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Voedselintoleranties
Feiten en Fabels

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Gastroenterology and Hepatology University Hospitals Leuven
Leuven Intestinal Failure and Transplantation (LIFT)
Translational Research Center for Gastrointestinal Disorders (TARGID)

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Overzicht

- Voedselallergie vs. intolerantie
- Prikkelbare Darmsyndroom
- Specifieke Intoleranties: - Lactose
  - Fructose
  - FODMAPs
  (- Gluten)



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Overzicht

- **Voedselallergie vs. intolerantie**
- Prikkelbare Darmsyndroom
- Specifieke Intoleranties: - Lactose
  - Fructose
  - FODMAPs



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Voedselallergie vs. intolerantie

Allergie: - Immunologische reactie (IgE of non-Ig E) tegen specifiek allergeen

- 1-3% prevalentie bij volwassenen (>< 15% bij zelf rapportering)
- Stijgende incidentie zonder duidelijke verklaring.
- Geen overtuigend verband met IBS
- Extraintestinale symptomen (jeuk, rash, dyspnoe, …)
- Meestal typisch, stereotiep patroon bij ingestie 1 product
- Diagnostiek: Huidtesten
  Specifieke IgE bepaling
  (dubbel-blinde) Orale Provocatietesten
  Géén rol voor IgG_1 en IgG_4 bepalingen

Intolerantie: niet-immunologisch gemedieerde symptomen na voedselinname

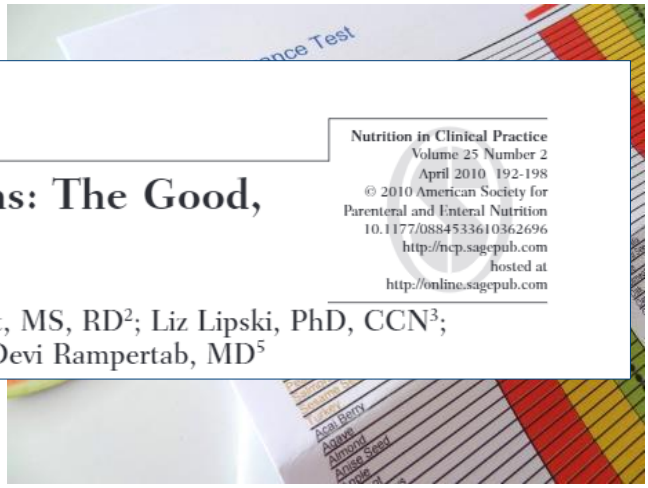
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Rona et al. J Allergy Clin Immunol 2007

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Voedselallergie vs. intolerantie

The Great Plains Laboratory, Inc.

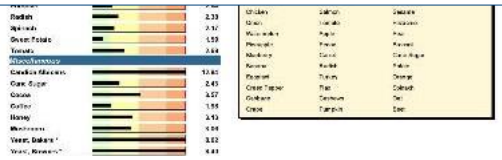


Techniques, Materials, Devices

Testing for Food Reactions: The Good, the Bad, and the Ugly

Gerard E. Mullin, MD[1]; Kathie M. Swift, MS, RD[2]; Liz Lipski, PhD, CCN[3]; Laura K. Turnbull, BS, MSNc[4]; and S. Devi Rampertab, MD[5]

Nutrition in Clinical Practice
Volume 25 Number 2
April 2010 192-198
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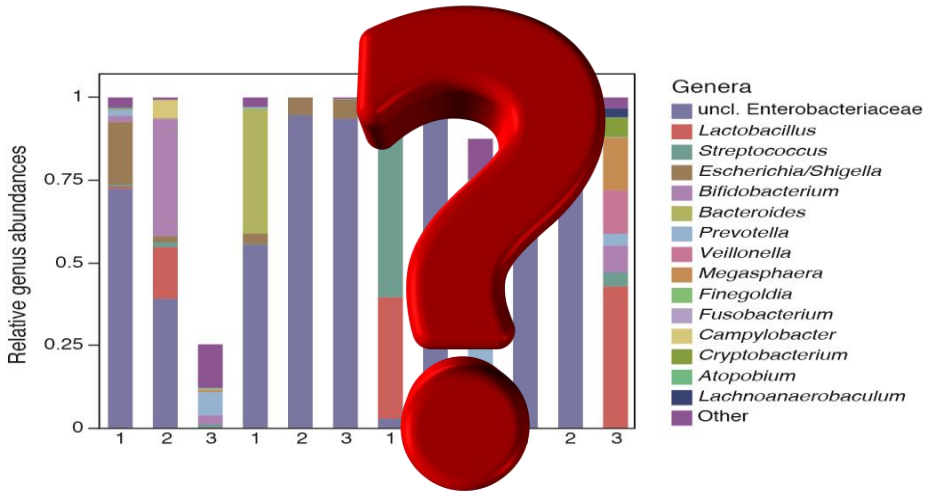


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http://www.labtestsplus.com

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Voedselallergie vs. intolerantie

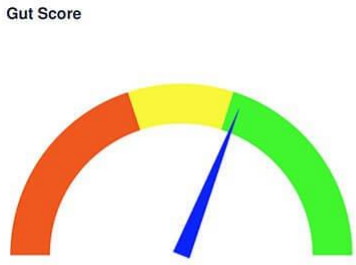


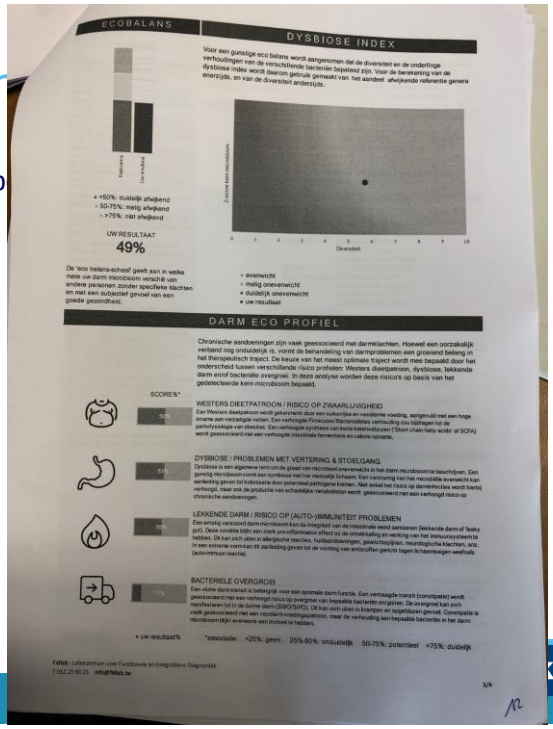
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Voedselallergie vs. in

Wildgroei aan commerciële, niet terugb





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IgG testing?

150 IBS patients (Rome II)

IgG ELISA against 29 common food antigens (YorkTest laboratories Ltd)

Sham diet vs. IgG-based diet during 12 weeks

‘Designed by the staff of YorkTest laboratories’

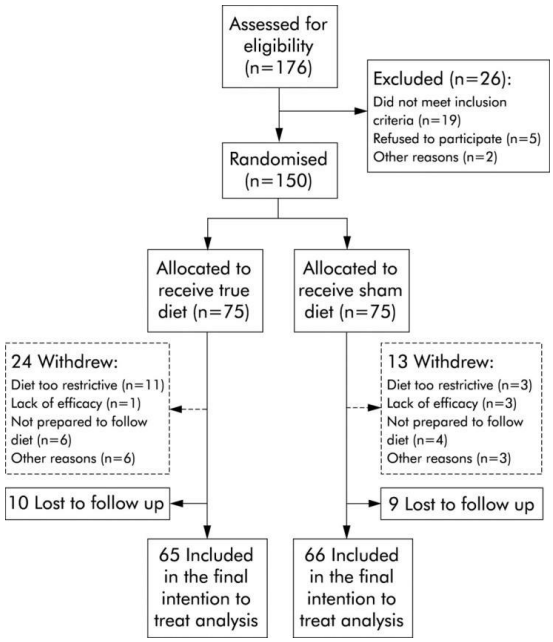
Same number of food items eliminated as in the ‘true diet’

Cow’s milk -> potato
Wheat -> rice
Yeast -> egg
Specific nuts -> other nuts
Specific legumes -> other legumes

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Atkinson et al. Gut 2004

IgG testing?



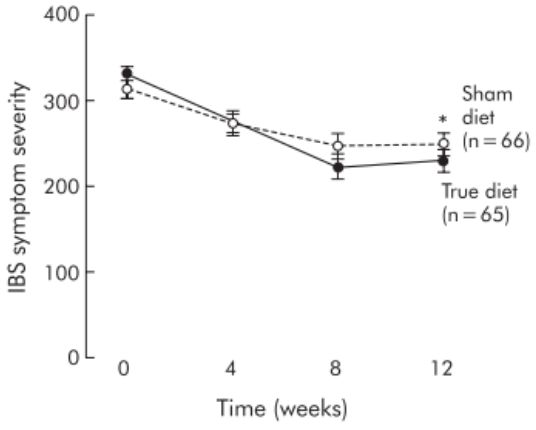
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Atkinson et al. Gut 2004

9

IgG testing?

Food	Treatment group	Sham group
Barley	26.7	9.3
Corn	22.7	14.7
[illegible]	[illegible]	[illegible]
Fish mix	17.3	28
Whole egg	57.3	26.7
Yeast	86.7	0



Atkinson et al. Gut 2004

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Overzicht

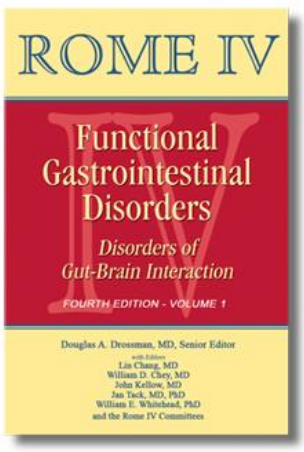
- Voedselallergie vs. intolerantie
- **Prikkelbare Darmsyndroom**
- Specifieke Intoleranties: - Lactose
  - Fructose
  - FODMAPs
  - Gluten



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Prikkelbare Darmsyndroom (IBS): Rome IV



Recurrent abdominal pain **>1 day/week in the last 3 months**

+ 2 or more of

A	B	C
Related to defecation	**Associated with change in frequency of stool**	**Associated with change in form of stool**

Criteria present for the last 3 months and onset at least 6 months prior to diagnosis

In the absence of an organic, systemic or metabolic cause likely to explain the symptoms.

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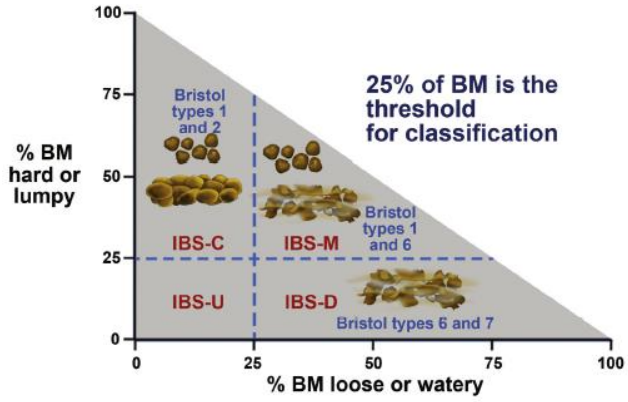
Lacy et al. Gastroenterology 2016

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Prikkelbare Darmsyndroom (IBS): Rome IV

Bristol Stool Form Scale

	Type 1 Separate hard lumps, like nuts (hard to pass)
	Type 2 Sausage-shaped, but lumpy
	Type 3 Sausage-shaped, but with cracks on surface
	Type 4 Sausage or snake like, smooth and soft
	Type 5 Soft blobs with clear-cut edges (easy to pass)
	Type 6 Fluffy pieces with ragged edges, mushy
	Type 7 Watery, no solid pieces (entirely liquid)

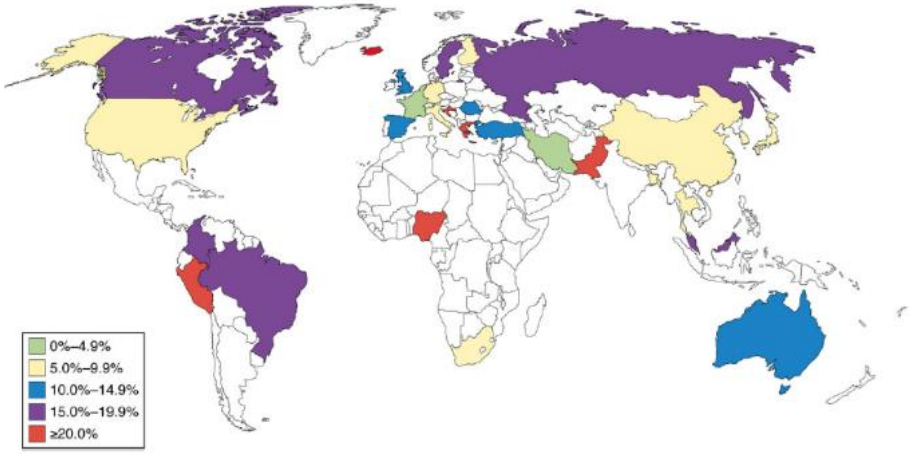


Lacy et al. Gastroenterology 2016

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IBS: Facts and Figures

- 5 – 15 % prevalentie wereldwijd



Lovell et al. Clin Gastroenterol Hepatol 2012

14

IBS: Facts and Figures

- 5 – 15 % prevalentie wereldwijd
- Meest frequente diagnose binnen gastro-enterologie: 28%
- Vrouwen > Mannen
- Negatieve impact of levenskwaliteit



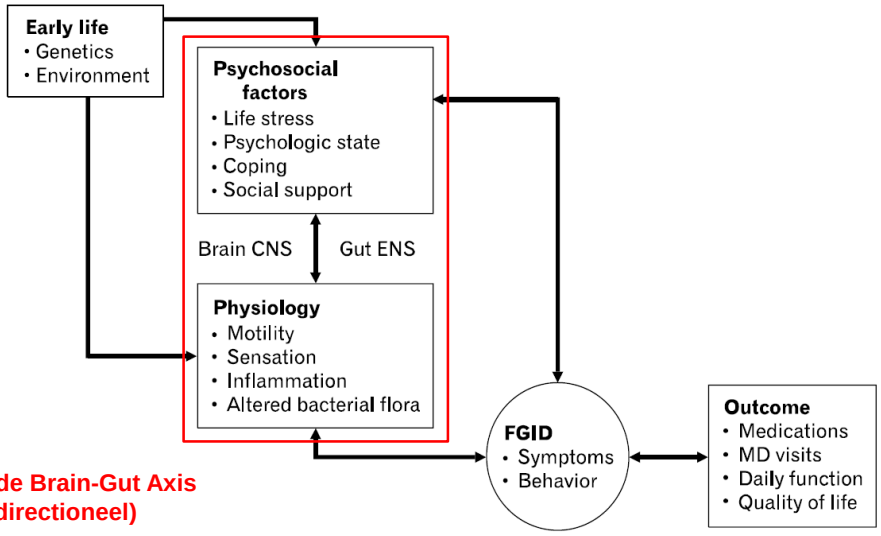
"I'm afraid that your irritable bowel syndrome has progressed. You now have furious and vindictive bowel syndrome."

Creed et al. Ann Intern Med 2001 Monnikes et al. J Clin Gastroenterol 2011 Koloski et al. Qual Life Res 2012

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IBS: Biopsychosociaal Model



Ontregelde Brain-Gut Axis (bi-directioneel)

Drossman et al. Gut 1999 Tanaka et al. J Neurogastroenterol Motil 2011

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IBS: rol van voeding

60-85% associeert S/ met voeding

Food	Most common symptom		
	1	2	3
Cabbage 188 (57%)	Gas problems 99 (30%)	Pain 38 (12%)	Distension 25 (8%)
Onion 186 (56%)	Gas problems 96 (29%)	Pain 41 (12%)	Dyspepsia 28 (8%)
Peas/beans 153 (46%)	Gas problems 76 (23%)	Pain 27 (8%)	Distension 21 (6%)
Hot spices 149 (45%)	Pain 44 (13%)	Dyspepsia 22 (6%)	Loose stools 20 (6%)
Deep-fried food 145 (44%)	Dyspepsia 41 (12%)	Pain 35 (11%)	Gas problems 22 (6%)
Pizza 144 (44%)	Pain 38 (12%)	Dyspepsia 36 (11%)	Loose stools 27 (8%)
Coffee 128 (39%)	Dyspepsia 34 (10%)	Pain 33 (10%)	Loose stools 30 (9%)
Cream 122 (37%)	Pain 41 (12%)	Loose stools 36 (11%)	Dyspepsia 30 (9%)
Smoked food 116 (35%)	Dyspepsia 30 (9%)	Pain 29 (9%)	Reflux 13 (4%)
Fried food 115 (35%)	Pain 31 (9%)	Dyspepsia 30 (9%)	Gas problems 14 (4%)

2/3 patiënten past voeding aan

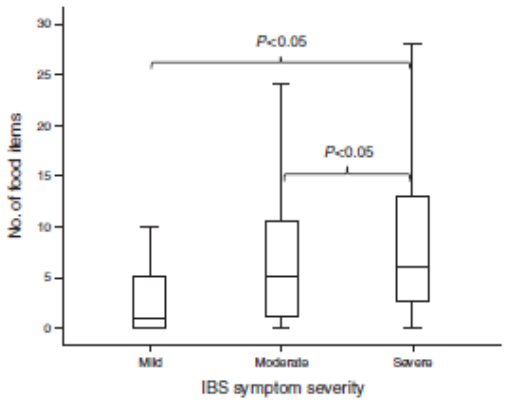
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Simren et al. Digestion 2001 Monsbakken et al. Eur J Clin Nutr 2006 Bohn et al . Am J Gastroenterol 2013

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IBS: rol van voeding

60-85% associeert S/ met voeding
Het aantal gerapporteerde intoleranties hangt samen met ernst van IBS



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Bohn et al . Am J Gastroenterol 2013

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IBS: rol van voeding

25 patients with diagnosis of IBS-D
Limit diet to 1 meat, 1 fruit and distilled water
Followed by reintroduction steps

FOOD INTOLERANCE: A MAJOR FACTOR IN THE PATHOGENESIS OF IRRITABLE BOWEL SYNDROME

V. ALUN JONES P. MCLAUGHLAN
M. SHORTHOUSE E. WORKMAN
J. O. HUNTER

Department of Gastroenterology, Addenbrooke's Hospital, Cambridge, and Department of Immunology, University of Cambridge

Results:
4 patients refused to try the diet
14/21 were free of symptoms
Provoking food items: wheat (9), corn (5), dairy (4), coffee (4), tea (3), citrus (2)

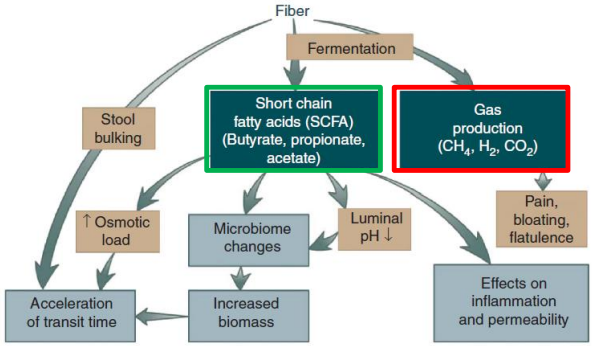
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Jones et al. Lancet 1982

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Vezels

- Koolhydraten
- Niet verteerd of geabsorbeerd in maag en dunne darm
- Effect door fermentatie in het colon tot korte keten vetzuren en gassen



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Eswaran et al. Am J Gastroenterol 2013

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Vezels

- Koolhydraten
- Niet verteerd of geabsorbeerd in maag en dunne darm
- Effect door fermentatie in het colon tot korte keten vetzuren en gassen

- toegenomen fecale massa (microbioom + vezel + vocht)
- rechtstreekse energiebron voor colonocyten
- versnelde transit

Vezelparadox

- flatulentie
- abdominale opzetting
- pijnklachten

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Eswaran et al. Am J Gastroenterol 2013

21

Vezels

- Koolhydraten
- Niet verteerd of geabsorbeerd in maag en dunne darm
- Effect door fermentatie in het colon tot korte keten vetzuren en gassen

Fibre source	Better	Worse	Unchanged
Bran	10 (10%)	55 (55%)	35 (33%)
Cornflakes	0	0	88 (100%)
Rice Crispies	0	0	81 (100%)
Porridge	0	9 (12%)	66 (88%)
Muesli	0	21 (27%)	58 (73%)
Vegetables	3 (3%)	24 (25%)	71 (72%)
Fruit	5 (5%)	42 (45%)	47 (50%)
Pulses	0	22 (25%)	65 (75%)
Nuts	0	23 (27%)	61 (73%)
Proprietary fibre	27 (39%)	15 (22%)	27 (39%)

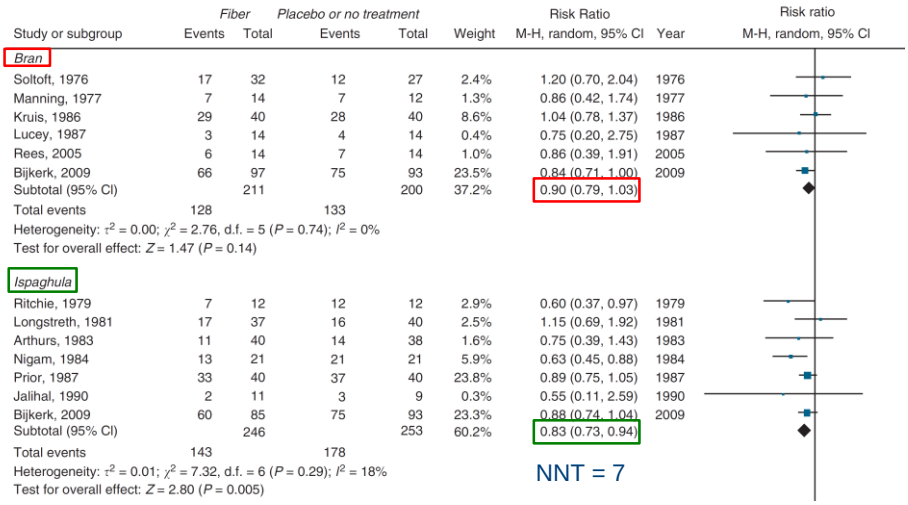
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Francis and Whorwell Lancet 1994

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Vezels

Study or subgroup	Fiber Events	Fiber Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio M-H, random, 95% CI	Year
Bran							
Soltoft, 1976	17	32	12	27	2.4%	1.20 (0.70, 2.04)	1976
Manning, 1977	7	14	7	12	1.3%	0.86 (0.42, 1.74)	1977
Kruis, 1986	29	40	28	40	8.6%	1.04 (0.78, 1.37)	1986
Lucey, 1987	3	14	4	14	0.4%	0.75 (0.20, 2.75)	1987
Rees, 2005	6	14	7	14	1.0%	0.86 (0.39, 1.91)	2005
Bijkerk, 2009	66	97	75	93	23.5%	0.84 (0.71, 1.00)	2009
Subtotal (95% CI)		211		200	37.2%	0.90 (0.79, 1.03)	
Total events	128		133				
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 2.76$, d.f. = 5 ($P = 0.74$); $I^2 = 0\%$							
Test for overall effect: $Z = 1.47$ ($P = 0.14$)							
Ispaghula							
Ritchie, 1979	7	12	12	12	2.9%	0.60 (0.37, 0.97)	1979
Longstreth, 1981	17	37	16	40	2.5%	1.15 (0.69, 1.92)	1981
Arthurs, 1983	11	40	14	38	1.6%	0.75 (0.39, 1.43)	1983
Nigam, 1984	13	21	21	21	5.9%	0.63 (0.45, 0.88)	1984
Prior, 1987	33	40	37	40	23.8%	0.89 (0.75, 1.05)	1987
Jalihal, 1990	2	11	3	9	0.3%	0.55 (0.11, 2.59)	1990
Bijkerk, 2009	60	85	75	93	23.3%	0.88 (0.74, 1.04)	2009
Subtotal (95% CI)		246		253	60.2%	0.83 (0.73, 0.94)	
Total events	143		178				
Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 7.32$, d.f. = 6 ($P = 0.29$); $I^2 = 18\%$							
Test for overall effect: $Z = 2.80$ ($P = 0.005$)							



NNT = 7

Beperkte rol van oplosbare vezels (e.g. psyllium) bij IBS-C.
Weinig gegevens over vezelrijke voeding.

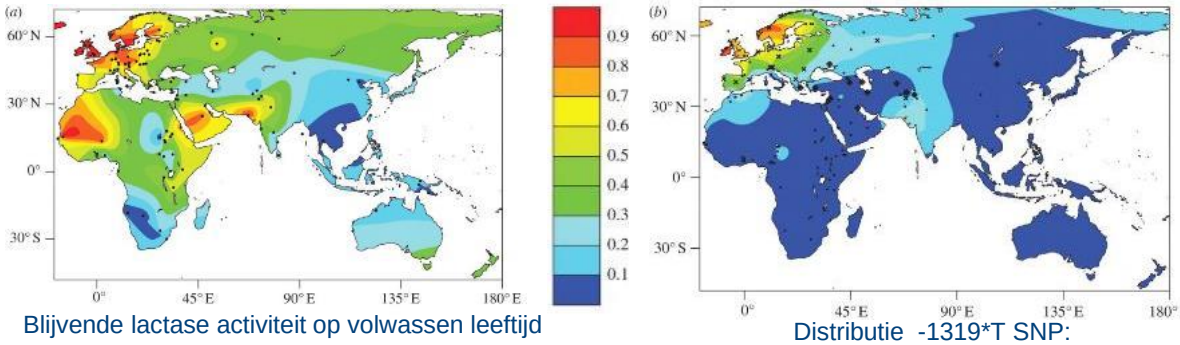
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Moayyedi et al. Am J Gastroenterol 2014

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Lactose

- Disaccharide in melk van zoogdieren (koemelk 4,7g/100mL)
- Omgezet tot galactose en glucose door lactase (brush border dunne darm)
- Snelle daling activiteit van lactase na de geboorte bij 70% van wereldbevolking



Blijvende lactase activiteit op volwassen leeftijd

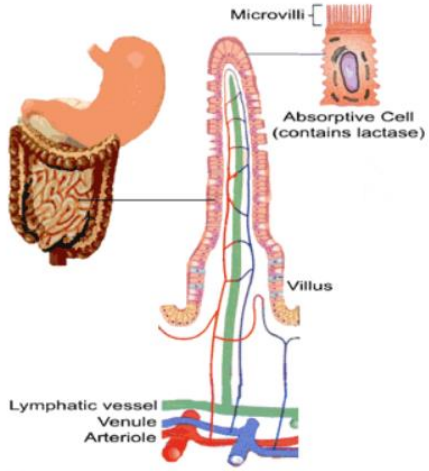
Distributie -1319*T SNP:
Persisterende lactase functie

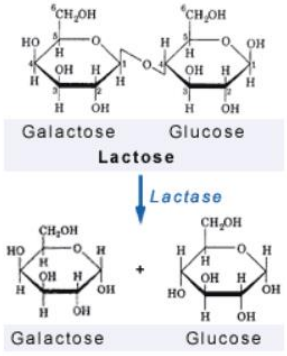
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Gerbault et al. Phil Trans R Soc B 2011

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Lactose





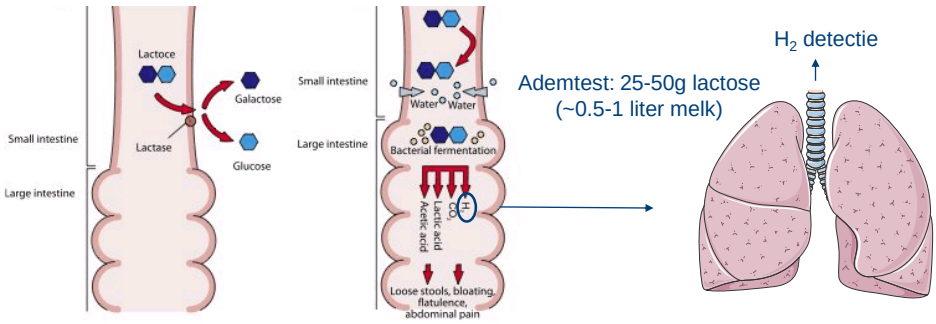
▲ Lactase: enzyme found in microvilli cells of small intestine that hydrolyzes lactose.

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Lactose

- Disaccharide in melk van zoogdieren (koemelk 4,7g/100mL)
- Omgezet tot galactose en glucose door lactase (brush border dunne darm)
- Snelle daling activiteit van lactase na de geboorte bij 70% van wereldbevolking
- Fermentatie in het colon tot gassen en vrije vetzuren bij maldigestie



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Gerbault et al. Phil Trans R Soc B 2011

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Lactose

- Disaccharide in melk van zoogdieren (koemelk 4,7g/100mL)
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- Fermentatie in het colon tot gassen en vrije vetzuren bij maldigestie
- Belang bij IBS symptomen is (meestal) zeer beperkt

Organic GI Disease	IBS Patients (Pretest Probability) (%)	General Population (Prevalence) (%)
Colitis/IBD	0.51–0.98	0.3–1.2*
Colorectal cancer	0–0.51	4–6*
Celiac disease	4.67	0.25–0.5†
Gastrointestinal infection	0–1.7	N/A‡
Thyroid dysfunction	6	5–9§
Lactose malabsorption	22–26	25¶

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Cash et al. Am J Gastroenterol 2002

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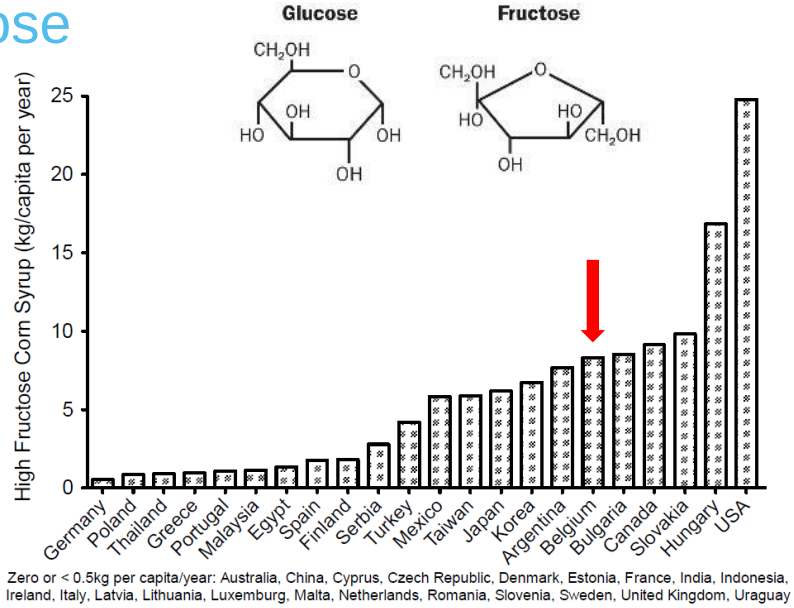
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- Fermentatie in het colon tot gassen en vrije vetzuren bij maldigestie
- Belang bij IBS symptomen is (meestal) zeer beperkt
- Lactose intolerantie ≠ Koemelkallergie
- Behandeling lactose-intolerantie: **relatieve** beperking van zuivelproducten

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Fructose



Zero or < 0.5kg per capita/year: Australia, China, Cyprus, Czech Republic, Denmark, Estonia, France, India, Indonesia, Ireland, Italy, Latvia, Lithuania, Luxemburg, Malta, Netherlands, Romania, Slovenia, Sweden, United Kingdom, Uraguay

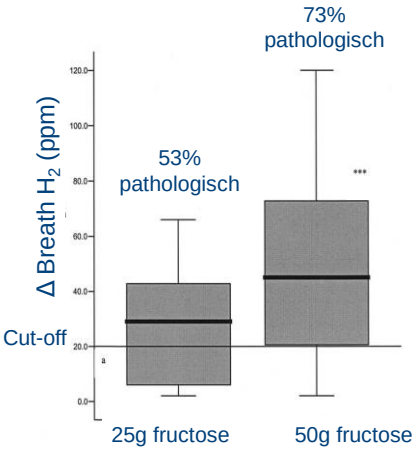
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Goran et al. Global Public Health 2013

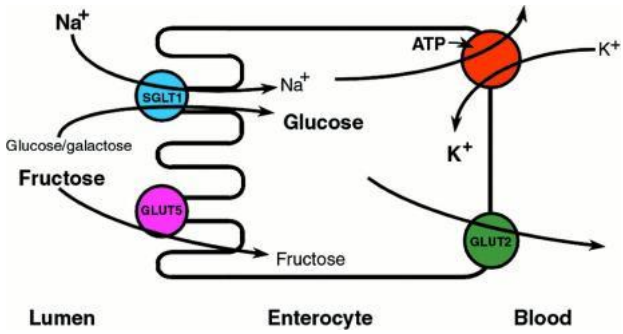
29

Fructose

- 'Fructose malabsorptie' is een fysiologisch fenomeen (≠ hereditary fructose intolerance!!!)



15 gezonde vrijwilligers



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Beyer et al. J Am Diet Assoc 2005

30

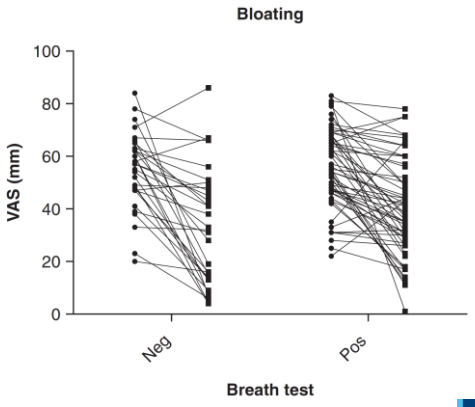
Fructose

- ‘Fructose malabsorptie’ is een fysiologisch fenomeen
- Fructose ademtest voorspelt geen respons op fructose-arm dieet

N= 88 IBS patiënten (Rome II)
Fructose ademtest (50g)
Effect van Fructose-arm dieet

Conclusies:
- Gunstig effect van fructose-arm dieet onafhankelijk van ademtest

- Significant beter effect vergeleken met ‘controle’ IBS dieet.



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Berg et al. Scand J Gastroenterol 2013

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Disaccharides → **Lactose**



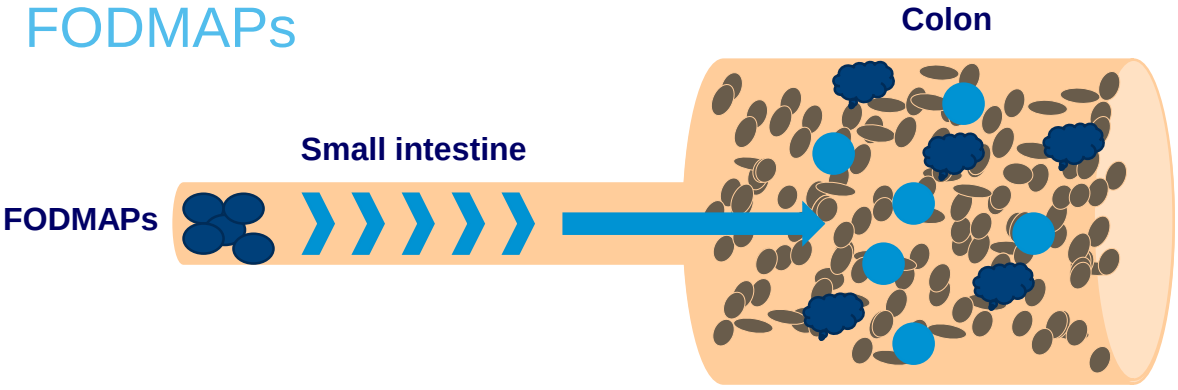
Monosaccharides → **Fructose** (in excess of glucose)



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FODMAPs



↑ water delivery

↑ gas production

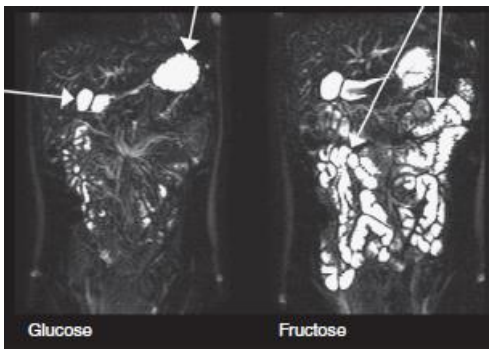
Luminal distension
Altered motility

Pain, bloating, distension, flatulence, constipation +/- diarrhoea

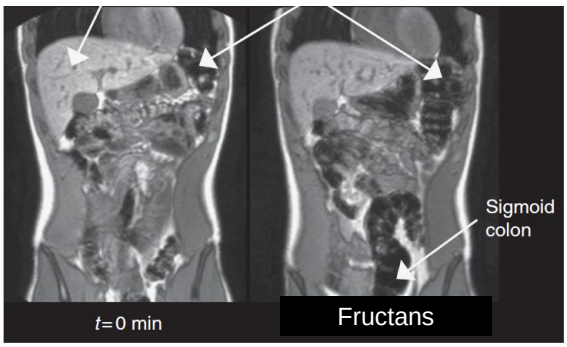
Slide Courtesy by Dr. Jessica Biesiekierski

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FODMAPs



Vochtinhoud dunne darm ↑

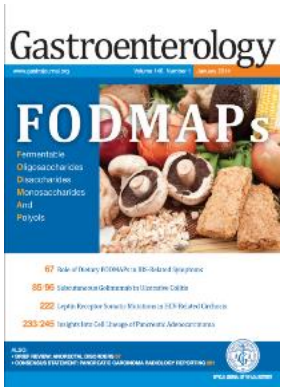


Gasinhoud colon ↑

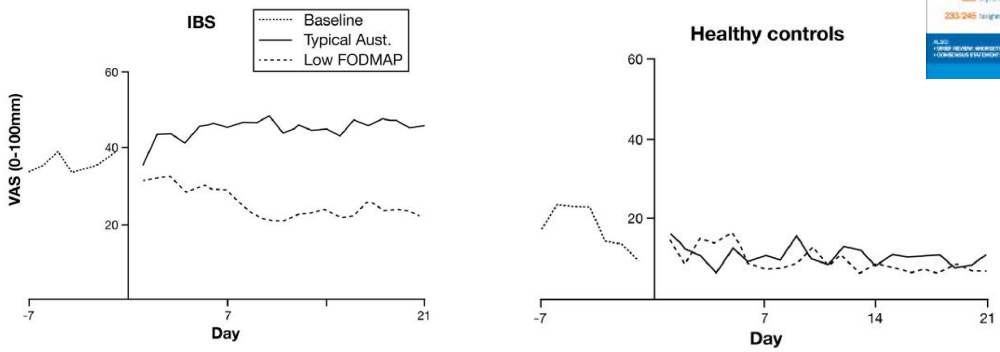
Murray et al. Am J Gastroenterol 2014

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FODMAPs



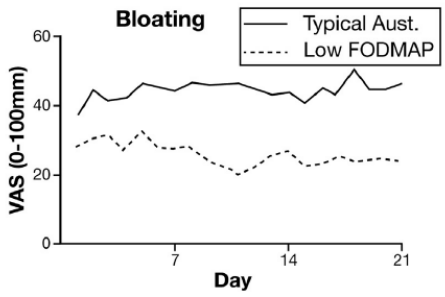
- PDS pts (n=30) en gezonde vrijwilligers (n=8)
- 21 dagen patiënt-geblindeerde cross-over studie
- Low FODMAP (3,05 g/d)
  vs. 'standaard' Australisch dieet (23,7 g/d)

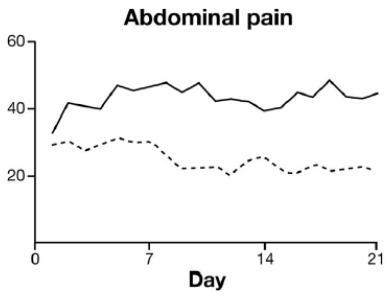


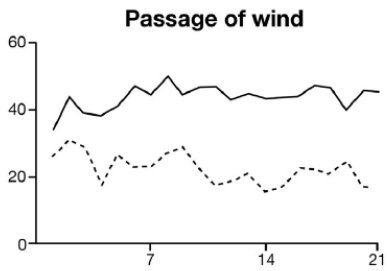
Halmos et al. Gastroenterology 2014

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FODMAPs







Halmos et al. Gastroenterology 2014

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FODMAPs



- <u>Praktisch:</u>
  2-4(-6) weken strikt FODMAP-arm dieet onder deskundige begeleiding
  - bij gunstige respons (68-86%): geleidelijke herinvoering per categorie
  - geen respons na 6 weken: stop dieet
- <u>Caveats:</u>
  - Invloed op microbioom: reductie Clostridium coccoides (butyraat)
    toename Ruminococcus species (mucus afbraak)
    afname Bifidobacteria
  - Lange termijn resultaten
  - Nutritionele deficiënties

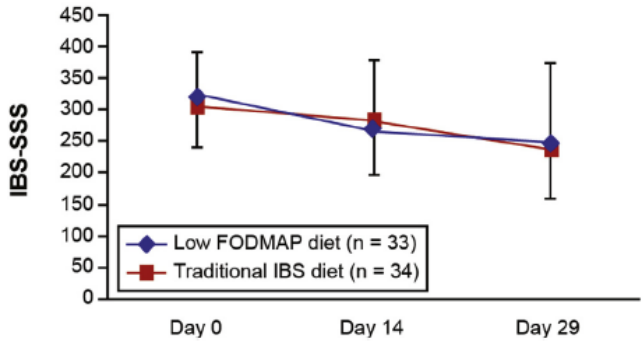
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Halmos et al. Gut 2015 Staudachter et al. J Nutr 2012

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FODMAPs

- Randomized Controlled Trial in IBS (Rome III)
- 4 weeks of Low FODMAP diet vs. 'traditional IBS diet' (NICE)
  3 meals + 3 snacks – avoid heavy meals – avoid high intake of fat, insoluble fibers, carbonated beverages, gas-producing foods, spicy food, coffee, artificial sweeteners, alcohol.



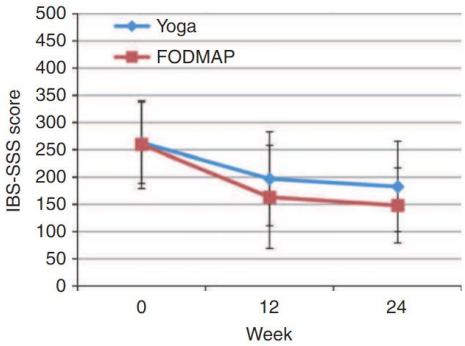
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Böhn et al. Gastroenterology 2015

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Of Yoga?

59 IBS patients
Randomized, single-blind design
3 FODMAP instruction visits vs. 24 yoga classes





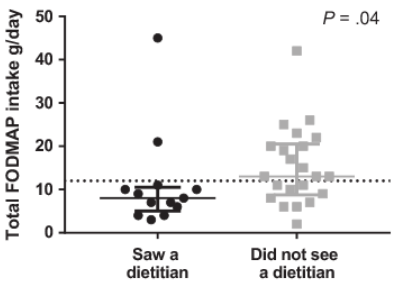
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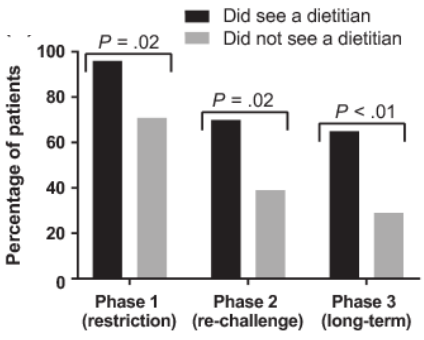
Schumann et al. Aliment Pharmacol Ther 2018

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FODMAPs

Diëtiste met voldoende kennis van het low FODMAP dieet is onontbeerlijk!





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Tuck et al. Neurogastroenterol Motil 2019

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Conclusies

- Belang van differentiatie allergie vs. intolerantie
- Rol van geïsoleerde lactose- of fructose-intolerantie is beperkt
- Low FODMAP dieet als standaard behandeling bij functionele gastrointestinale klachten
- Denk aan coeliakie!

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