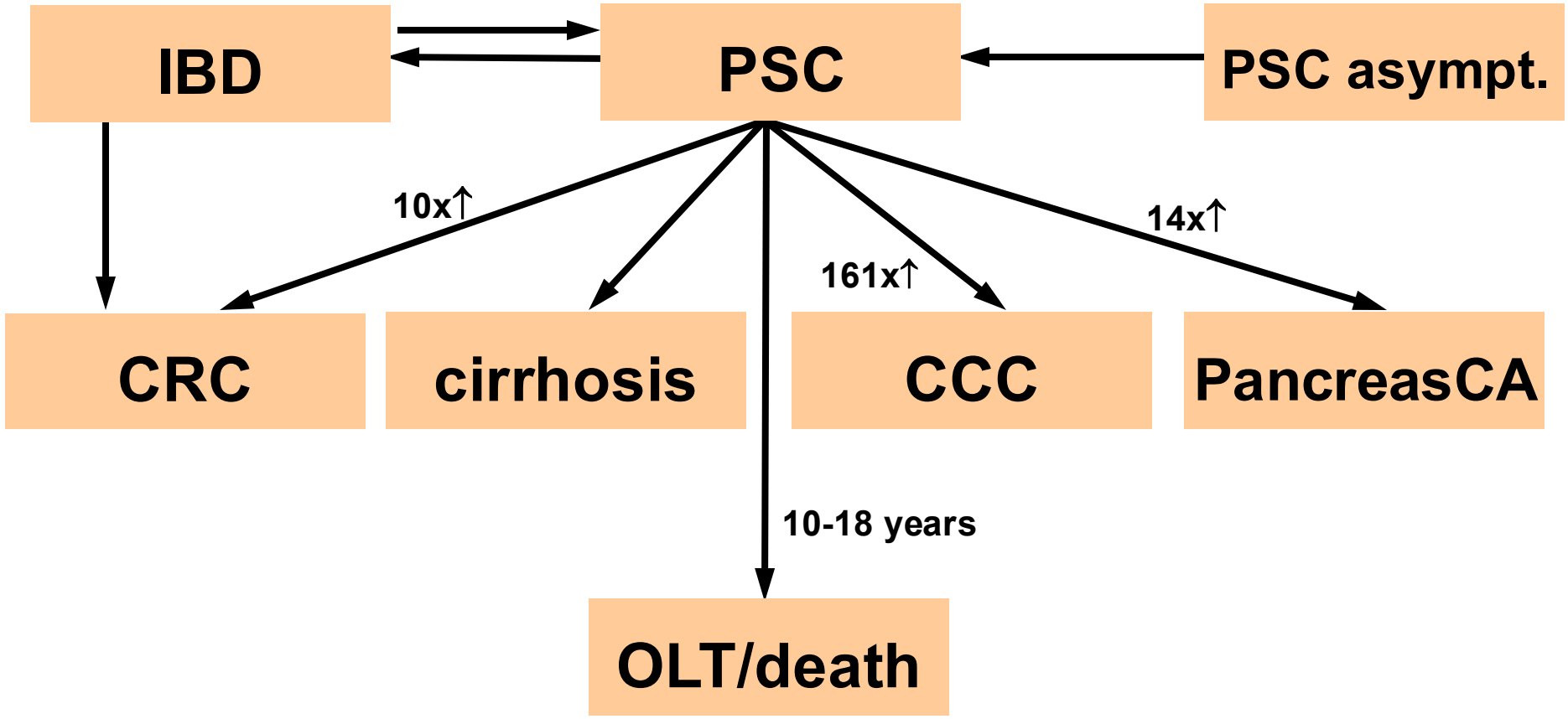
PSC: Risiko für die Progression und Krebsrisiko



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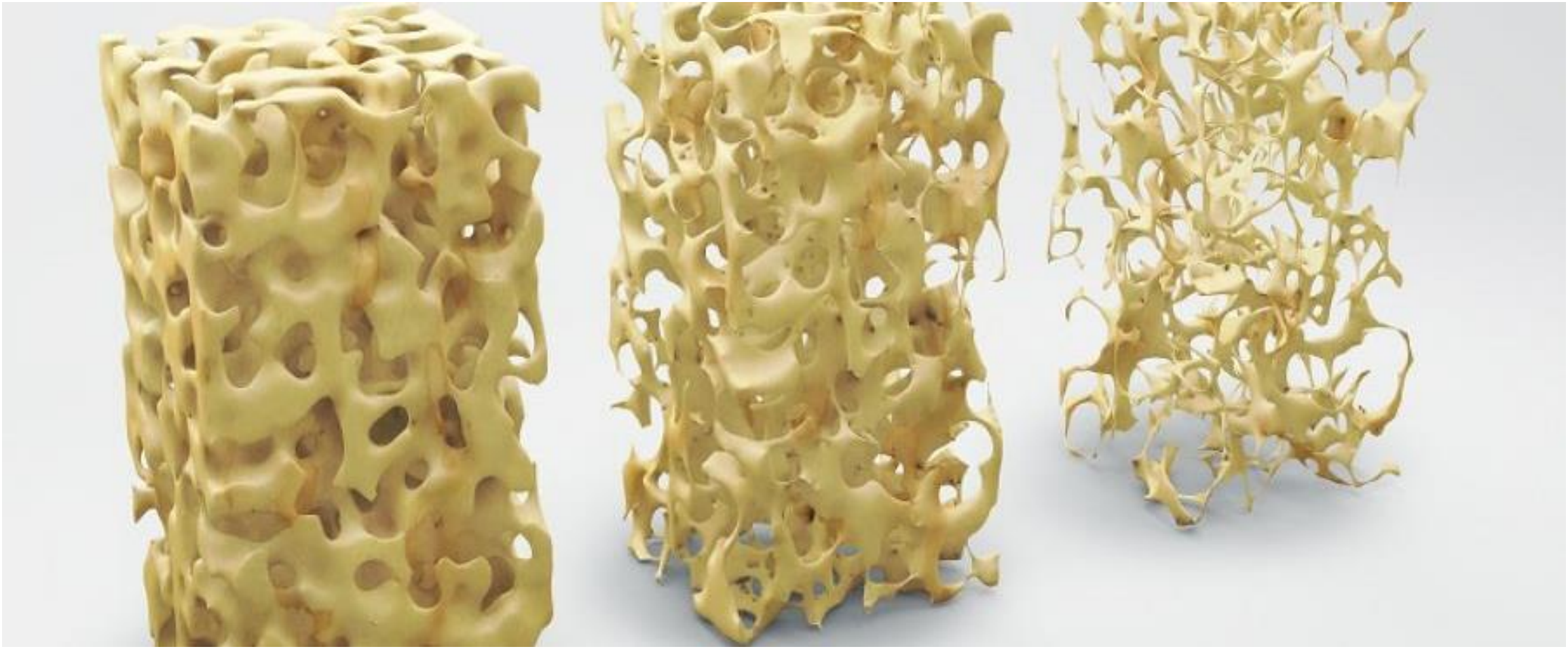
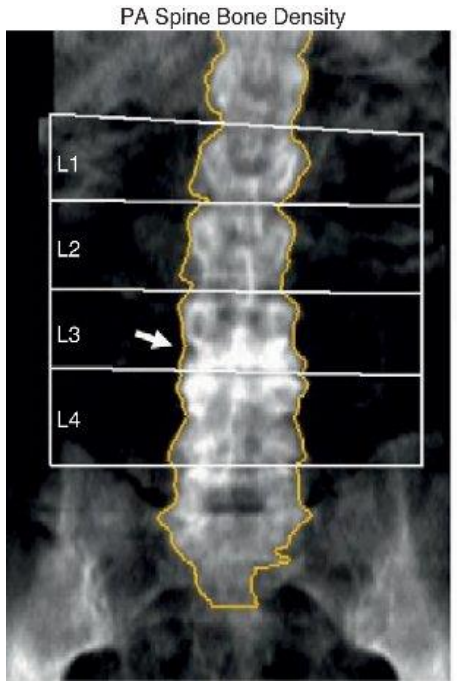
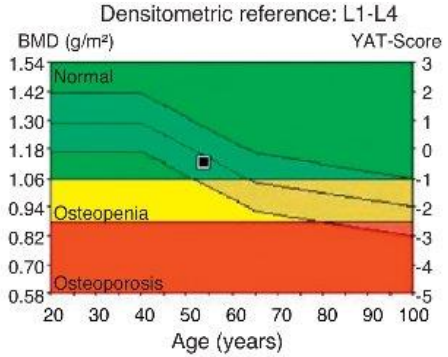
Osteoporose



Osteoporosis

- Tiefe Knochendichte (Osteopenie) – Osteoporose (20-50%)
- Risikofaktoren : chronische Entzündung, Steroide, Malabsorbtion durch Entzündung/Resektion, Rauchen, wenige kröperliche Aktivität
- Diagnose: Knochendichtemessung (Dexa)



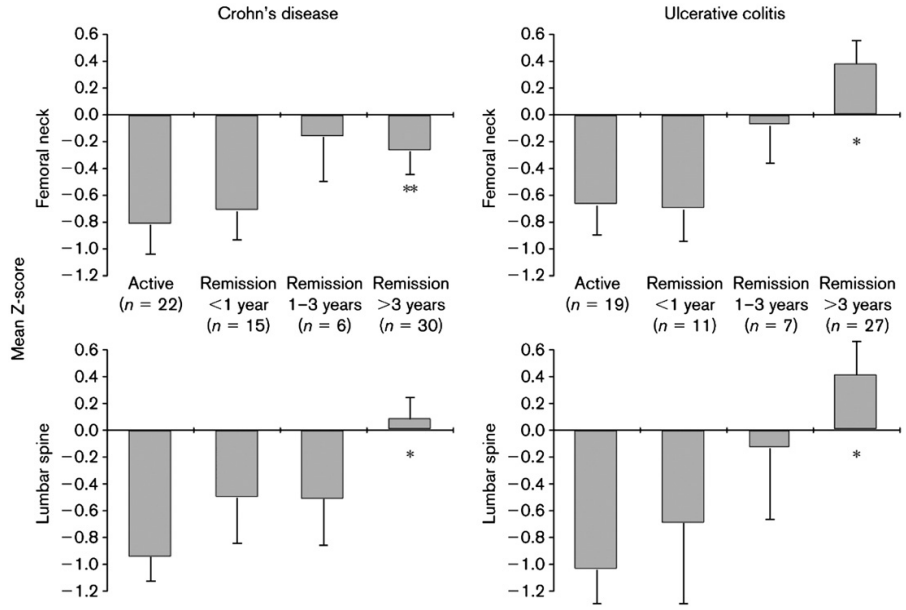


Region	BMD [1] (g/m²)	Young adult [2] (%)	T-score	Adj. to age [3] (%)	Z-score
L1	0.883	78	-2.1	80	-1.8
L2	0.991	83	-1.7	85	-1.5
L3	1.326	111	1.1	113	1.3
L4	1.217	101	0.1	104	0.4
L1-L4	1.122	95	-0.5	97	-0.3
L2-L4	1.184	99	-0.1	101	0.1

Table 1 Bone density in patients with inflammatory bowel disease

Normal bmd $T>-1$	Osteopenia $T<-1>-2,5$	Osteoporosis $T<-2,5$	Author
Crohn's disease			
42%	23%	35%	von Tirpitz et al. (1999)[3]
8%	55%	7%	Ardizzone et al. (2000)[4]
37%	50%	13%	Siffledeen et al. (2004)[5]
Ulcerative colitis			
15%	67%	18%	Ardizzone et al. (2000)[4]

Proportion of patients with normal bone mineral density (bmd), osteopenia $T<1$and >-2.5 and osteoporosis in %.



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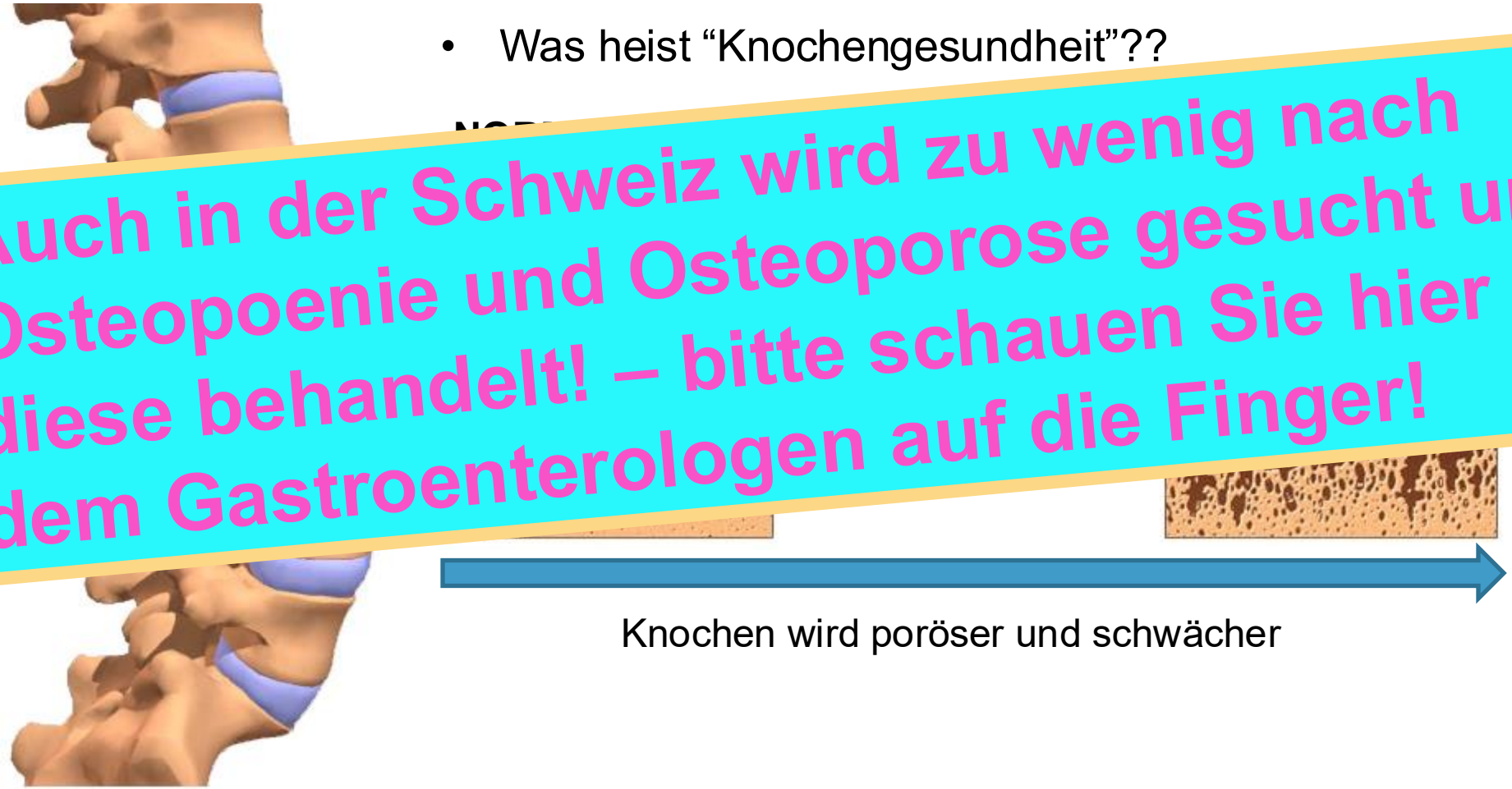
Osteopenie und Osteoporose



- Was heist “Knochengesundheit”??

Auch in der Schweiz wird zu wenig nach Osteopoenie und Osteoporose gesucht und diese behandelt! – bitte schauen Sie hier dem Gastroenterologen auf die Finger!

Knochen wird poröser und schwächer

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Bone health in patients with inflammatory bowel disease

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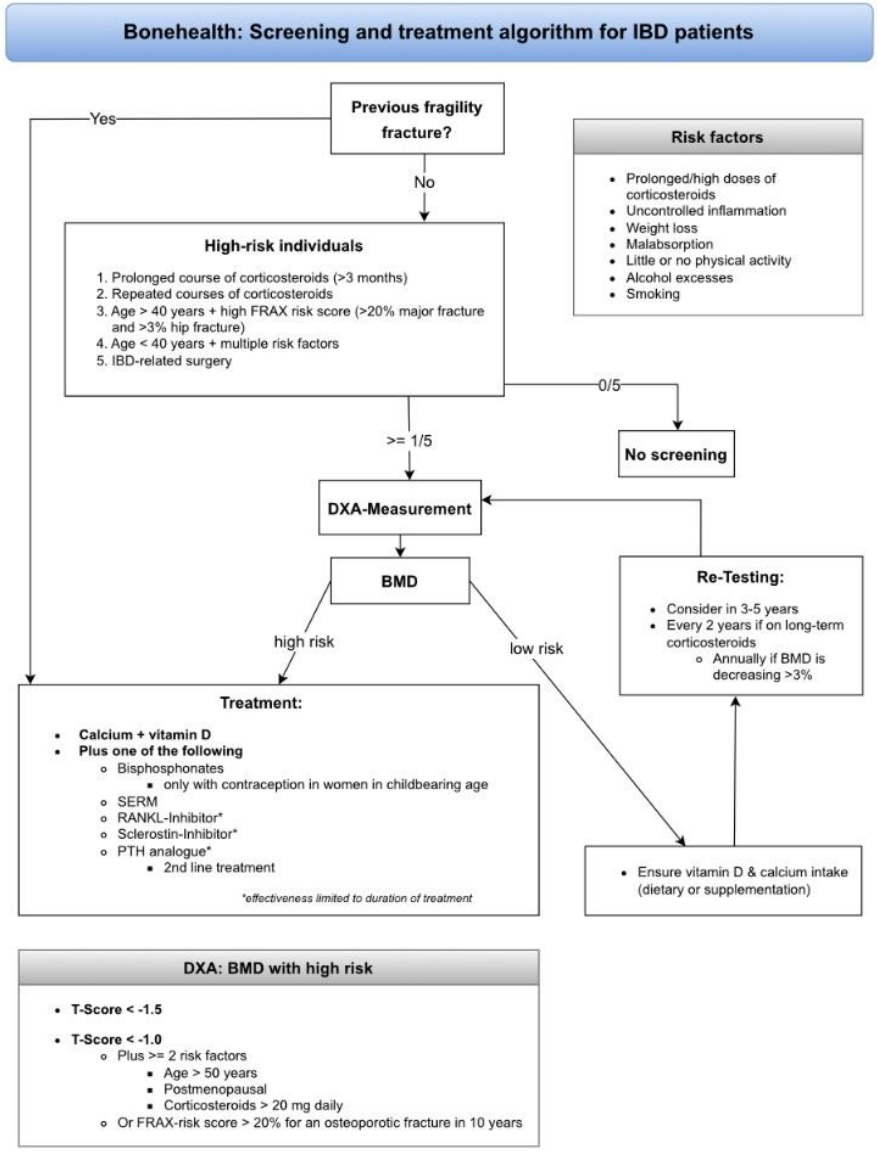

Fragen?


Herzlichen Dank für die
Aufmerksamkeit