

Advances in Nutrition Therapies and Technology in IBD and Cirrhosis

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Objectives

- Describe the rationale for using diet as therapy in IBD and present supportive pilot data
- Discuss the role of nutrition optimization and anti-inflammatory diets in the treatment of IBD
- Discuss nutrition optimization and implications in cirrhosis on clinical outcomes
- Introduce an approach to using technology to empower patients to self-manage diet and stress in chronic diseases

Microbiota

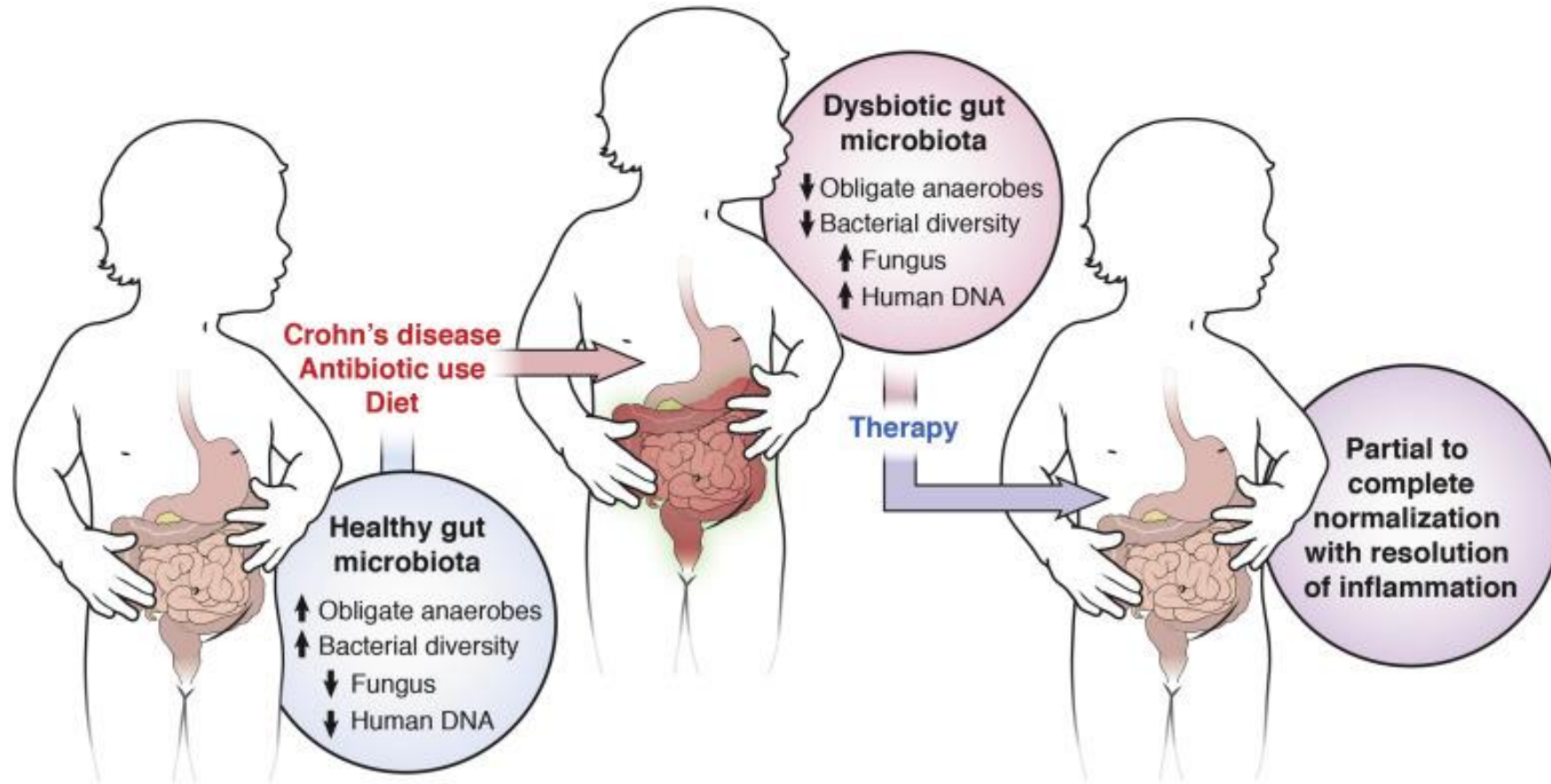
- GI tract is densely colonized with 100 trillion diverse microbes
- Healthy individuals microbiota live symbiotically with host
 - Digestion of otherwise indigestible CHO's to produce SCFA's
 - Regulate fat metabolism
 - Synthesize vitamins / essential AA, transform conjugated bile acids
 - Protect against epithelial injury
 - Maintain epithelial barrier function
 - Intestinal immune homeostasis

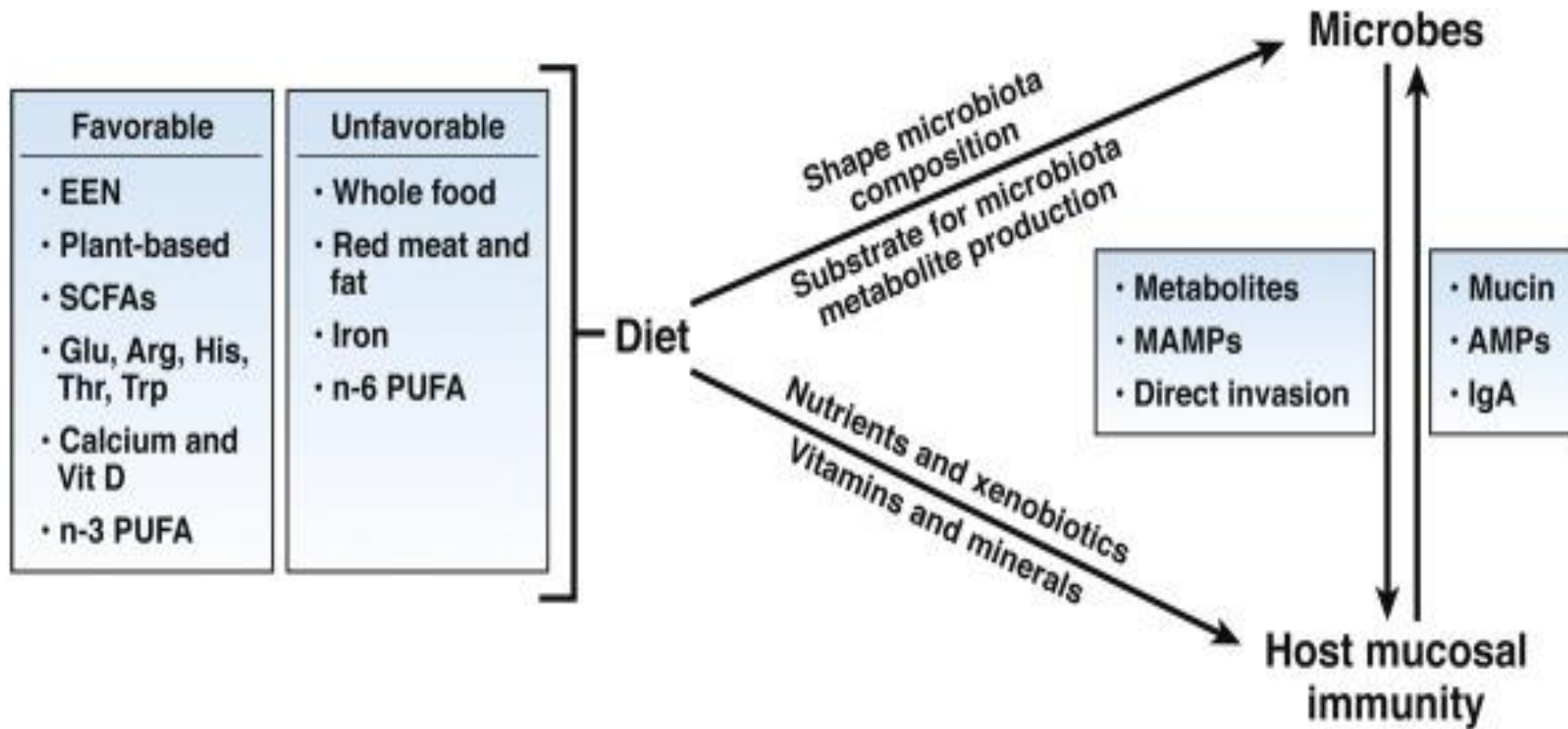
The microbiome in IBD







Table 1. Changes in the Microbiome Linked to IBD

Microbial composition	<ul style="list-style-type: none">Decrease in α diversityDecrease in Bacteroides and FirmicutesIncrease in GammaproteobacteriaPresence of E coli, specifically adherent-invasive E ColiPresence of FusobacteriumDecrease in Clostridia, Ruminococcaceae, Bifidobacterium, LactobacillusDecrease in F prausnitzii
Microbial function	<ul style="list-style-type: none">Decrease in SCFAs, butyrateDecrease in butanoate and propanoate metabolismDecrease in amino acid biosynthesisIncrease in auxotrophyIncrease in amino acid transportIncrease in sulfate transportIncreased oxidative stressIncrease in type II secretion system, secretion of toxins

Effects of dietary and pharmacologic interventions on dysbiosis in patients with CD





■ Butyrate	■ Acetate	■ Propionate
Resistant starch		
 <p data-bbox="1429 177 2084 244">Intact or milled grains, dry beans, pasta, banana, fruits, uncooked potatoes, maize, cooked potatoes and bread, processed foods</p>		
Insoluble fiber (90%) and FOS (10%)		
 <p data-bbox="1888 358 2084 382">Wheat bran</p>		
Insoluble fiber : Cellulose		
 <p data-bbox="1378 511 2084 535">Fruits and vegetables, seeds, whole grains</p>		
Soluble fiber : Beta glucan		
 <p data-bbox="1531 691 2084 715">Oat bran (outer husk of oat grain)</p>		
Soluble fiber : Guar gum		
 <p data-bbox="1182 862 2084 939">From the endosperm of guar bean, used as a thickening, stabilizing and binding agent in soups, juices, salad dressings, jams, dairy products, cheeses</p>		
Soluble fiber : Pectin		
 <p data-bbox="1156 1039 2084 1116">Peaches, apples, oranges, apricots, grapefruits, carrots, tomatoes, potatoes, used as a stabilizer for jams and jellies, dairy products and soft drinks</p>		
Bacterial phyla		
<ul style="list-style-type: none"> Roseburia/Eubacterium rectale group Eubacterium hallii Faecalibacterium prausnitzii Eubacterium cylindroides 	<ul style="list-style-type: none"> Ruminococcus obeum Ruminococcus bromii Ruminococcus flavefaciens Atopobium spp. Bacteroides-Prevotella group Proteobacteria Lactobacillus/Enterococcus Eubacterium cylindroides Lachnospira spp. 	<ul style="list-style-type: none"> Clostridial cluster IX Bacteroides-Prevotella group

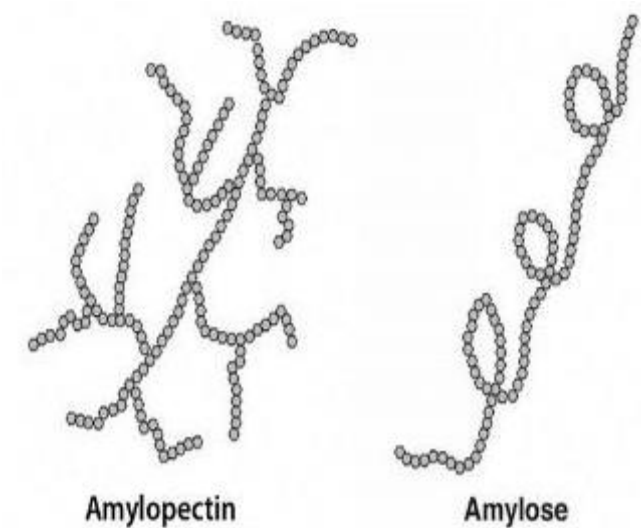


Limitations of dietary studies in IBD

- Largely Retrospective, few prospective, food recall studies
- Single nutrient interventions
 - Fiber Supplements
 - Probiotics
 - Omega-3 Fatty Acids
- Few studies exploring efficacy of holistic diverse diets

Specific carbohydrate diet (SCD)

- Evolved from a diet for celiac disease mid-20th century
 - Based on hypothesis that patients with IBD have a dysfunction of disaccharidases, necessary to digest and absorb disaccharides and amylopectin
 - Therefore, higher amounts of disaccharides would enter the colon, leading to bacterial overgrowth, bowel injury and intestinal permeability



Mean Clinical Disease Activity Index and Mean Laboratory Measures for Patients with IBD on the SCD (Mean \pm SD)

Elements	Enrollment	2 wk	8 wk	12 wk
PCDAI	28.1 \pm 8.8	14.8 \pm 12.8	7.9 \pm 11.23	4.6 \pm 10.3
PUCAI	28.3 \pm 23.1	8.3 \pm 2.9	6.7 \pm 2.9	6.7 \pm 11.6
CRP (mg/L)				
Seattle (normal < 8.0)	24.1 \pm 22.3	18.3 \pm 27.0	7.9 \pm 1.6	7.1 \pm 0.4
Atlanta (normal < 4.9)	20.7 \pm 10.9	13.4 \pm 15.4	12.0 \pm 14.6	4.8 \pm 4.5
Sedimentation rate (mm/h)				
Seattle (normal 0-20)	15.3 \pm 11.0	11.0 \pm 9.6	8.3 \pm 6.0	7.4 \pm 5.5
Atlanta (normal 0-32)	35.7 \pm 1.2	26.7 \pm 16.6	11.7 \pm 6.4	12.0 \pm 12.7
Albumin (g/dL)				
Seattle (normal 3.8-5.4)	4.1 \pm 0.77	4.1 \pm 0.7	4.5 \pm 0.6	4.4 \pm 0.4
Atlanta (normal 3.5-5.5)	3.2 \pm 0.76	3.4 \pm 0.5	3.7 \pm 0.6	3.4 \pm 0.7
Calprotectin (μ g/g)				
Seattle (normal < 50)	642.3 \pm 648.6	—	—	202.6 \pm 245.2
Atlanta (normal < 50)	110.0 \pm 100.0	—	—	209.0 \pm 159.8

PCDAI indicates pediatric Crohn's disease activity index; PUCAI, pediatric ulcerative colitis activity index.

Autoimmune protocol diet

Extension of paleolithic diet with avoidance of:

- Gluten, Refined sugar
- Food Additives
- Initial phase – dairy, eggs, legumes, nightshades
- Fresh, nutrient dense, fermented

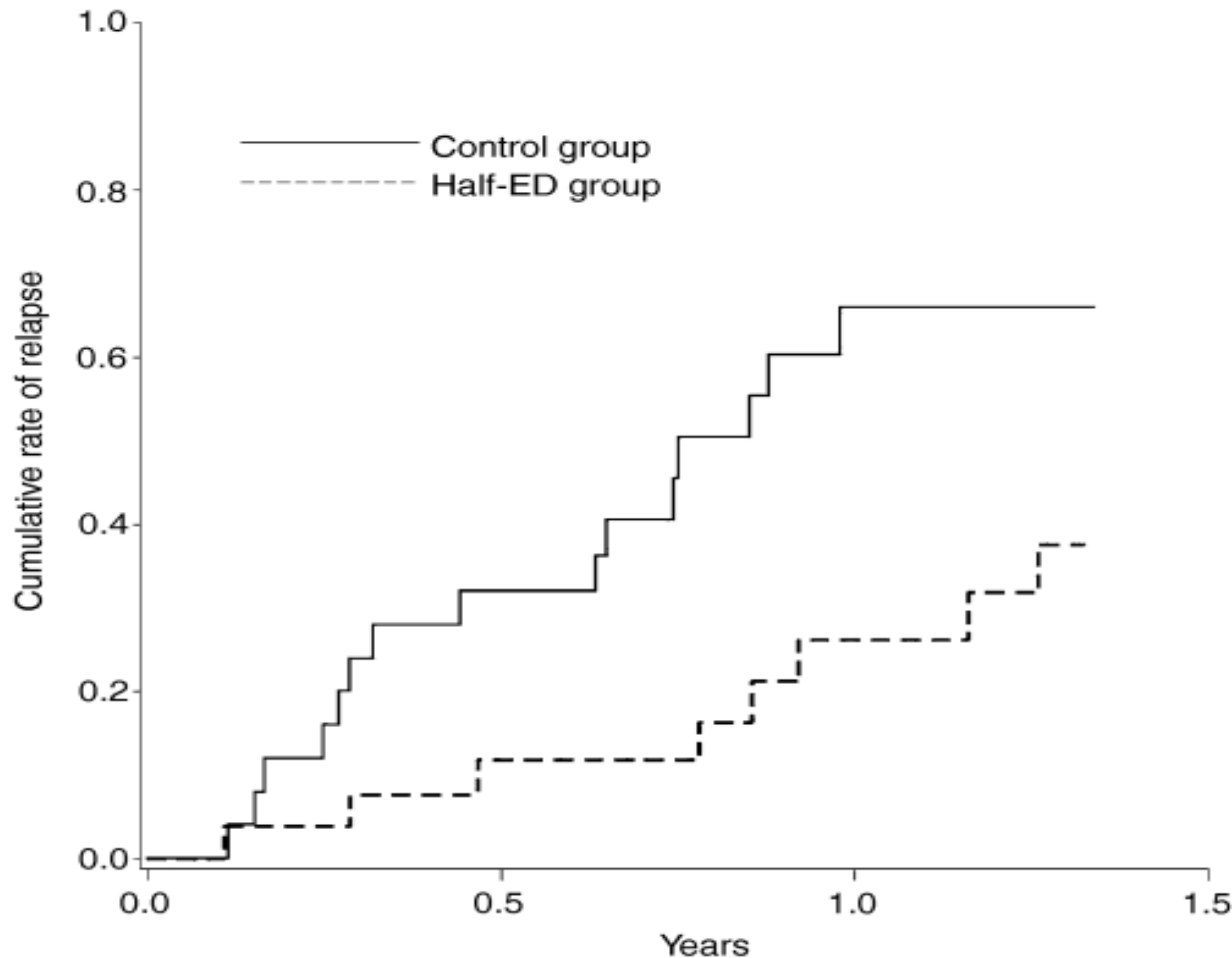
	Week 0	Week 6	<i>P</i> (week 6 vs 0)	Week 11	<i>P</i> (week 11 vs 0)
Crohns Disease HBI, mean (SD)	6.7 (1.5)	3.3 (1.8)	0.001	3.4 (2.6)	0.004
UC					
Partial Mayo score, mean (SD)	5.8 (1.2)	1.2 (2.0)	0.01	1.0 (2.0)	0.007
Stool frequency, mean (SD)	2.0 (0.9)	0.2 (0.4)	0.012	0.2 (0.4)	0.012
Rectal bleeding, mean (SD)	1.8 (0.8)	0.5 (0.8)	0.025	0.3 (0.8)	0.017
Physician global assessment, mean (SD)	2.0 (0.0)	0.5 (0.8)	0.007	0.5 (0.8)	0.007
Fecal calprotectin (µg/g) , mean (SD), n=6	471 (562)			112 (104)	0.12
Baseline FC > 50 µg/g, mean (SD), n=4	701 (563)			139 (113)	0.09

Partial enteral nutrition vs regular diet, N=51

- To examine the effectiveness of half elemental diet + half regular meals compared to habitual diet alone in Crohn's patients in remission
- RCT
- Elemental formula (900-1200kcal/day)
- Primary Outcome was the occurrence of relapse over the 2-year intervention period

Characteristics	Half ED (n = 26)	Free diet (n = 25)	P-value
Men	20	17	0.48
Mean age (s.d.; years)	30.8 (11.1)	28.9 (8.1)	0.49
Mean body mass index (s.d.)	20.1 (3.1)	20.0 (3.6)	0.85
Duration of disease (s.d.; years)	4.1 (4.2)	5.6 (6.5)	0.32
Disease site			
Small bowel only	8	7	0.50
Colon only	3	6	
Both	15	12	
Perianal lesions	12	10	0.66
Previous gut operation	11	11	0.90
Frequency of relapse			
High (not <0.5/year)	10	9	0.98
Low (<0.5/year)	7	7	
First attack	9	9	
Administration of azathioprine	2	4	0.42
Inductive therapy (+surgery)			
Total enteral nutrition	12 (0)	10 (3)	0.67
Total parenteral nutrition	12 (1)	13 (1)	
Administration of prednisolone	0 (0)	1 (0)	
Administration of infliximab	2 (0)	1 (0)	

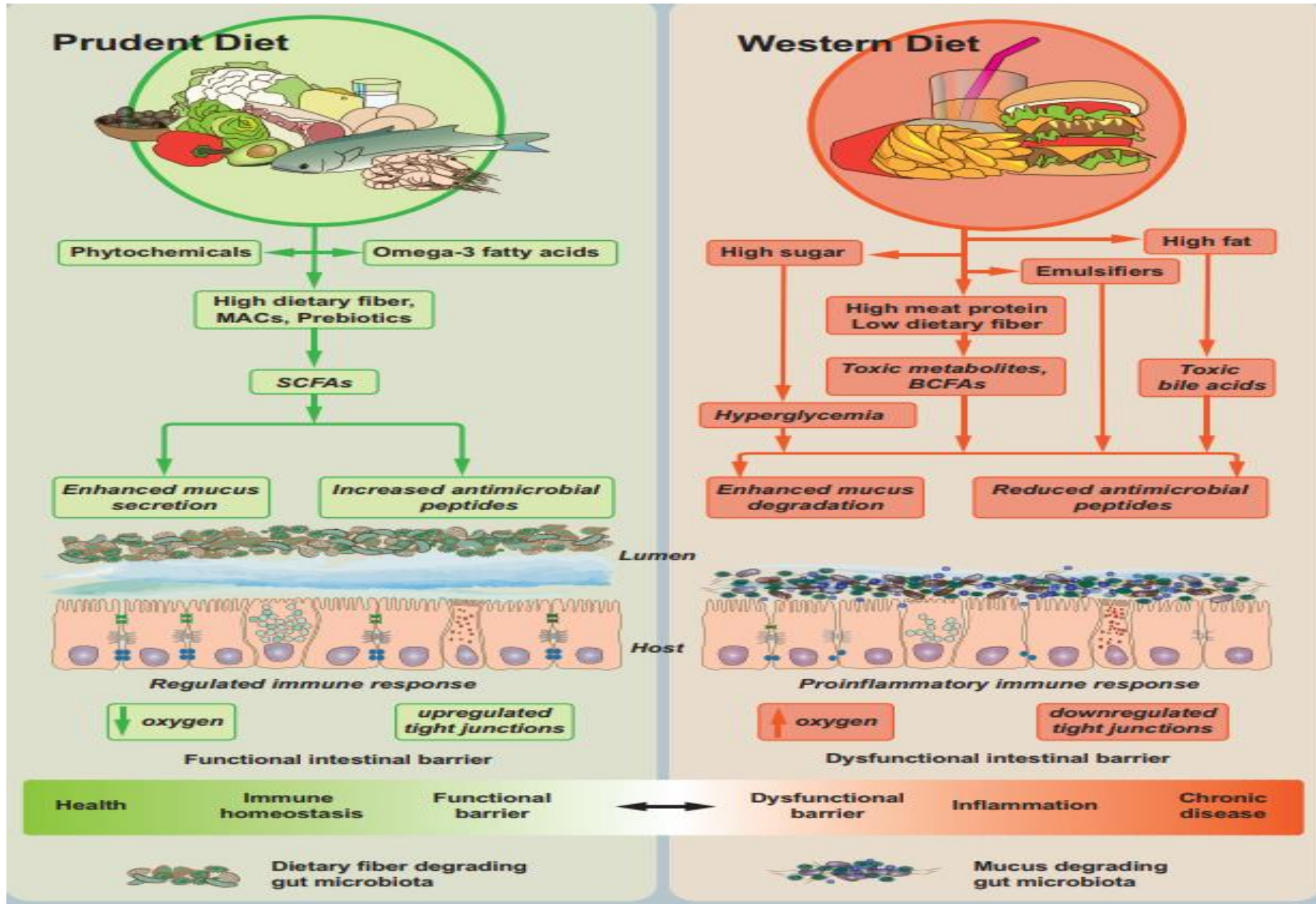
Partial enteral nutrition vs regular diet and relapse rates



	Treatment Half ED	Treatment Free Diet
Number of cases	9	16
Age and sex adjusted HR (95% CI)	0.36 (0.15-0.83)	1.00 (reference)
Multivariate HR (95% CI)	0.40 (0.16-0.98)	1.00 (reference)

Crohn's Disease dietary intervention Objectives

- 1) To characterize the gut microbiome in patients with CD in remission stratified by dietary diversity.
- 2) To examine the effect of a personalized dietary intervention on the microbiome in patients consuming a non-anti-inflammatory diet (NAID)



Makki et al. Cell Host and Microbe 2018

Hypotheses

- Crohn's patients in remission consuming a NAID will have a significantly different gut microbiome compared to patients consuming an anti-inflammatory diet (AID)
- **NAID (Non-anti-inflammatory Diet)**
 - ≤ 3 servings Fruit/Veg/day
 - ≥ 3 servings Red Meat per week
 - ≤ 15 g/day dietary Fiber

Methods

- Prospective intervention study
- Patients in remission recruited from IBD clinics at U of C
- Maintenance of remission using biologic therapies
- Excluded if on antibiotics, probiotics or corticosteroids
- RD assessment and if NAID = intervention x 3 months
- Stool Samples = Baseline x 3, monthly x 3

Dietary intervention

- Emphasize an AID using Mediterranean diet Principles
 - Move away from emphasizing single nutrients
- 25-30 kcal/kg (Remission)
- 0.8-1.2 g/kg protein
- Fat intake 20-35% energy (PUFA + Monounsaturated)
 - < 10% saturated fat
- < 10% energy refined sugars
- Fiber 25 g/day females and 38 g/day males
 - Emphasis on prebiotic rich foods
- Fruits/Vegetables 7 servings/day
- Poultry < 3 X/week
- Fish = 2 servings / week
- 2 servings probiotic, fermentable foods (minimum 10 billion CFU)

Patient demographics and health information

	Female N=34	Male N=33
Age in years (mean, SD)	44.7 (14.4)	49.7 (12.7)
BMI (kg/m ² ; mean, SD)	27.8 (6.1)	26.7 (3.9)
Anti-TNF n, (%)	30 (88.2%)	24 (72.7%)
IMM n, (%)	15 (44.1%)	14 (42.4%)
Previous bowel surgery n, (%)	7 (20.6%)	11 (33.3%)

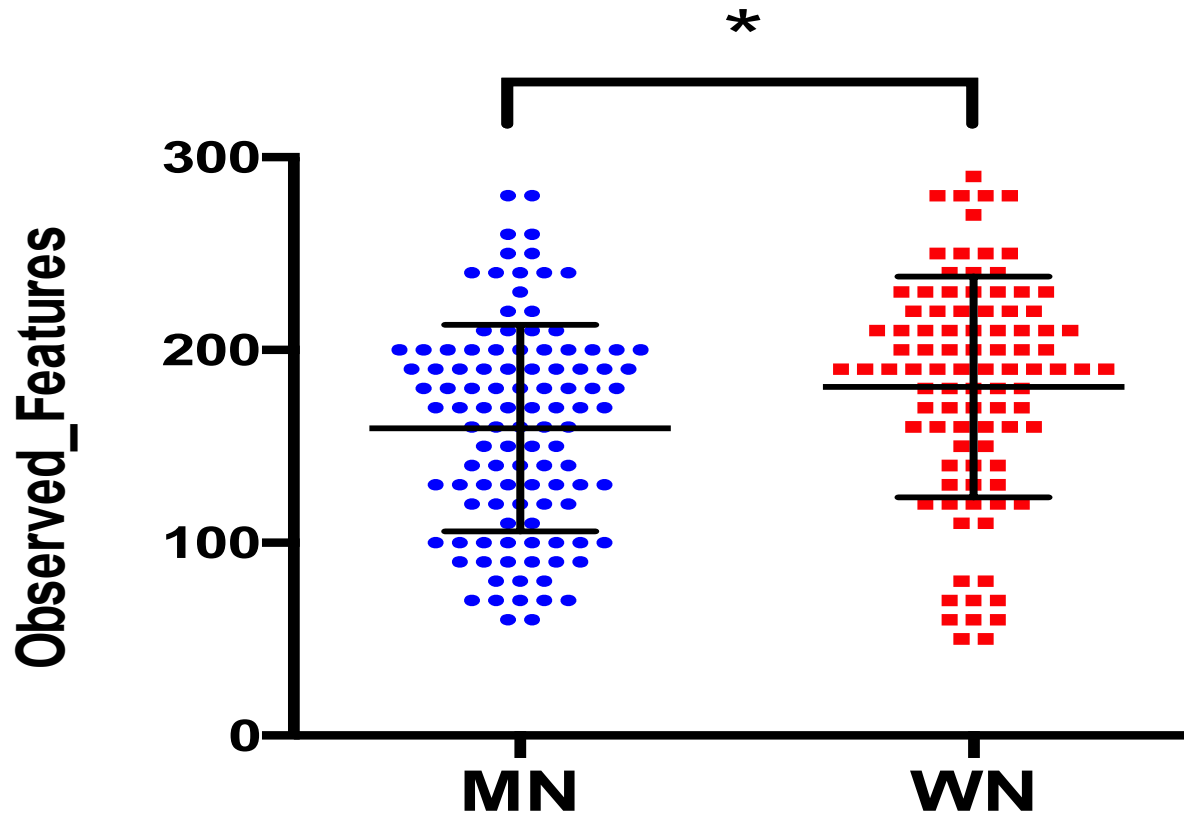
Macronutrient composition compared to current guidelines

Macronutrient	DRI Acceptable Macronutrient Distribution Range (AMDR) and Adequate Intake (AI) [29]	Academy of Nutrition and Dietetics [30]	Crohn's Patients (N = 67; Mean ± SE)		Representative Sample (N = 1547; Mean ± SE) [27]	
			M (N = 33)	F (N = 34)	M (N = 721)	F (N = 826)
Total energy intake (kcal/d)	Male = $662 - (9.53 \times \text{age (y)}) + \text{PA} \times \{(15.91 \times \text{weight (kg)}) + (539.6 \times \text{height (m)})\}$, Female/Women = $354 - (6.91 \times \text{age (y)}) + \text{PA} \times \{(9.36 \times \text{weight (kg)}) + (726 \times \text{height (m)})\}$		2358 (95.3)	1881 (86.5)	2346 (61)	1730 (42)
Protein (% total energy)	10–35% total energy		18.3 (1.0)	18.0 (0.7)	17.0 (0.4)	16.8 (0.3)
Carbohydrate (% total energy)	45–65% total energy		47.1 (1.5)	48.1 (1.1)	48.7 (0.9)	48.5 (0.6)
Fiber (g/day) ^	M: 30–38 F: 21–25		22.8 (1.4) *	20.9 (1.6) *	19.2 (0.6)	13.9 (0.5)
Total fat (% total energy)	20–35% total energy		33.7 (1.2)	34.3 (1.0)	31.0 (0.8)	32.4 (0.6)
PUFA (% total energy)	5–10% total energy	3–10% total energy	4.5 (0.4) *	3.9 (0.3) *	5.6 (0.2)	5.6 (0.1)
Omega-6 (linoleic)	5–10% total energy	3–10% total energy	3.3 (0.4) *	2.8 (0.2) *	4.5 (0.1)	4.5 (0.2)
Omega-3 (α-linolenic)	0.6–1.2% total energy	0.6–1.2% total energy	0.6 (0.15)	0.5 (0.09) *	0.8 (0.04)	0.8 (0.02)
MUFA (% total energy)	No AI level	15–20% total energy	8.2 (0.6)*	7.1 (0.5) *	12.6 (0.4)	12.8 (0.2)
SFA (% total energy)	As low as possible	7–10% of total energy <7% to reduce CVD risk 5–6% to lower lipids	10.7 (0.4)	11.1 (0.5)	9.8 (0.2)	10.7 (0.3)
TransFA (% total energy)	As low as possible	<1% total energy	0.4 (0.1)	0.3 (0.1)	unavailable	

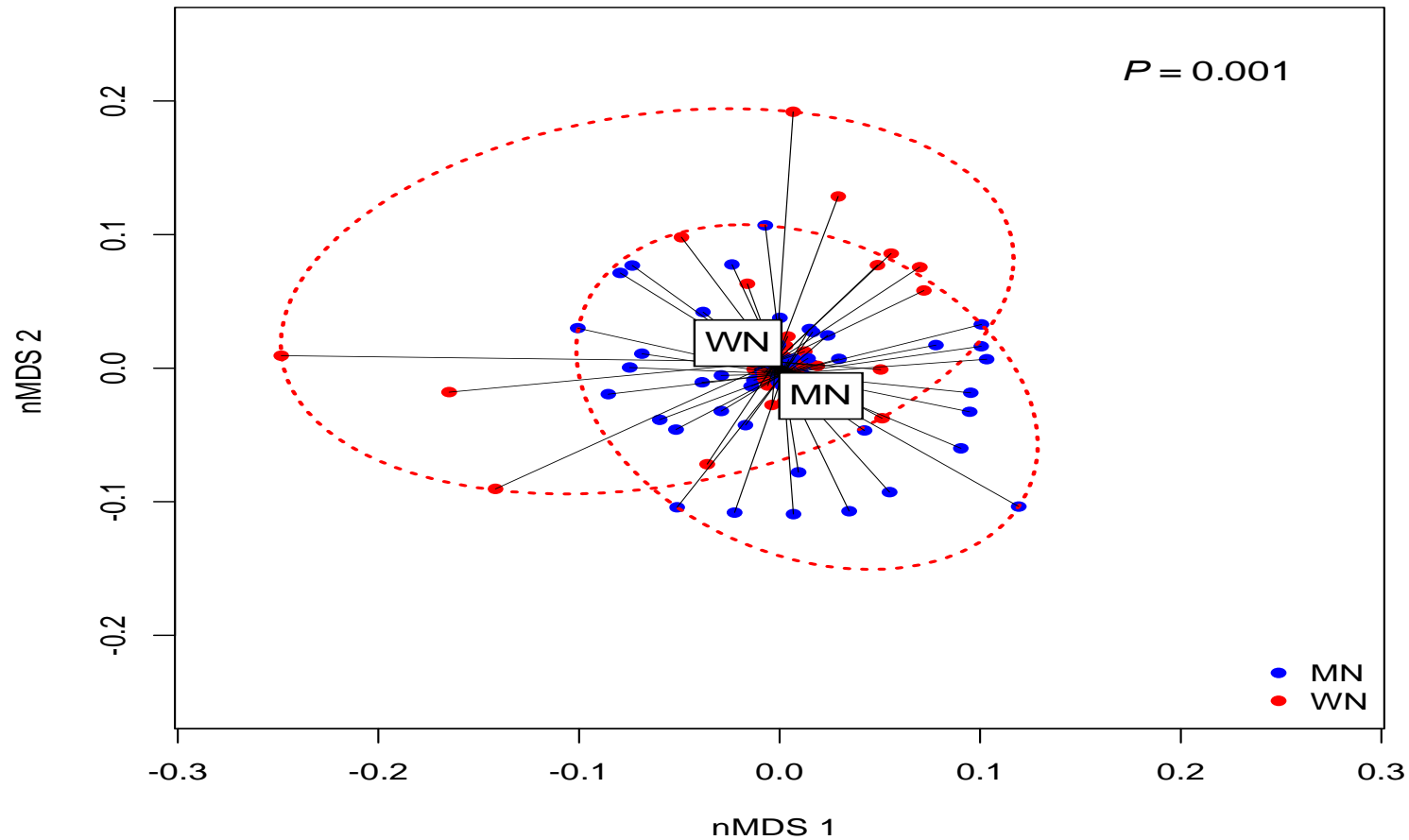
Vitamin composition compared to healthy population

Vitamins	DRI Adequate Intake/day (AI) ¹		Crohn's Patients (N=67)				Healthy Population (N=1547)	
	Males	Females	M (n=33) % of DRI	F (n=34) % of DRI	M (n=33) Daily intake (M±SE)	F (n=34) Daily intake (M±SE)	M (n=721) Usual intake ² (M±SE)	F (n=826) Usual intake ² (M±SE)
A RAE µg	900	700	69 (55)%	97 (162)%	609 (86)	682 (195)	667 (33)	577 (28)
D µg [@]	15-20		21 (20)%	16 (17)%	3 (0.5)**	2.5 (0.4)**	5.9 (0.3)	5.0 (0.3)
E α-tocopherol mg	15		48 (59)%	32 (28)%	5 (1.5)	7.1 (0.7)	n/a	n/a
K µg	120	90	52 (46)%*	106 (101)%*	61 (9.7)	97 (15.7)	n/a	n/a
C mg (N=1484)	90	75	121 (78)%	108 (84)%	106 (12)**	82 (11)**	143 (8) 92 (7)	113 (4)
Thiamin, B1 mg	1.2	1.1	115 (60)%*	82 (41)%*	1.4 (0.12)**	0.9 (0.08)**	2.0 (0.07)	1.4 (0.04)
Riboflavin, B2 mg	1.3	1.1	141 (67)%	113 (52)%	1.8 (0.15)	1.3 (0.10)**	2.1 (0.07)	1.6 (0.05)
Niacin, B3 NE	16	14	212 (113)%*	161 (76)%*	34 (2)**	23 (2)**	46 (2)	32 (1)
Pantothenic Acid, B5 mg	5		87 (46)%	68 (35)%	4.4 (0.4)	3.4 (0.3)	n/a	n/a
Pyridoxine, B6 mg ^t	1.3-1.7	1.3-1.5	119 (64)%*	86 (45)%*	1.8 (1.0)	1.2 (0.7)**	2.1 (0.1)	1.6 (0.1)
Biotin, B7 mg	30		47 (42)%*	25 (19)%*	14 (2.2)	8 (1.0)	n/a	n/a
Folate, B9 DFE µg	400		72 (32)%	61 (59)%	287 (34)**	244 (33)	488 (15)	325 (41)
Cobalamin, B12 µg	2.4		177 (123)%	130 (109)%	4.2 (0.5)	3.1 (0.5)	4.9 (0.3)	3.5 (0.2)
Choline mg [^]	550	425	43 (26)%	39 (23)%	229 (25)	165 (17)	n/a	n/a

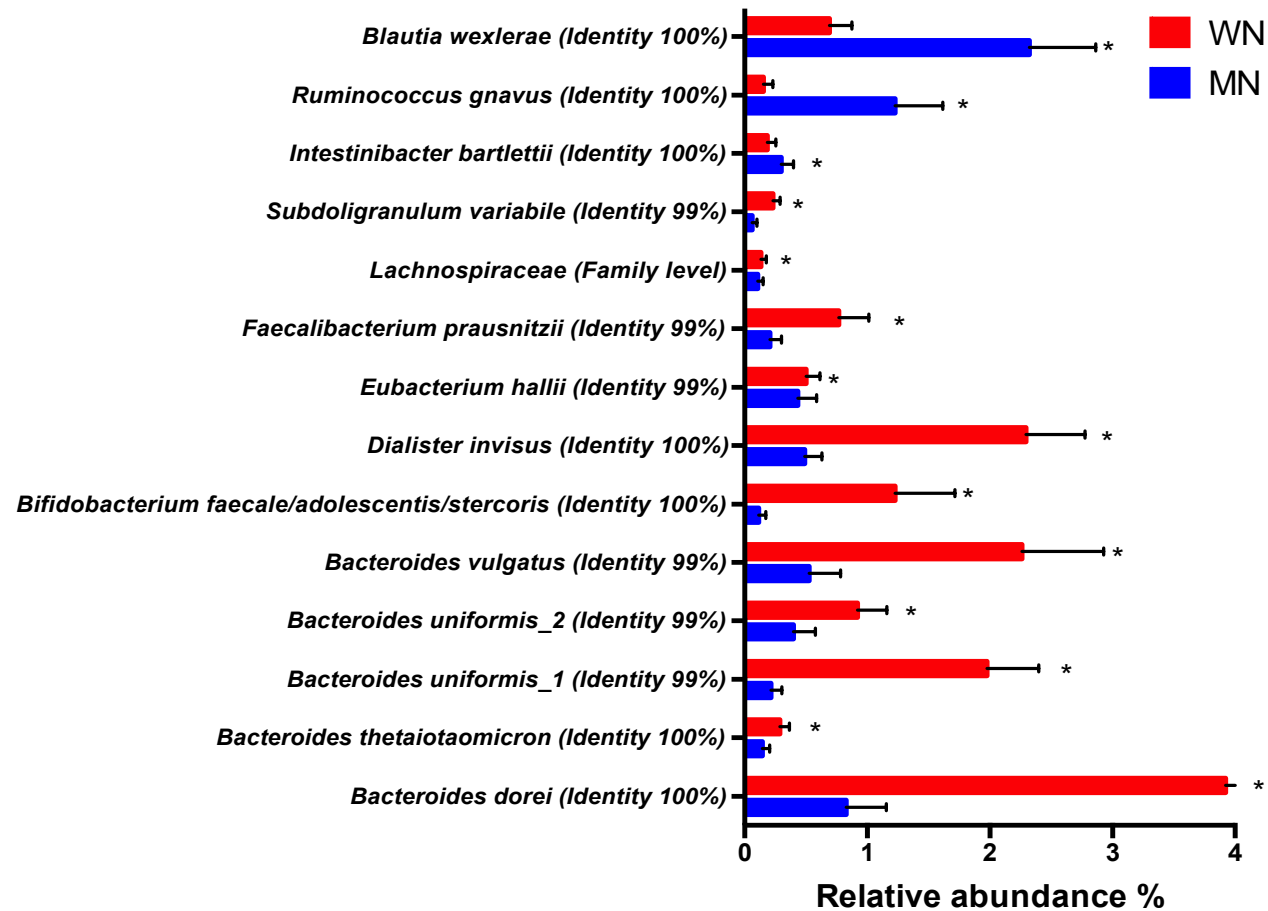
Comparison of α -diversity (richness) of gut microbiota between patients who have intake of AID vs NAID



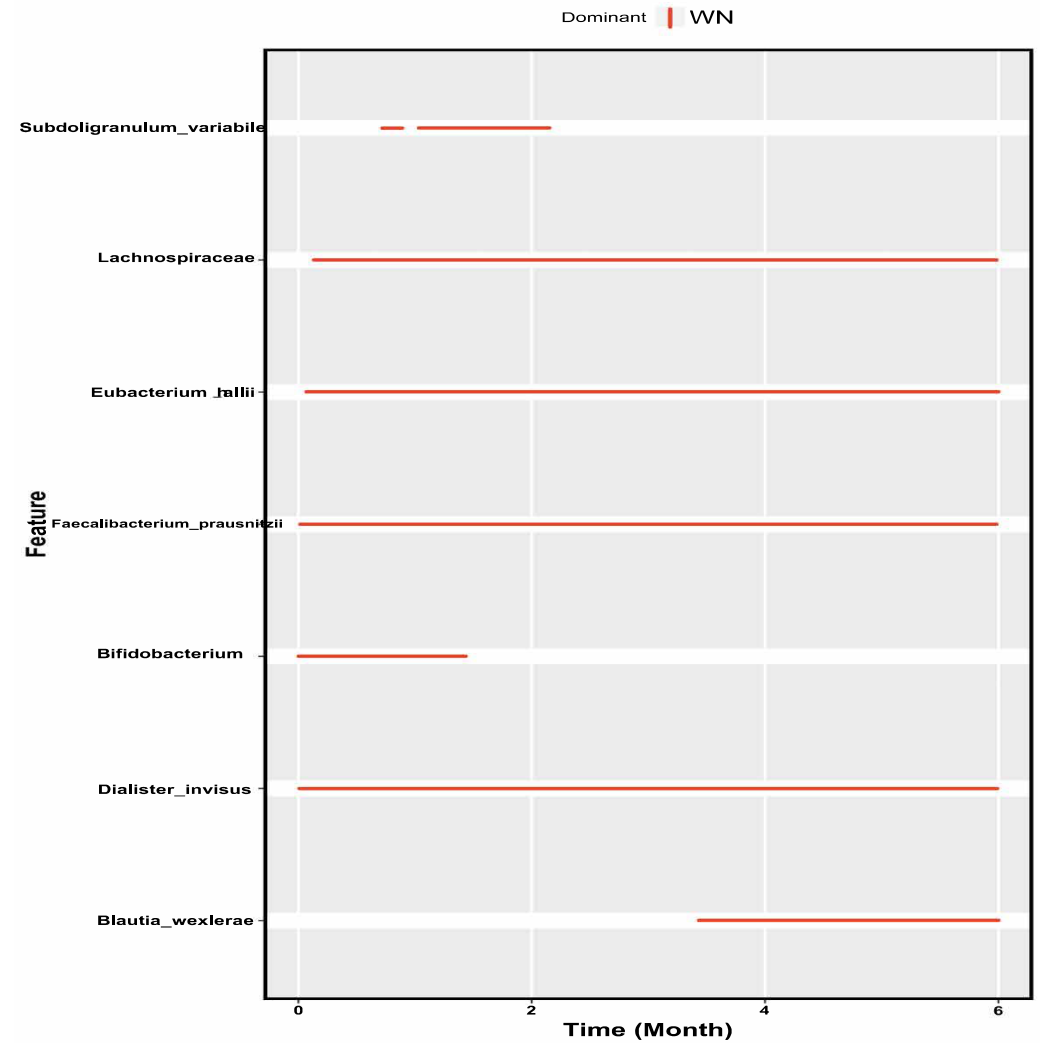
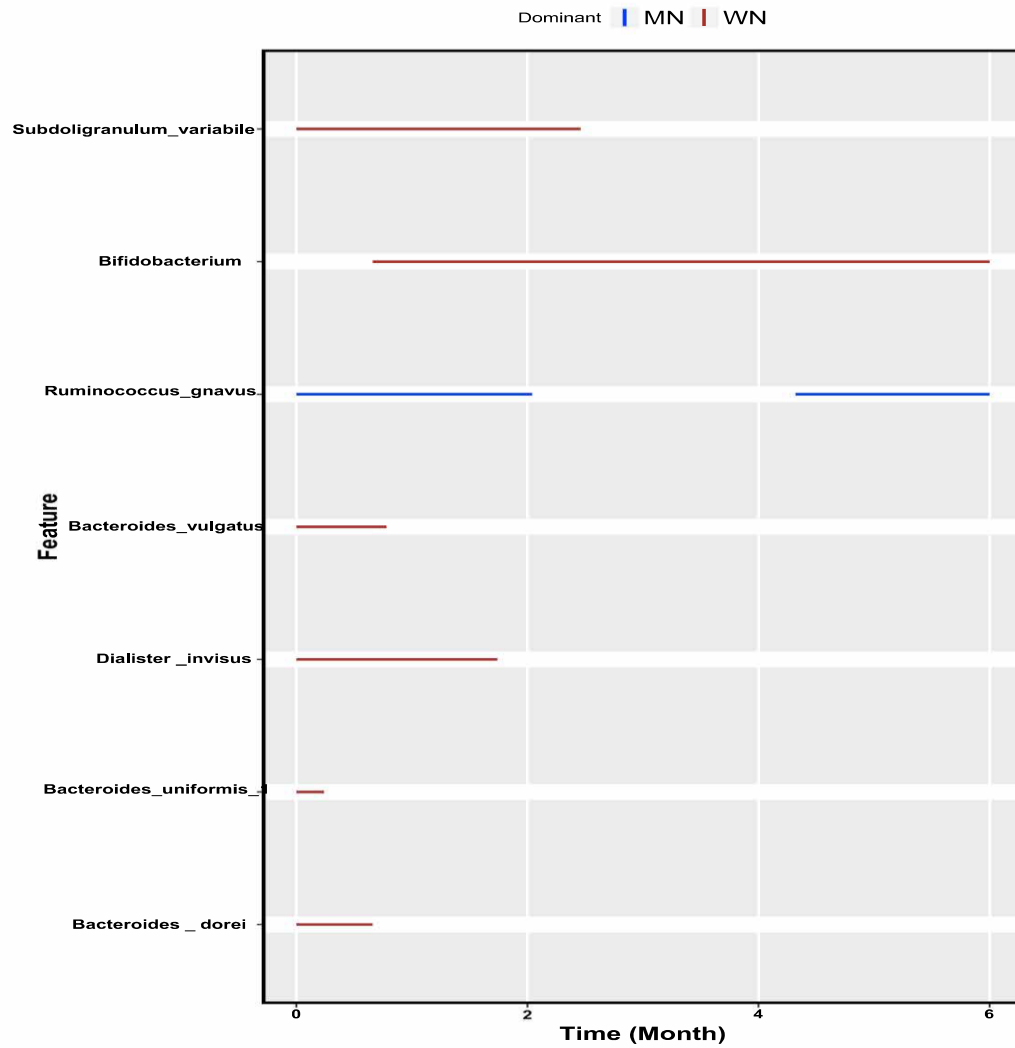
Comparison of β -diversity (richness) of gut microbiota between patients who have intake of AID vs NAID



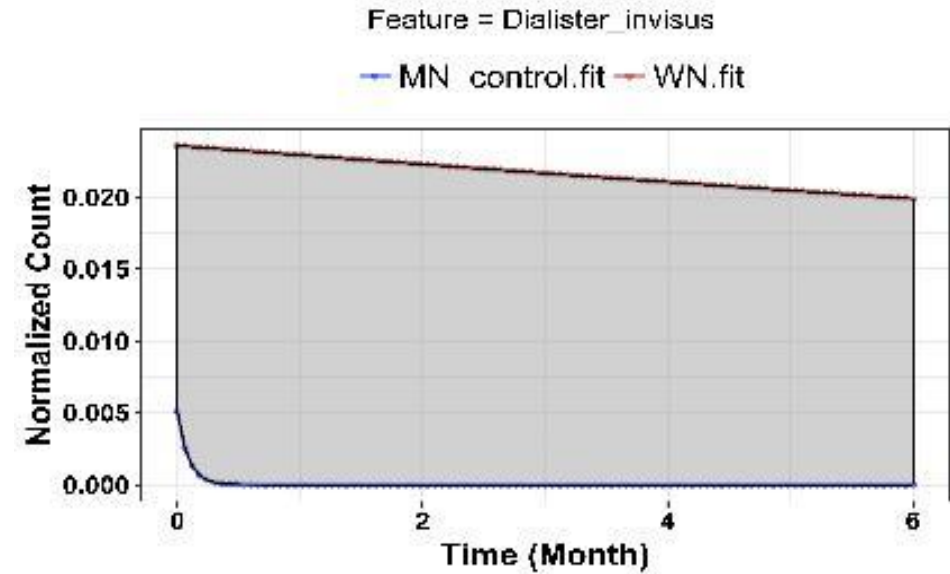
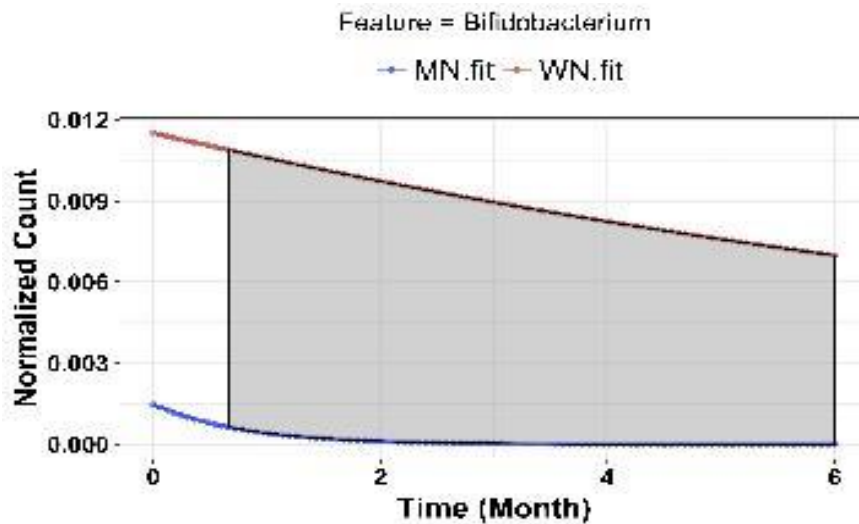
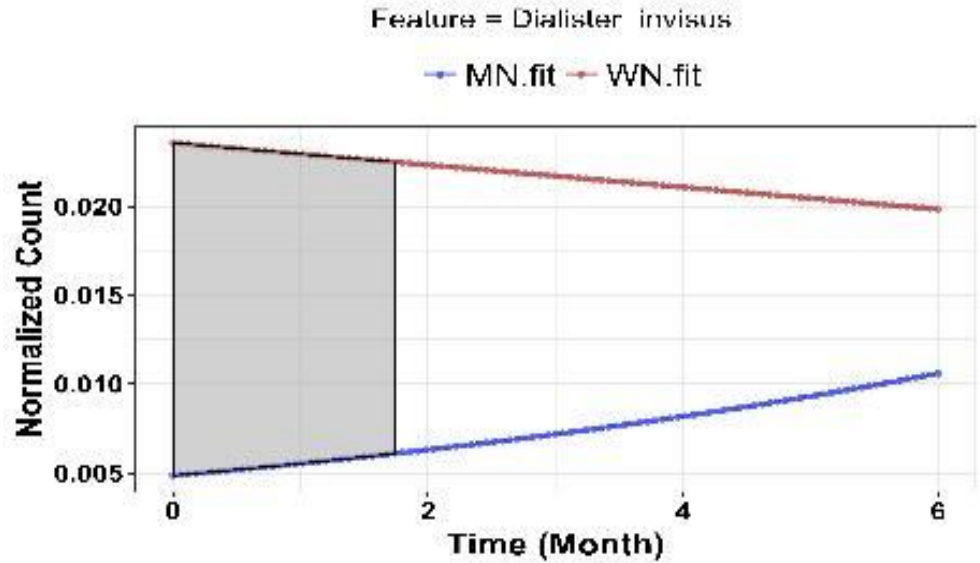
14 bacterial features in the gut microbial community show different relative abundance between AID and NAID



Shift in bacterial species dominance over time



Shift in bacterial species dominance over time



Relationship between MDS food groups and fecal calprotectin

MDS and Food Group Servings, mean (SD)	Fecal Calprotectin <250ug/g	Fecal calprotectin >250ug/g	P-value
MDS score out of 13	4.5 \pm 1.6	3.7 \pm 1.5	0.19
Total vegetables/day	2.2 \pm 2.2	1.4 \pm 1.1	0.26
Leafy greens/day	0.7 \pm 0.8	0.1 \pm 0.2	<0.01
Fruit/day	1.8 \pm 1.4	1.9 \pm 1.7	0.83
Red and processed meat/wk	0.5 \pm 0.7	0.9 \pm 1.1	0.24
Legumes/wk	0.7 \pm 1.3	0.0 \pm 0.0	0.01
Fish/wk	5.1 \pm 6.4	1.5 \pm 3.3	0.04

MDS score components and relationship with peripheral cytokines

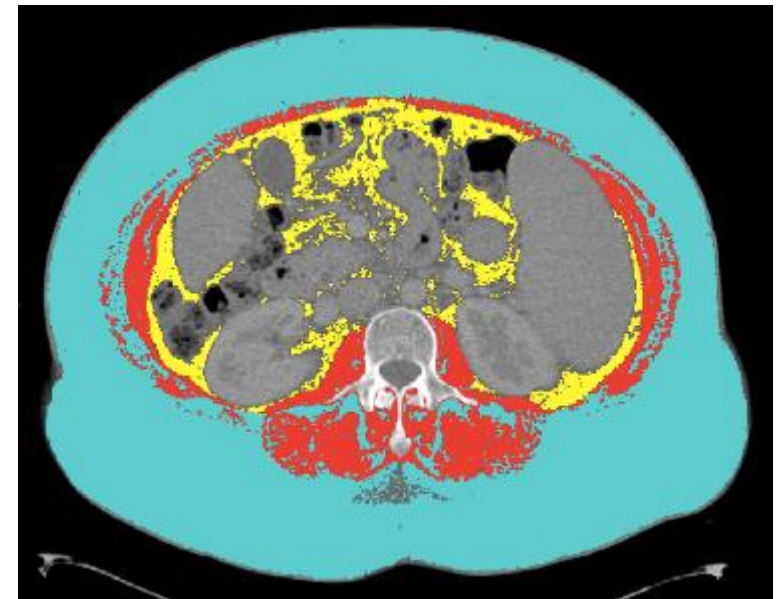
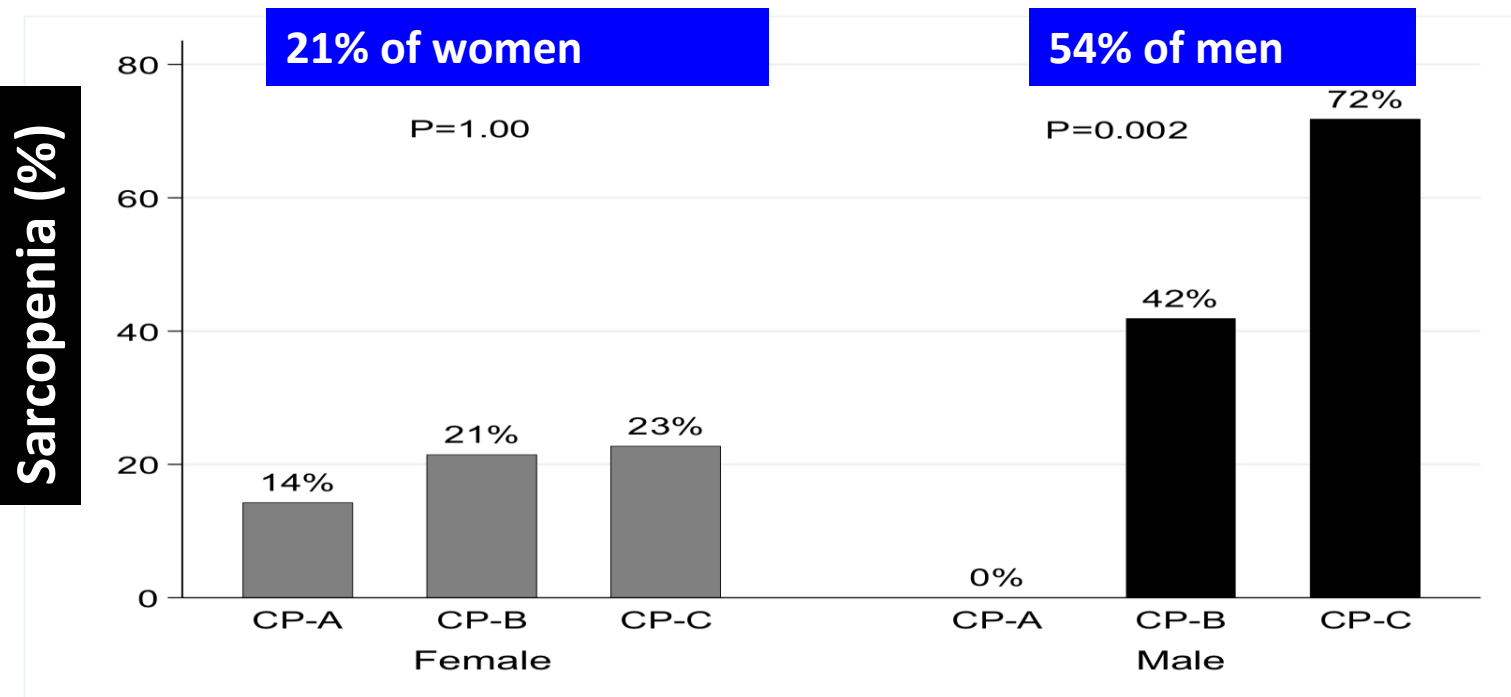
Dietary measure	Significant cytokines at month 3	Correlation
MDS Totals (mean, SD)	IFN-g	-0.4
Fruit *plus juice CFG servings (mean, SD)	IL-1b F: IL-1b F: IL-17A	0.4 0.5 0.5
Total veg CFG servings (mean, SD)	IFN-g	-0.5
Red and processed meat CFG servings (mean, SD)	F: IFN-g M: IL-27	0.7 -0.6
Legumes CFG servings / week (median, IQR)	CRP F: IL-6	-0.4 -0.6

Diet IBD conclusions

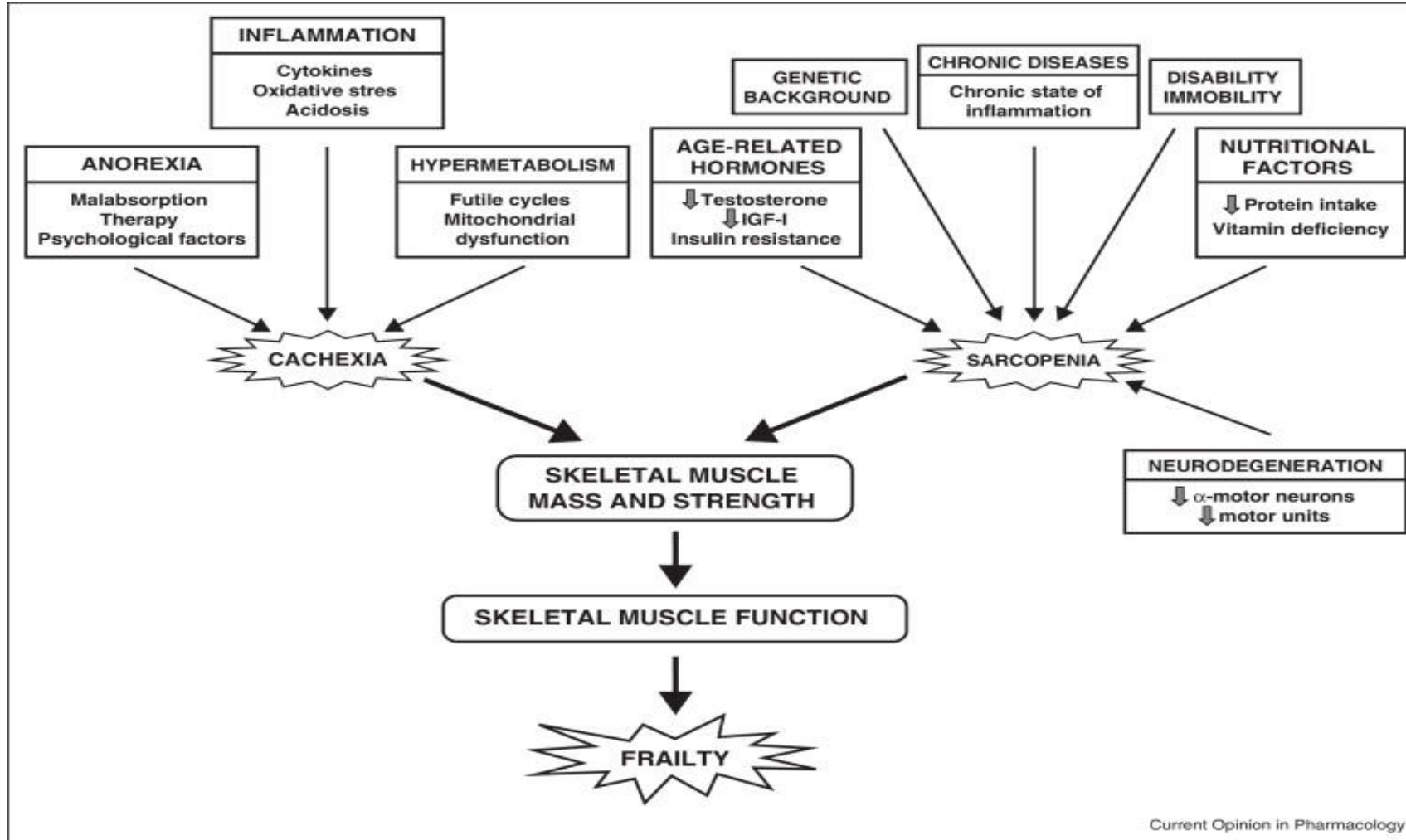
- Greater interest in exploring dietary patterns and composition
- Signals for clinical improvements
 - Anti-Inflammatory diets
 - SCD
 - Mechanistically plausible
 - Microbiome
 - Inflammatory markers
 - Relationship with fecal calprotectin
- **Further high quality trials needed**

Prevalence of malnutrition in cirrhosis

- **Malnutrition is common**, varies with the tool for measurement
- Prevalence increases with worsening liver disease severity



Differential factors involved in cachexia and sarcopenia

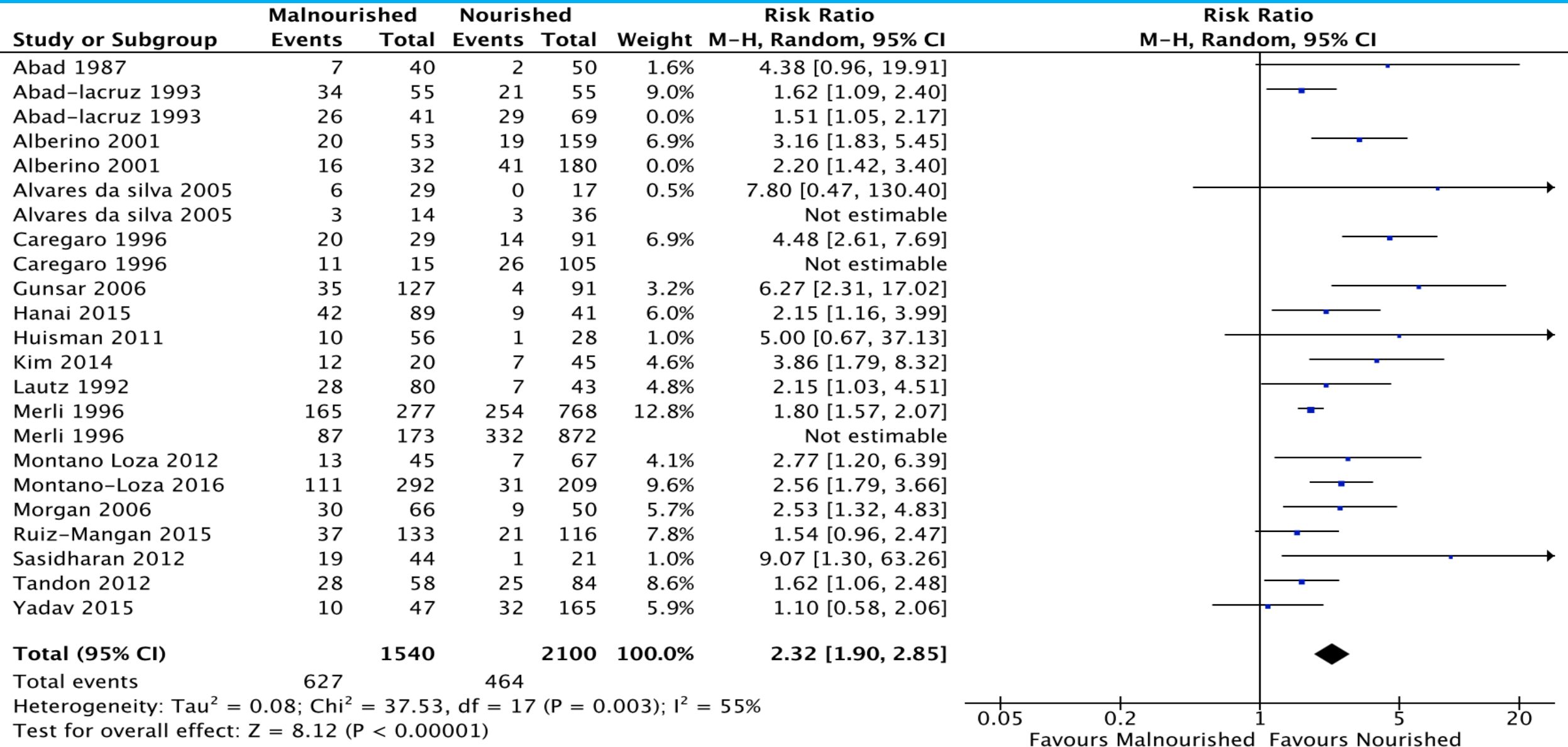


Research tools and clinical tools for diagnosing sarcopenia

Measurements of muscle mass, strength, and function in research and practice

Variable	Research	Clinical practice
Muscle mass	Computed tomography (CT) MRI Dual energy x-ray Absorptiometry (DXA) Bioimpedance analysis (BIA) Total or partial body potassium per fat-free soft tissue	BIA DXA Anthropometry
Muscle strength	Handgrip strength Knee flexion/extension Peak expiratory flow	
Physical performance	Short physical performance battery (SPPB) Usual gait speed Timed get-up-and-go test Stair climb power test	SPPB Usual gait speed Get-up-and-go test

Nutritional assessment tools predict pre-transplant mortality in a pooled analysis of 18 studies (N=3640 patients)



Malnutrition clinic

- High nutrition risk patients with cirrhosis (pre-transplant +) and IBD
- Combined assessment RD + MD
- Calorie / protein targets, nocturnal meals, diet quality, exercise
 - Recently updated nutrition guidelines
- F/U frequency based on nutrition assessment status

Malnutrition clinic

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Objective

- To identify if a personalized nutrition intervention in malnourished pre-transplant patients impacted clinical outcomes at 6-12 months following intervention

Methods

- Prospective cohort study
- Nutrition assessment data
 - SGA
 - HGS
 - MAC
- Clinical outcome data
 - Frequency of hospitalization
 - Infection
 - Hepatic encephalopathy
 - Mortality
 - Quality of Life

SGA and HGS predict mortality in patients with cirrhosis

	SGA		MUAC		HGS kg	
Mortality	$\chi^2(2) = 6.6, p=0.04$		$\chi^2(1) = 1.15, p=0.28$		$\chi^2(1) = 13.8, p<0.001$	
	Yes	No	Yes	No	Yes	No
Well nourished	A: 2, 9.5%	16, 35.6%	4, 19.0%	16, 35.6%	5,	34,
Less nourished	B: 9, 42.9%	19, 42.2%	17, 81%	29, 64.4%	23.8%	75.6%
	C: 10, 47.6%	10, 22.2%			16, 76.2%	11, 24.4%

Nutrition assessment and clinical outcome variables over time

Characteristic (n=43)	Baseline (mean \pm SD)	6-12 month F/U (mean \pm SD)	P-value
Dry BMI	22.7 \pm 3.9	23.5 \pm 3.9	<0.01
MAC (cm)	26.5 \pm 4.0	26.9 \pm 3.6	<0.01
HGS (Kg)	23.6 \pm 8.1	24.2 \pm 9.0	<0.01
MELD-Na	15.1 \pm 5.2	14.4 \pm 4.9	<0.01

- Significantly improved SGA status at follow-up
- Worsening SGA at follow-up vs. baseline was associated:
 - Increased infections ($X^2(1)=7.93$, $p<0.01$)
 - HE ($X^2(1)=5.82$, $p<0.05$)
 - Increased hospital length of stay (23 vs. 10 days)

Length of stay (bed days) by nutritional status

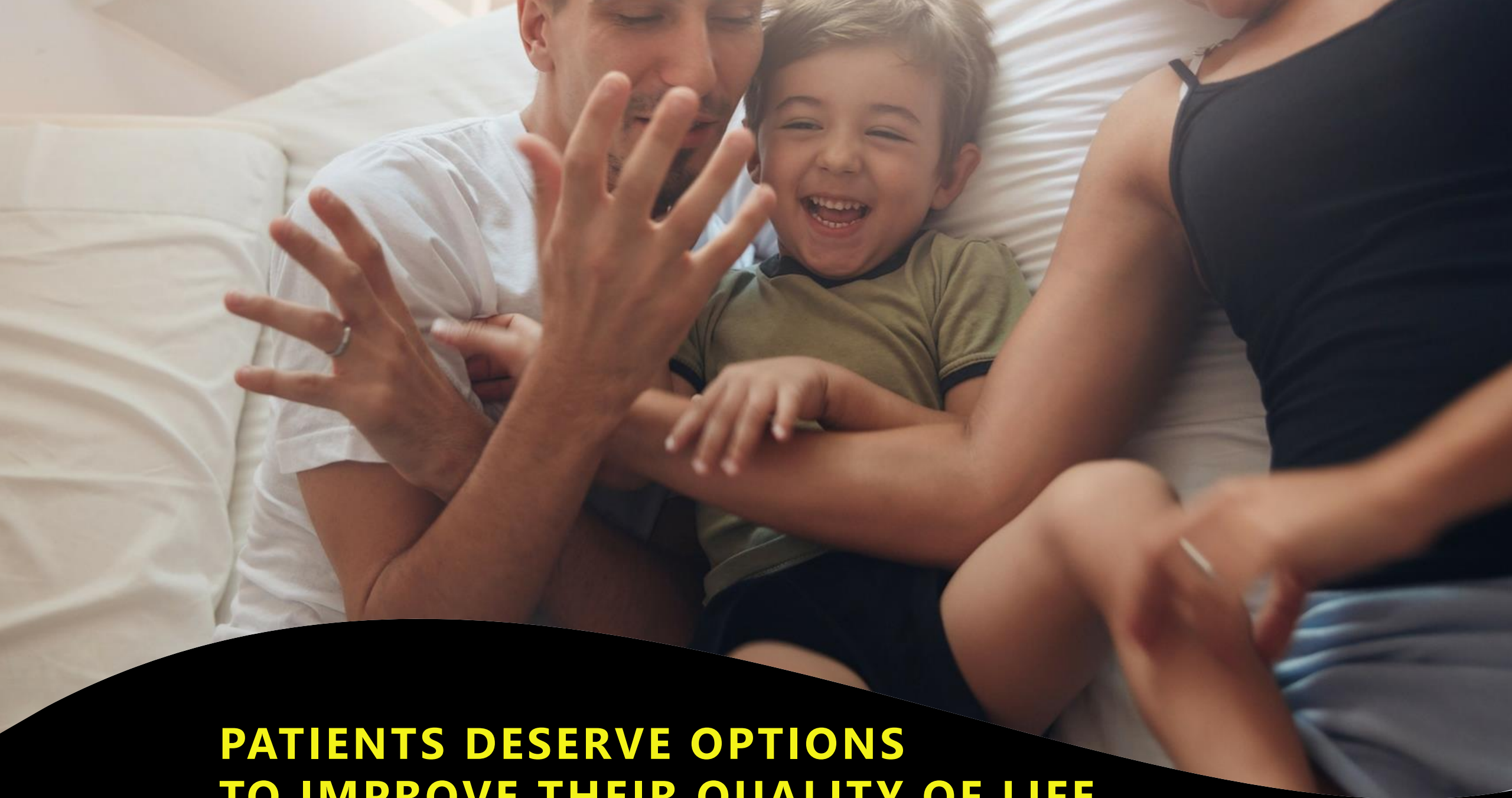
	Nourished	Moderately Malnourished	Severely Malnourished
Total N=958	8.43 [0.65]	11.66 [1.17]*	11.70 [0.96]*
Medical N=632	8.20 [0.95]	12.05 [1.32]*	12.05 [1.33]*
Surgical N=301	6.98 [0.65]	9.62 [1.39]*	8.75 [1.11]*

Costs by nutritional status

	Nourished	Moderately Malnourished	Severely Malnourished
Total N=958	\$5074 [512]	\$7931 [766]*	\$7989 [976]*
Medical N=632	\$4839 [593]	\$7825 [849]*	\$7823 [1042]*
Surgical N=301	\$4303 [681]	\$7154 [1660]*	\$6744 [1435]*

Associations between SF-36 subscales and NATs and MELD-Na

SF-36 Subscale	SGA	HGS	MAC	MELD-Na
Physical Function	✓	✓	✗	✗
Role Physical	✓	✗	✗	✗
Vitality	✓	✗	✗	✗
Social Function	✓	✗	✗	✗
Bodily Pain	✗	✗	✗	✗
General Health	✓	✗	✗	✗
Emotional Role	✓	✗	✗	✗
Mental Health	✗	✗	✗	✗



**PATIENTS DESERVE OPTIONS
TO IMPROVE THEIR QUALITY OF LIFE**

Appointment
help

Symptom
tracking

Support
network

Grocery lists
and orders

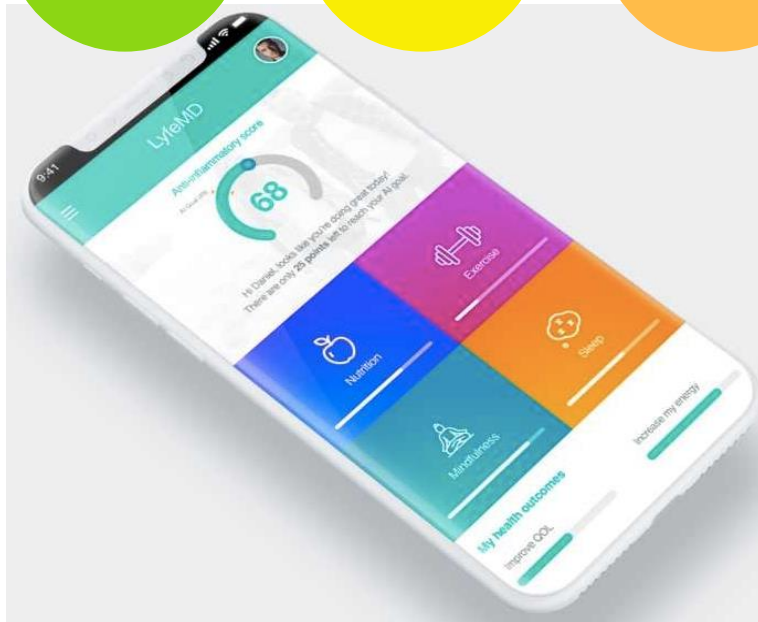
Nutrition
tracking

Anti-
inflammatory
index

Stress
management

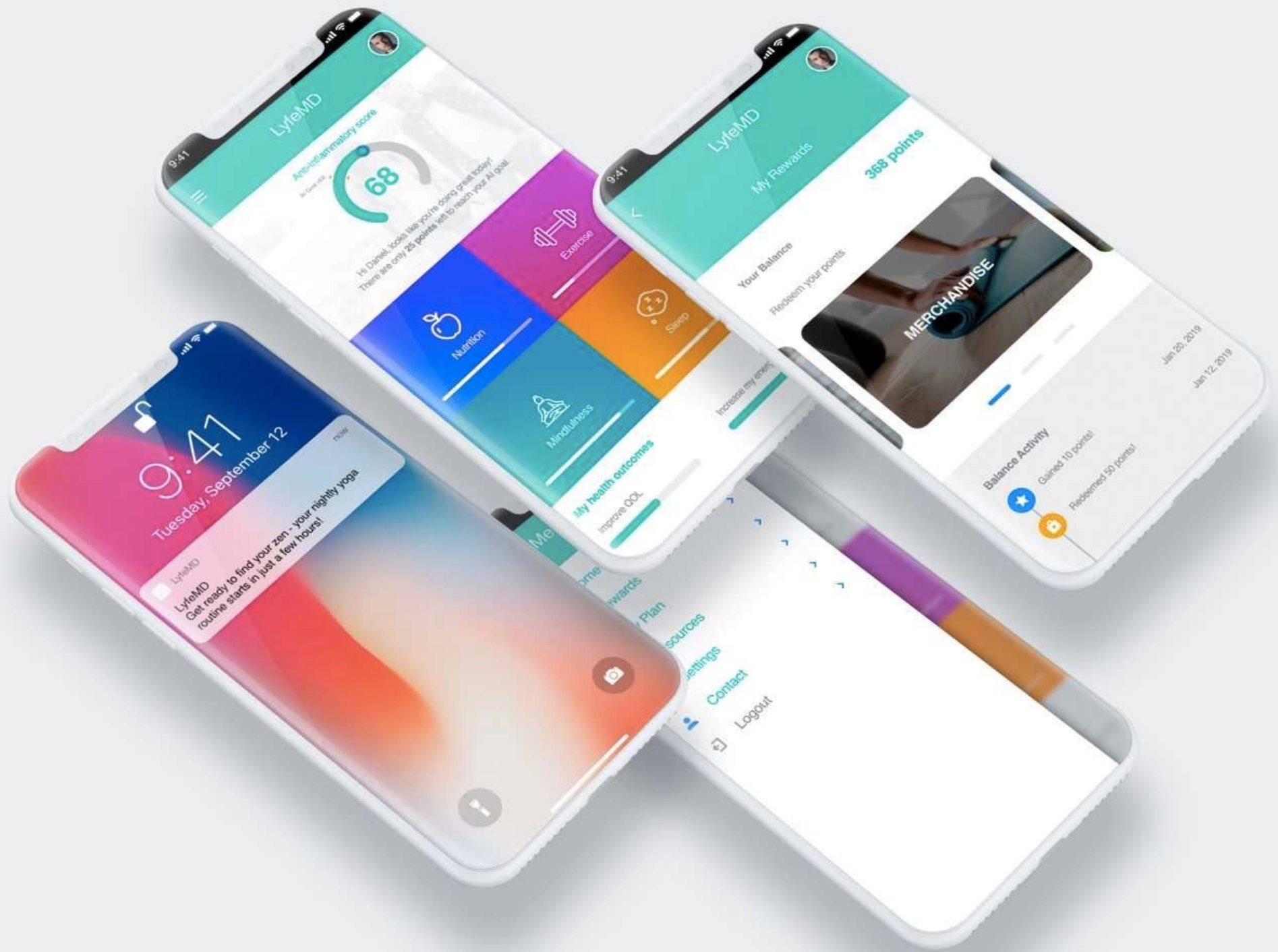
Personalized
meal plans

Nudges



THE Lyfe^{MD} APP

EMPOWERING PATIENTS
MANAGE IBD



LyfeMD



- Nutrition
- Exercise
- Sleep
- Mindfulness
- My health outcomes

LyfeMD

My Rewards

368 points

Your Balance

Redeem your points



Balance Activity

- Gained 10 points
- Redeemed 50 points

Jan 26, 2019

Jan 12, 2019

9:41

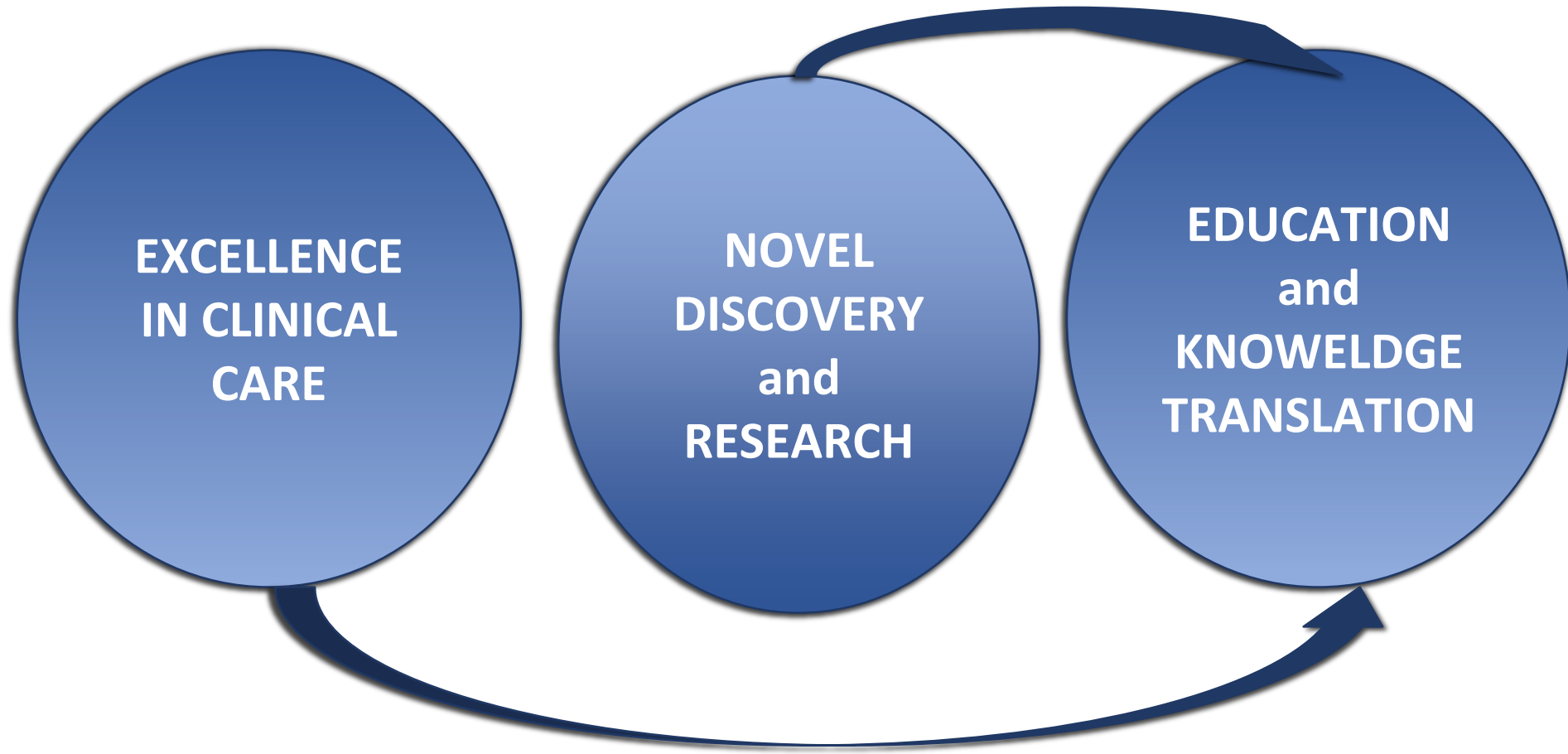
Tuesday, September 12

LyfeMD

LyfeMD
Get ready to find your zen - your nightly yoga routine starts in just a few hours!

- Home
- My Rewards
- My Plan
- Resources
- Settings
- Contact
- Logout

Ascend: Alberta's Collaboration of Excellence for Nutrition in Digestive Diseases



Conclusions

- Malnutrition is common in cirrhosis and associated with increased clinical complications and poor QOL
- Nutrition therapy is of benefit in malnourished patients with cirrhosis
- Consider integrating both SGA in addition to a muscle measure (HGS/MAC/US) to assess muscle mass and quality
- Integrate physical activity to optimize muscle health

Thanks

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- Dr. Mark Swain
- Dr. Leah Gramlich
- Mr. Ankush Kumar
- Dr. Nusrat Shommu

The logo for 'Ascend' features the word 'Ascend' in a white, sans-serif font, centered within a dark blue, stylized shape that resembles a wave or a drop. This shape is surrounded by several concentric, lighter blue layers, creating a sense of depth and movement. The overall design is clean and modern.

Ascend

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