Lactose intolerance: Insights and management strategies

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KING'S HEALTH PARTNERS

Guy's and St Thomas' NHS
NHS Foundation Trust

Conflicts of interest

Course Director of low FODMAP courses for dietitians

Personal fees from Janssen, Mayoly, Abbvie

Grants from Crohn's and Colitis UK, GSTT charity, NIHR-HTA

Lactose intolerance: Insights and management strategies

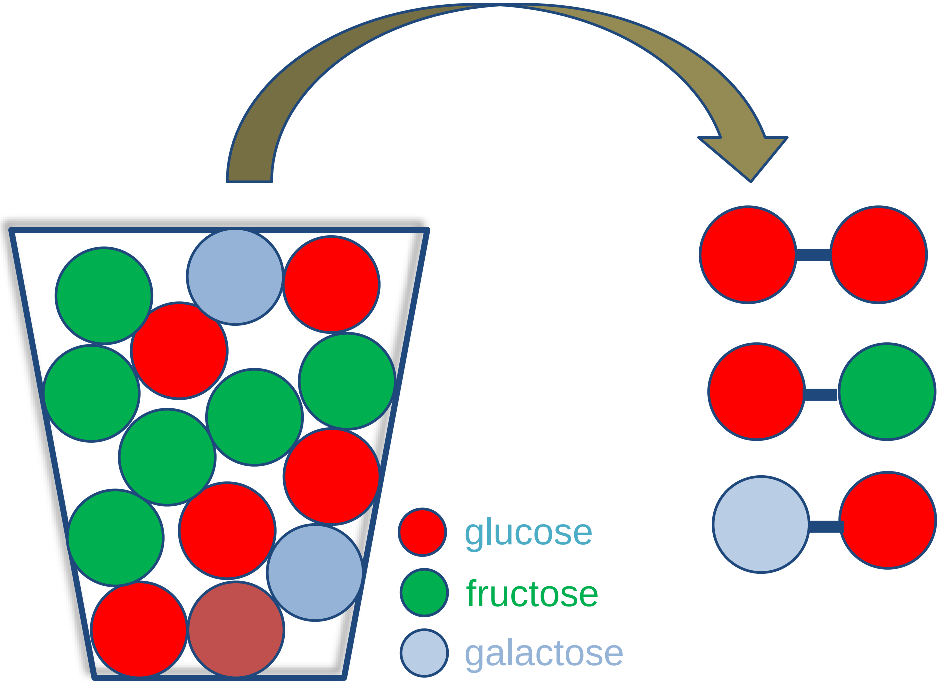
Mechanisms of lactose digestion

Lactose intolerance

Dietary management

Misconceptions

Lactose, is the natural milk sugar



maltose

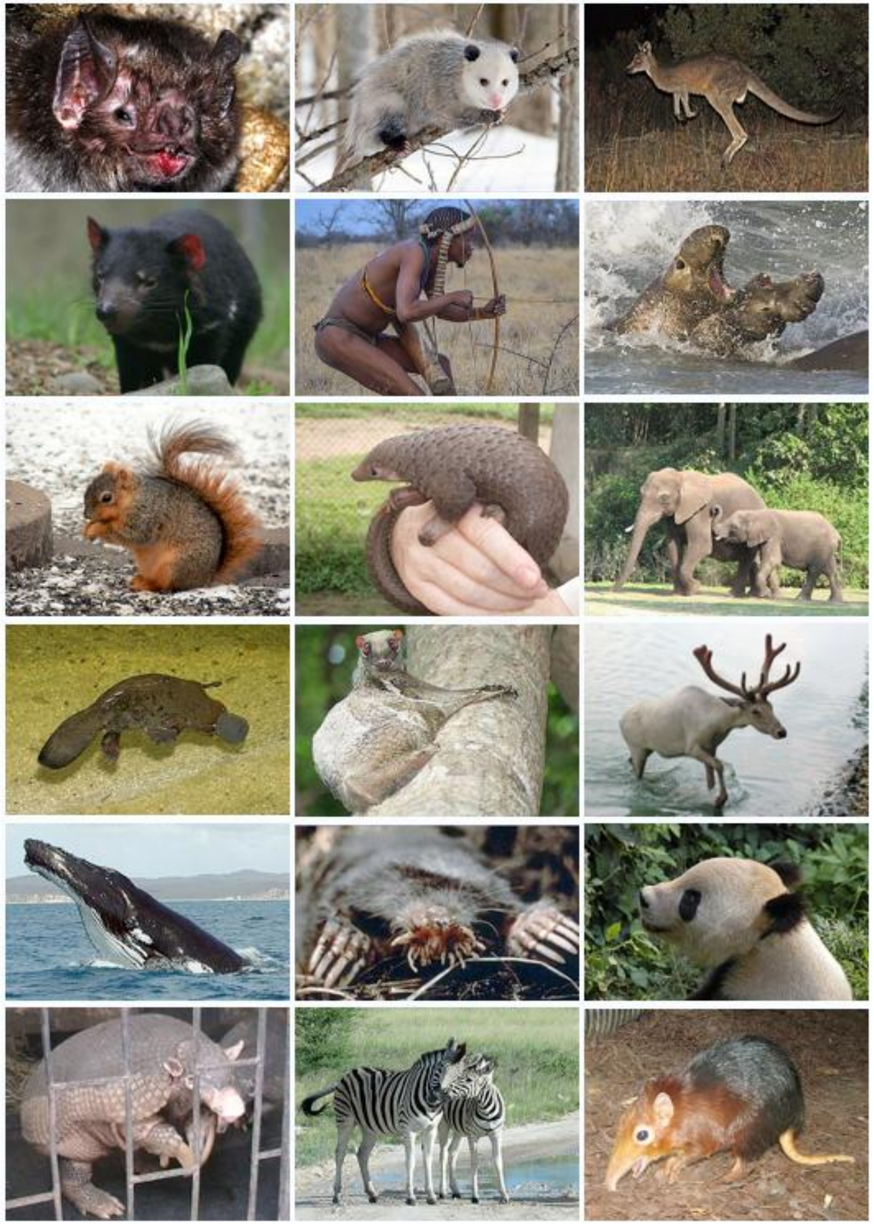
sucrose (saccharose / table sugar)

lactose

- Disaccharide exclusively present in milk (most mammals)
- Major component of milk:
  - Cow: 46g/L (4.6%)
  - Human: 70g/L (7%)
  - Used as energy source

Sugars have multiple other functions besides being energy sources

Sweetener
Taste enhancer
Filler
Gel former
Stabilizer
Coloring agent
Structure
Preservative



Milk is a unique feature of mammals

Definition:
Mammals (from Latin mamma "breast") are vertebrate animals constituting the class Mammalia, and characterized by the presence of **mammary glands which in females produce milk for feeding (nursing) their young**, a neocortex (a region of the brain), fur or hair, and three middle ear bones.

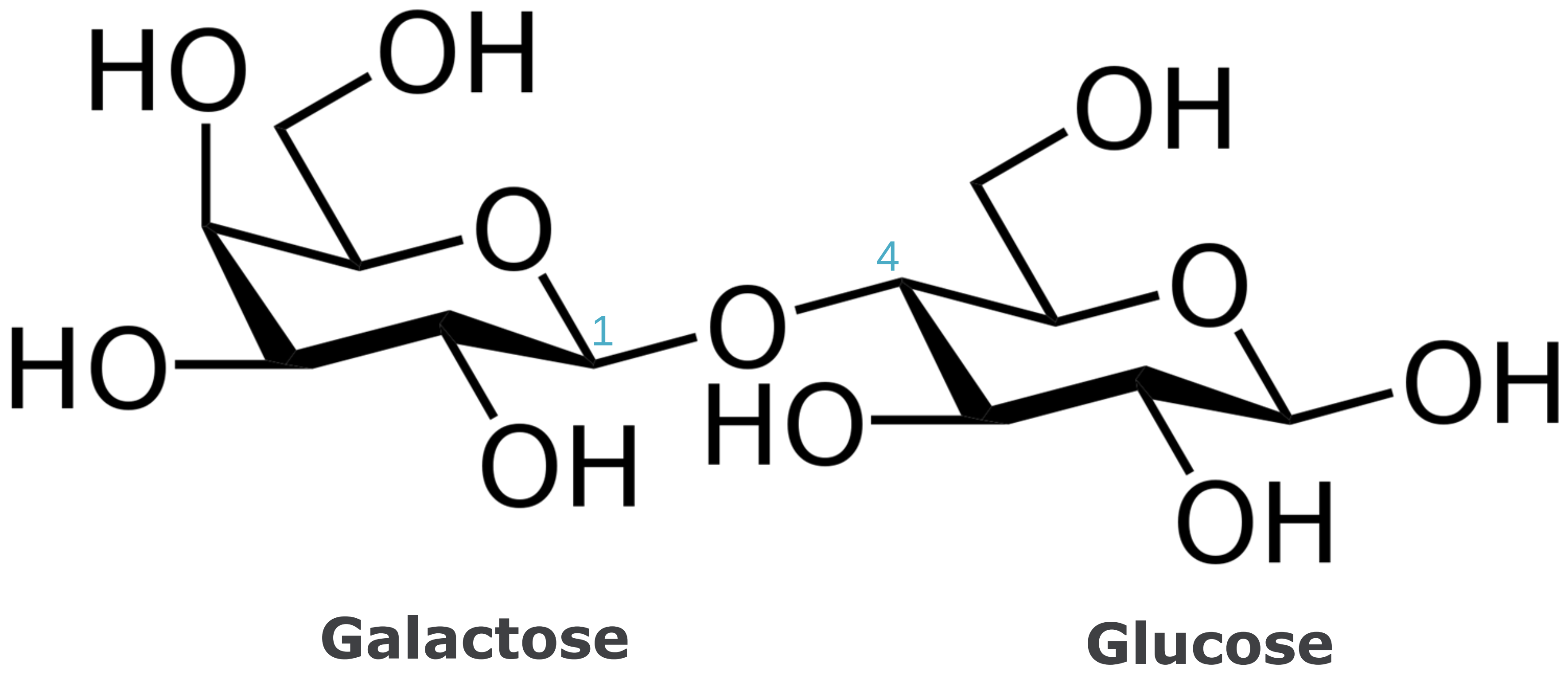
Galactose and glucose are present in all mammalian milks, but not always in the form of lactose (e.g. sea otter, certain marsupials, …)

Lactose has been evolutionary conserved in virtually all placental mammalian milks, with varying concentrations according to species. Of all milks currently analyzed by lactose-specific methods, human breast milk seems to have the highest amount

Mammal	Lactose content (%)
Seal	0.1
Black bear	0.4
Rabbit	3.0
Reindeer	3.9
Goat	4.3
Cow	4.6
Indian elephant	4.7
Sheep	4.8
Camel	5.0
Pig	5.5
Donkey	6.3
Human	7.5

Paques, M. and Lindner, C. (2019). Lactose. 1st ed. Academic Press

Lactose consists of galactose coupled to glucose via a specific bond

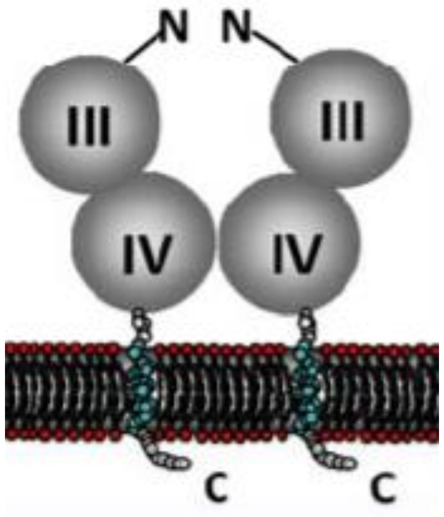


Jensen, R. G. (1995). Handbook of milk composition. Academic Press

Lactose = **galactose** coupled to **glucose** by a **β1,4 glycosidic bond**

Lactose is broken down by lactase (LCT), a.k.a. lactase phlorizin hydrolase (LPH)

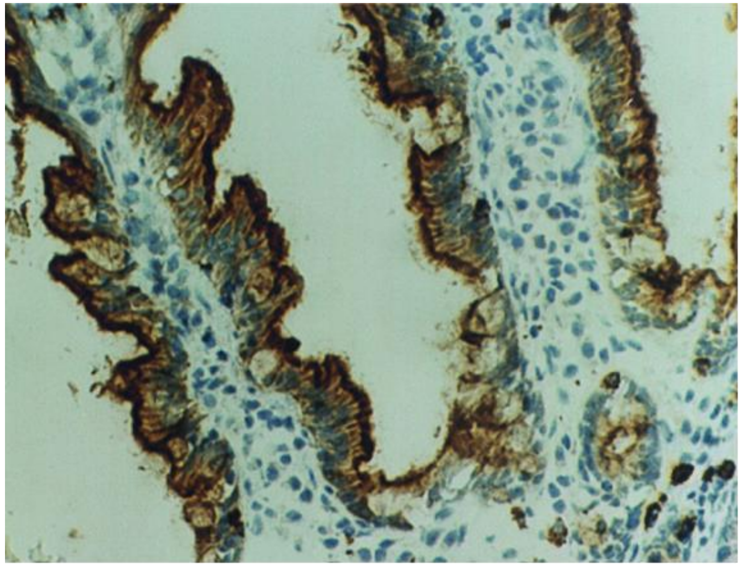
Lactose is enzymatically broken down in the small intestine by lactase

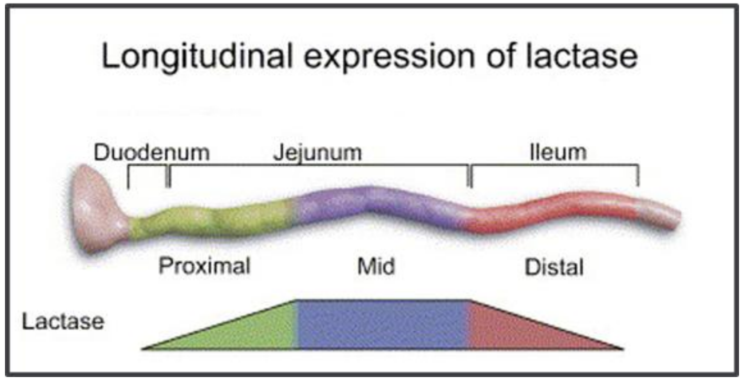


III: Phlorizin-hydrolase domains

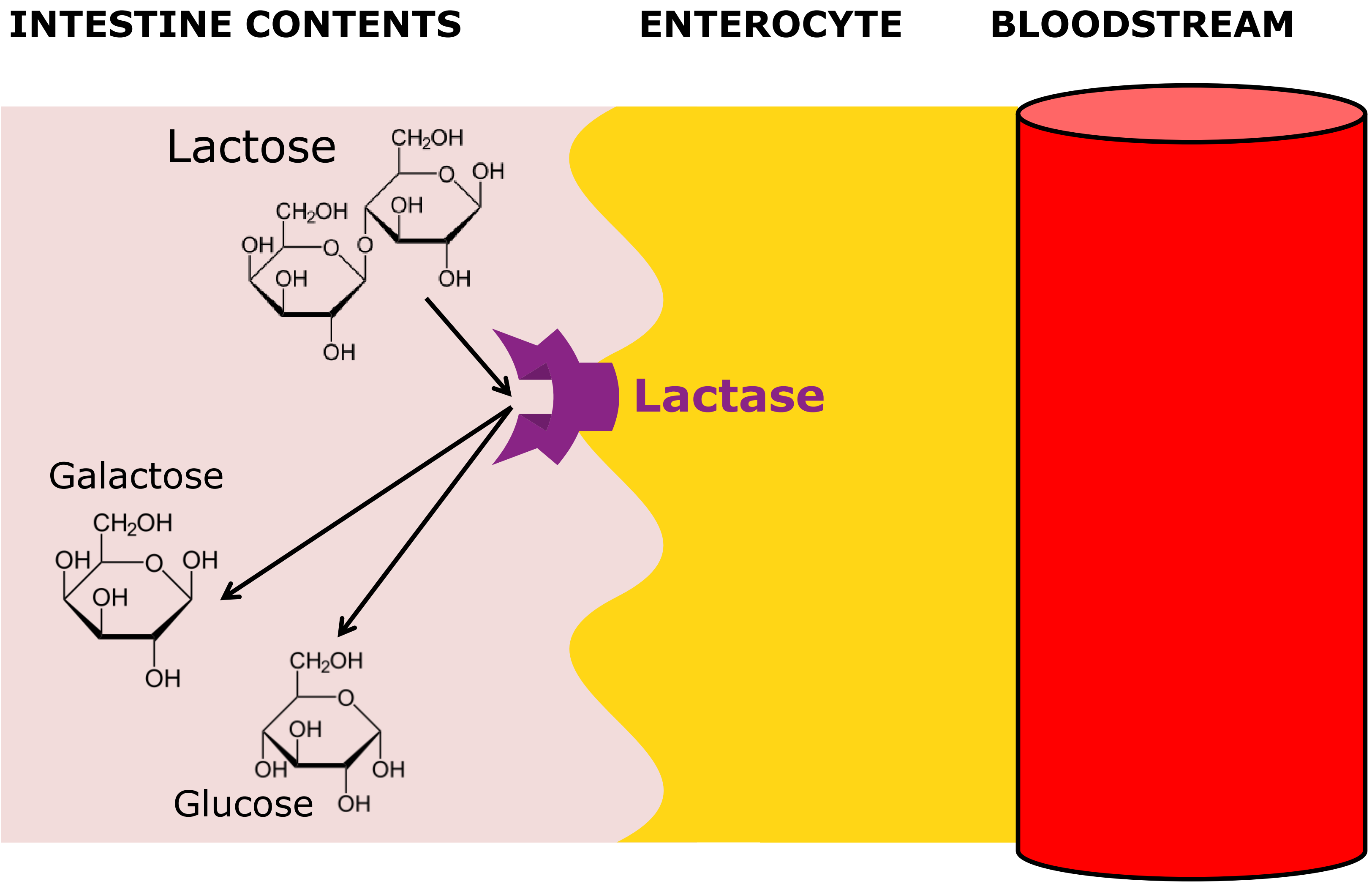
IV: Lactase domains

This is the "brush border" of an enterocyte, which is the side of the enterocyte that comes in contact with the contents of the small intestine. Lactase is stained brown

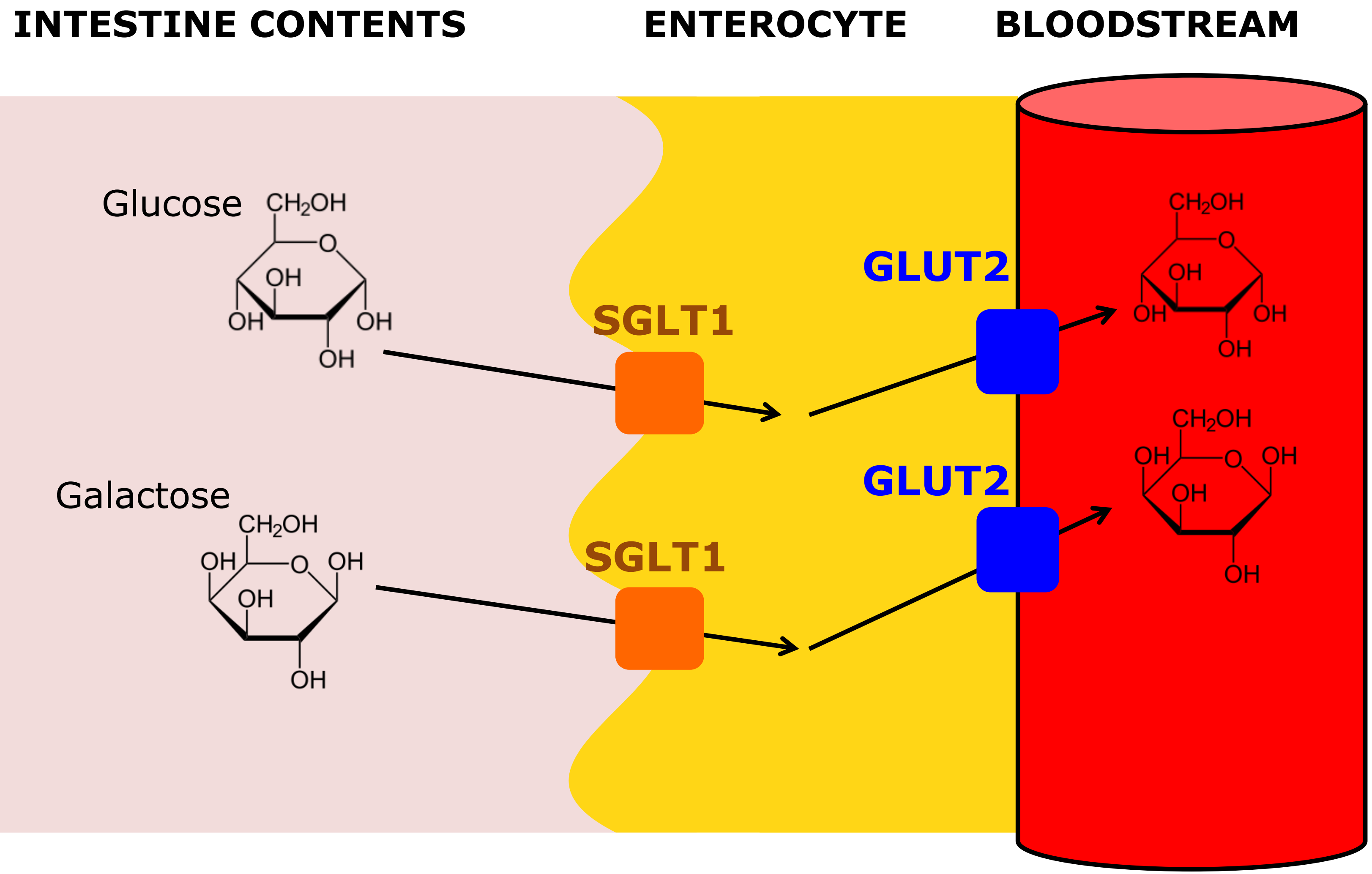




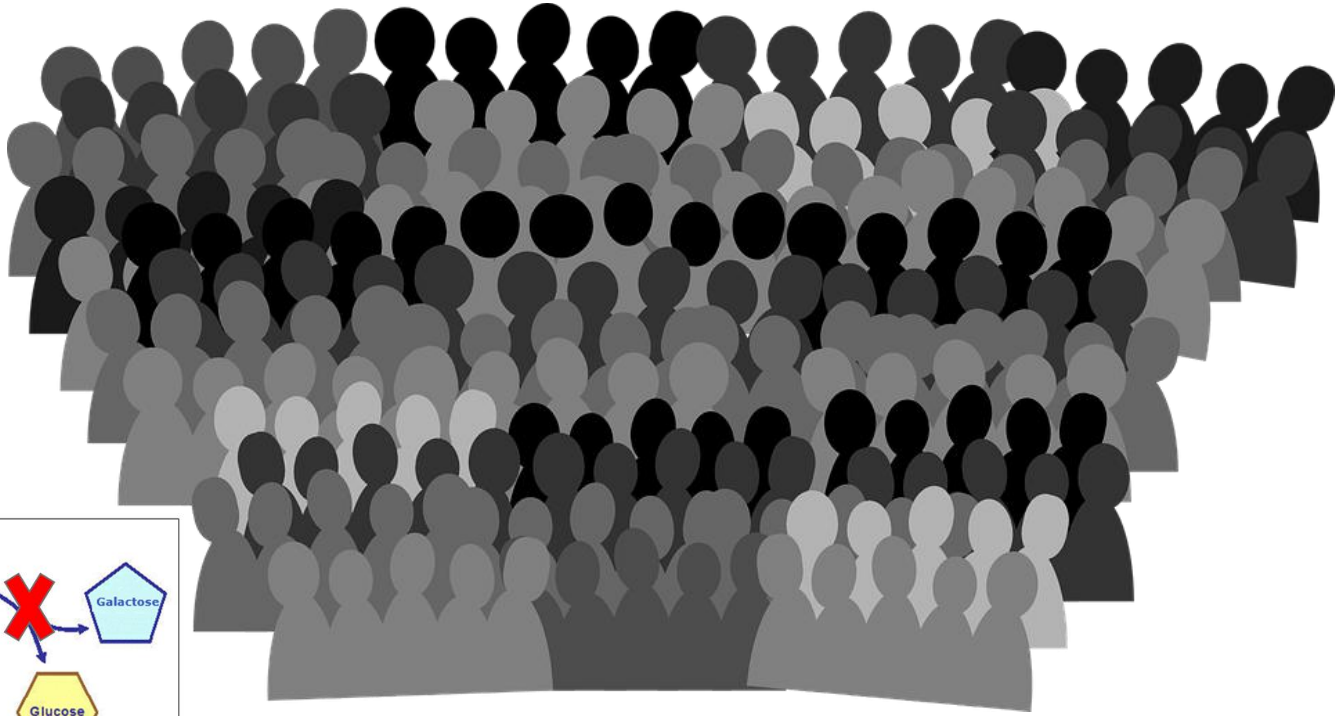
Lactase breaks down lactose

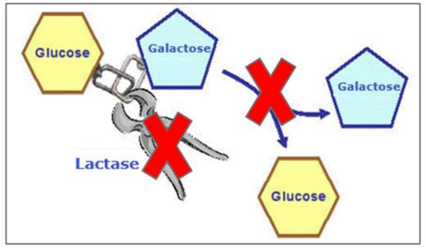


Glucose and galactose are absorbed



Lactase production decreases after weaning - ancestral trait for most people





Almost all known mammals – including the majority (~65%) of humans **–** experience a 90% to 95% **decrease in lactase production** in the years **after weaning** (a condition known as Lactase Non-Persistence (LNP)).
LNP individuals become **lactose mal-absorbers** (LM) and **can** suffer from **lactose intolerance** (LI) complaints when consuming milk and dairy products into adulthood*

Not everyone with lactose malabsorption develops symptoms of lactose intolerance

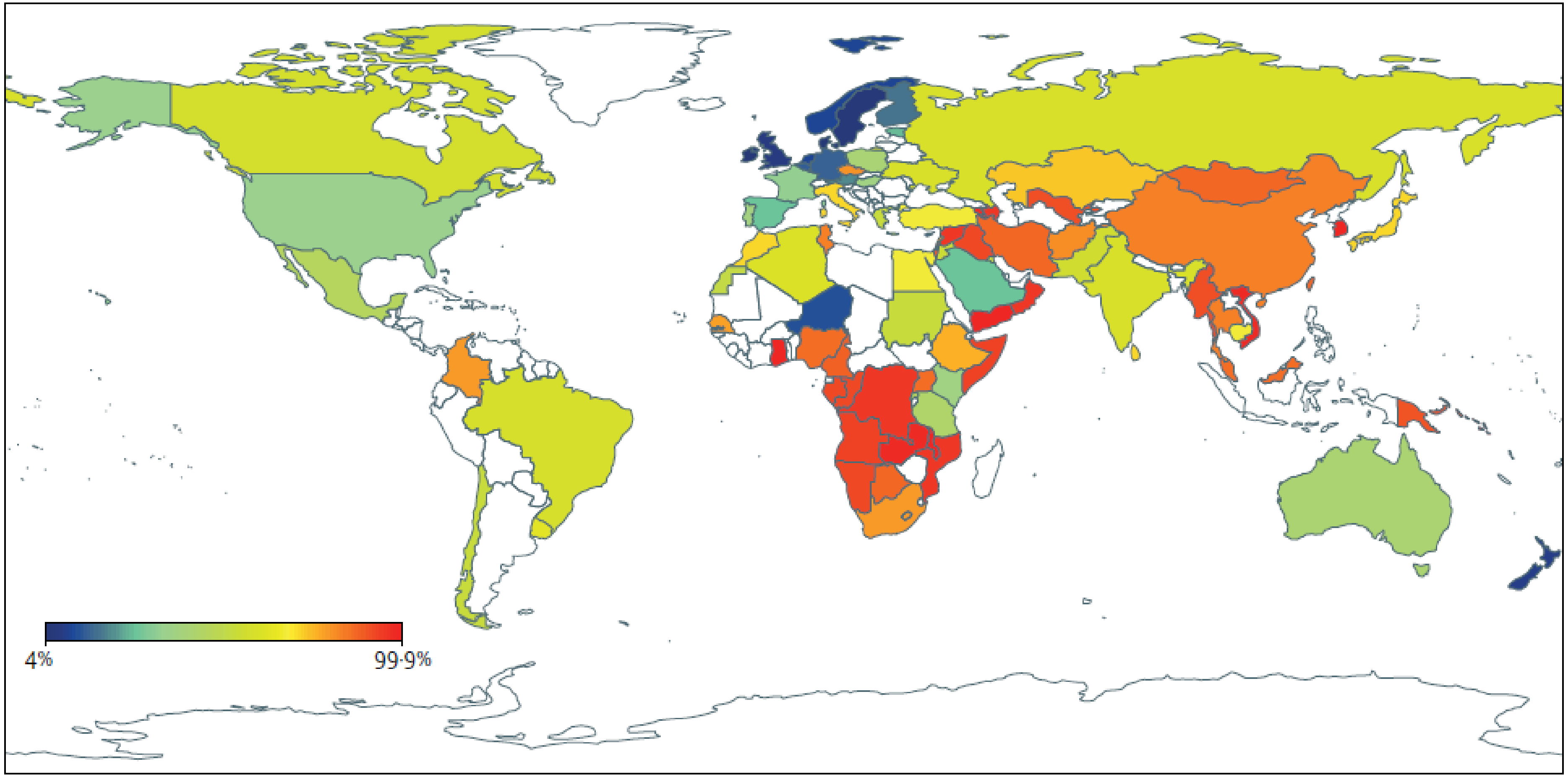
Variation across human populations in the estimated age when lactase is downregulated in LNP individuals

Population	Lactase downregulation age	Reference
Chinese	1–5 years	Sahi (1994)
	7–8 years	Yang, He, Cui, Bian, and Wang (2000)
Hong Kong Chinese	3–10 years	Chang, Hsu, Chen, Lee, and Hsu (1987)
Japanese	1–5 years	Sahi (1994)
Taiwanese	2–6 years	Chang et al. (1987)
Thai	By 5 years	Wang et al. (1998)
	Under 12 months to 3 years	Keusch, Troncale, Miller, Promadhat, and Anderson (1969)
Bangladesh	7–18 months to 3 years	Brown, Parry, Khatun, and Ahmed (1979)
African	Between 1 and 8 years	Northrop-Clewes, Lunn, and Downes (1997); Rasinperä et al. (2004)
Nigerian Yoruban	Under 12 months to 4 years	Kretchmer, Hurwitz, Ransome-Kuti, Dungy, and Alakija (1971)
East African Baganda	Some downregulation observed from 1 week to 5 months	Cook (1967)
Somalian	5–10 years	Rasinperä et al. (2004)
Ugandan	After 3 years	Cook and Kajubi (1966)
Sardinian	3–9 years	Schirru et al. (2007)
Greek	5–12 years	Ladas, Katsiyiannaki-Latoufi, and Raptis (1991)
Finnish	8–12 years	Rasinperä et al. (2004)
Finnish and Estonian	8–12 years	Sahi (1994)
Israeli Jewish	From 6.5 years	Gilat, Dolizky, Gelman-Malachi, and Tamir (1974)
Native American	1–5 years or later	Bose and Welsh (1973); Caskey et al. (1977); Johnson et al. (1977)
American Black ancestry	1–4 years	Bayless et al. (1975)
	3–9 years	Pribila, Hertzler, Martin, Weaver, and Savaiano (2000)
	6–11 years	Huang and Bayless (1967)
American Mexican ancestry	1–4 years	Bayless et al. (1975)
American European ancestry	5 years or later	Bayless et al. (1975)
Mexican	Under 4–13 years	Rosado et al. (1994)

Paques, M. and Lindner, C. (2019). Lactose. 1st ed. Academic Press

Worldwide prevalence of lactose malabsorption

Down-regulation of lactase production leads to lactose malabsorption



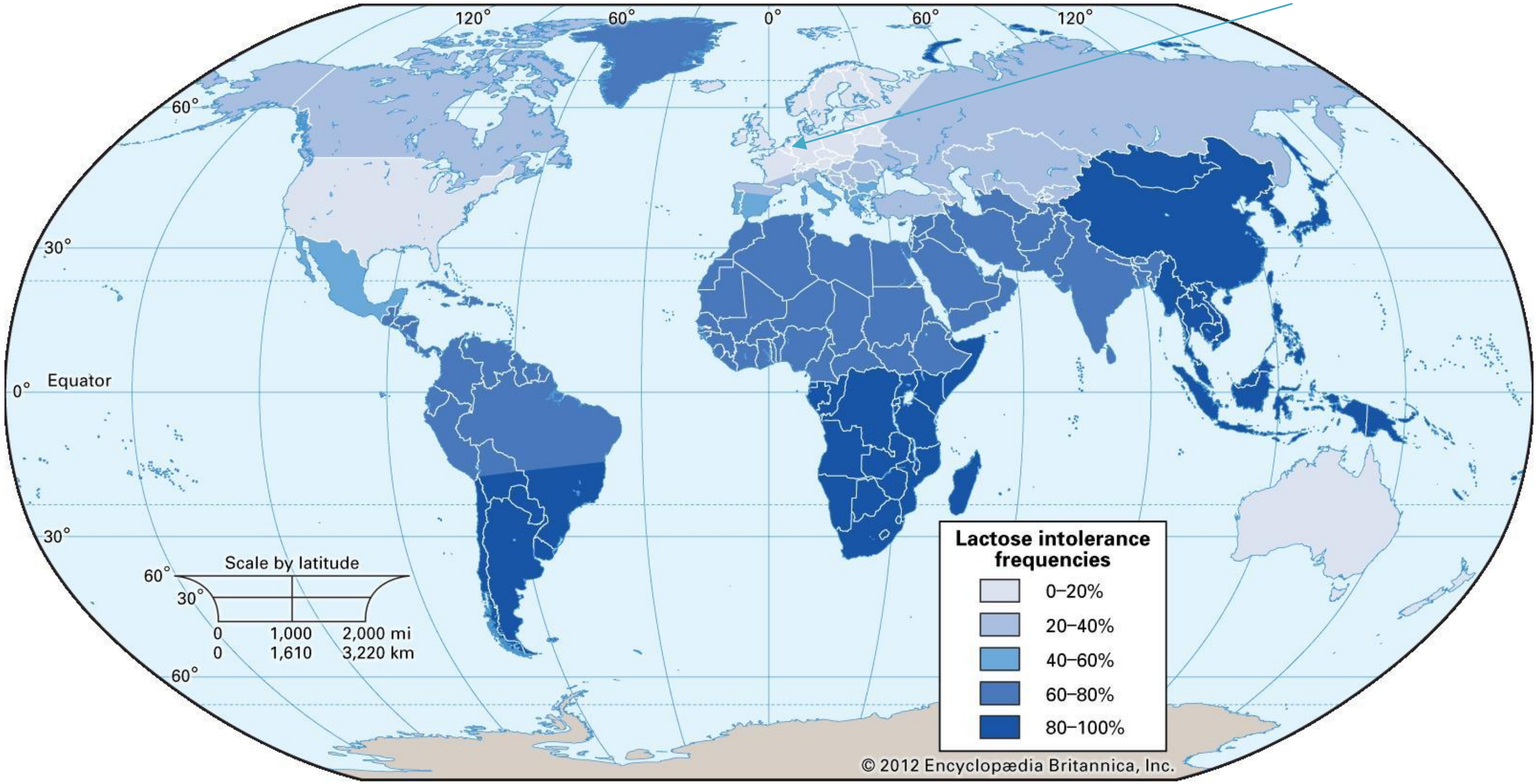
Storhaug *et al.*, 2017

Estimated lactose intolerance frequencies

probably 3 to 5 times lower than lactose malabsorption frequency (Savaiano *et al*., 2003)

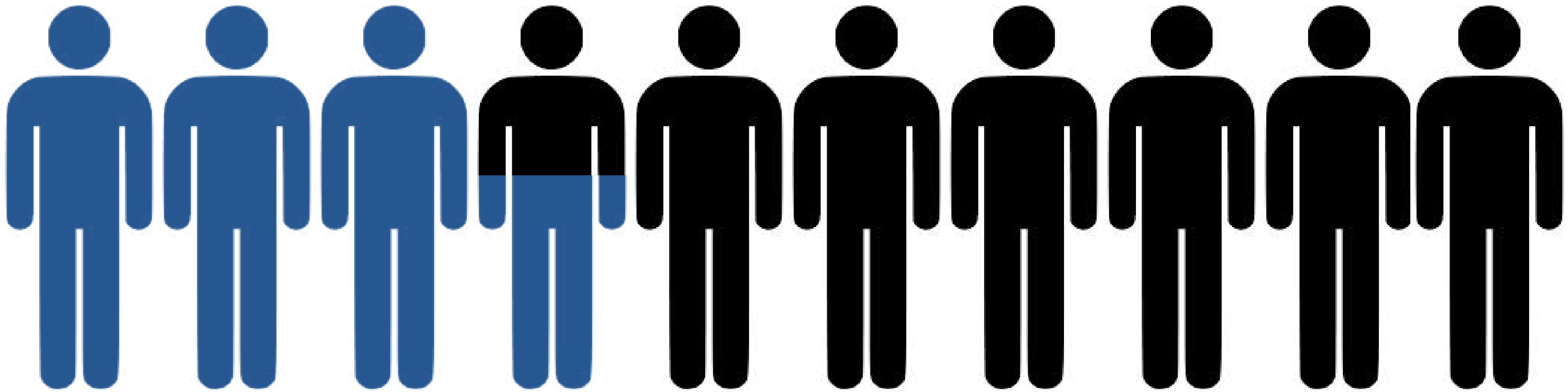
Lactose malabsorption can be objectively measured, lactose intolerance cannot

NL: ~2-3%



~35% of humans persistently continue to produce lactase after weaning

…and are therefore able to continue to consume milk and other dairy products into adulthood, a situation known as “lactase persistence” (LP)



Lactase non persistence

- Congenital lactase deficiency
- Primary lactase deficiency
  - 70% of the population, ranging from 5% British to 90% Asian (Lomer 2008)
  - 18-82% of individuals with IBS (Staudacher et al., 2014)
  - Not all people have "lactose intolerance"
- Secondary lactase deficiency
  - Coeliac disease, gastroenteritis

Lactose malabsorption

the incomplete hydrolysis of lactose and the presence of unabsorbed lactose in the colonic lumen

Lactose intolerance

the occurrence of gastrointestinal symptoms due to unabsorbed lactose in the colonic lumen. It is dependent on self reported symptoms after lactose ingestion

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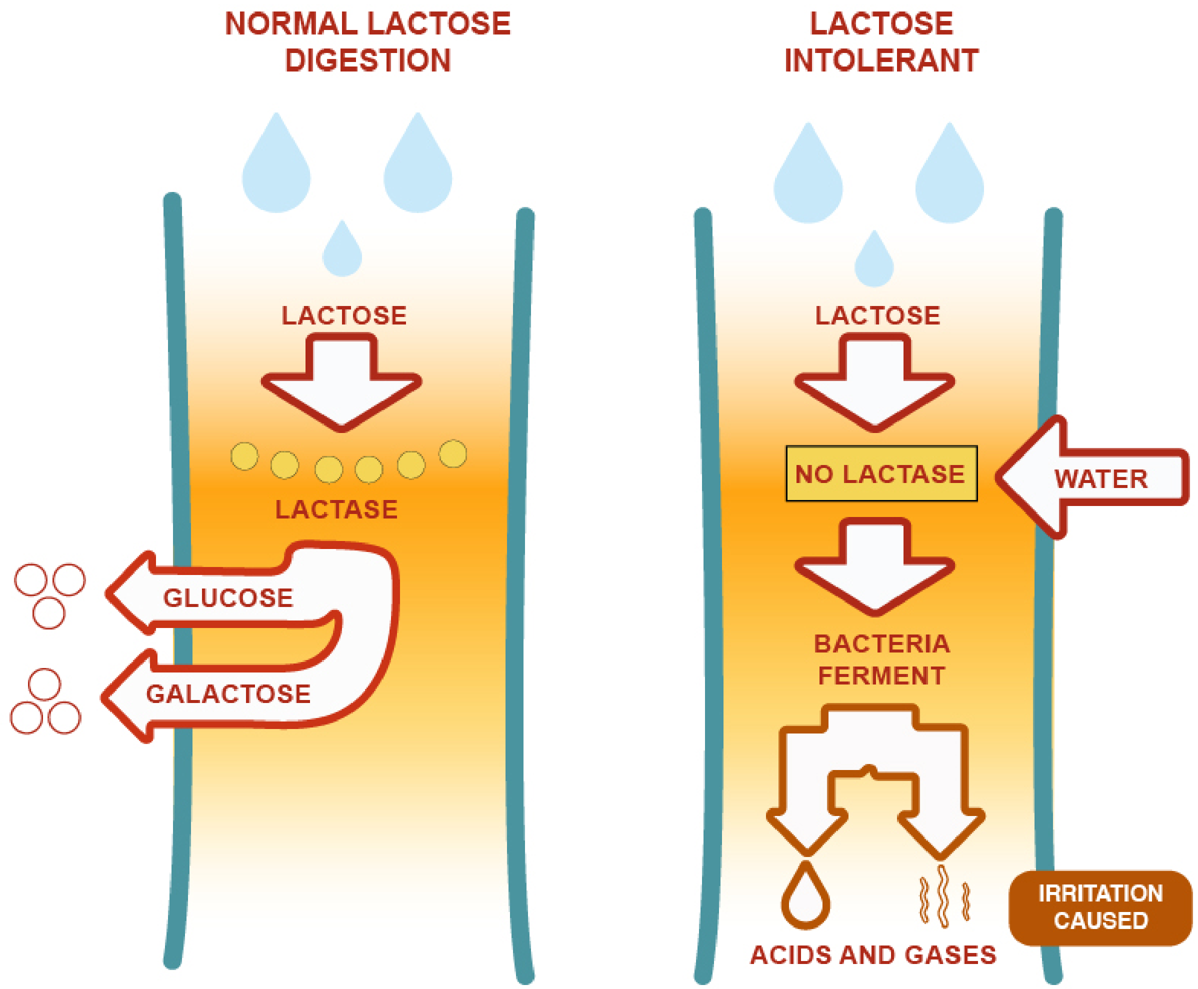
Not everyone with lactose malabsorption has lactose intolerance

The pathophysiology of lactose-intolerance



Several tests exist for measuring lactose malabsorption

	Test	Method	Interpretation	Comments
direct	Intestinal biopsy	Crosby capsule swallowed by patients	Lactase U/g of tissue Normal 18.3 U/g	Ratio of lactase to sucrase used as sucrase is not usually downregulated May be variable due to age-related fluctuations of lactase levels
	Quick R test	Endoscopic biopsy with rapid results	Similar to above but more rapid at bedside	Limited use at this time
	^{14}C-labeled lactose	Isotopically labeled glucose measured	Similar to measuring rise of glucose	Early method. More labor intensive and not widely used except in research
indirect	Blood glucose (aka lactose tolerance)[a]	Ingestion of lactose (20–50 g) Measure blood glucose every 30 min for 2 h	A rise above 1.1-1.4 mmol/L is positive in a lactose digester	Outcome modified by underlying diabetes, small intestinal disorders, or gastrointestinal problems. May not concur with breath hydrogen test results, but agrees with genetic tests
	Blood galactose	Same as blood glucose	A rise in galactose >0.3 mmol/L is positive in a lactose digester. Result measured by change in absorbance by the release of galactonic acid and reduced nicotinamide adenine dincleotide	Rarely used as other tests like the glucose or breath tests are more readily available
	Breath hydrogen[a]	Measurement of hydrogen and methane after a load of lactose for 3 h	Lactose digesters do not increase breath hydrogen $\geq$ 20 ppm or methane $\geq$ 10 ppm	Most common clinical test. Lactose load varies but 25 g best clinical use, 50 g more sensitive for correlation with genetic tests. Multiple variables can interfere with interpretation (e.g. rapid intestinal transit, bacterial overgrowth with ageing, secondary lactase deficiency)
	Urinary galactose	Measurement of galactose in urine 5 h after a 50 g lactose load	Normal lactose digesters: $\mu = 45\ mg\ 5\ h$ Lactose maldigesters: $\mu < 8\ mg\ 5\ h$	Surpassed for clinical use by blood glucose or breath hydrogen tests
	Genetic tests	DNA from blood, saliva, or other tissue sources	Confirms the presence of absence of alleles associated with lactose hydrolysis into adulthood	Most clinical tests assess the C/T -13910 allele

[a]Breath tests and blood glucose tests are most commonly used in clinical practice

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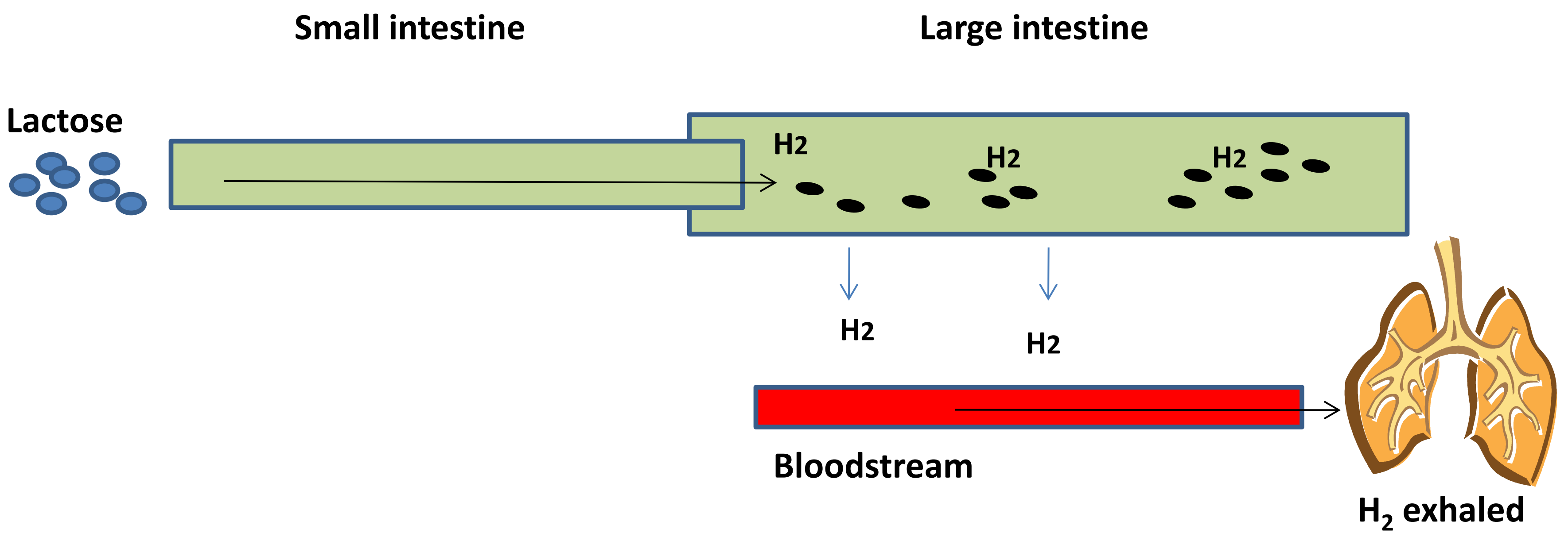
What is a breath test

Measurement of hydrogen or methane in the breath after ingestion of a test sugar solution



What is involved?

Pre-test instructions

No antibiotics or prebiotics for 4 weeks

No bowel prep 4 weeks

No laxatives or anti-diarrhoea medication for 3 days

Avoidance of test (fermentable) sugars for 24 hours

Fast - 10 hours

No chewing gum or smoking pre test

What is involved?

Baseline (0 min) breath sample

Ingestion of test liquid

25g lactulose or lactose in 250ml fluid

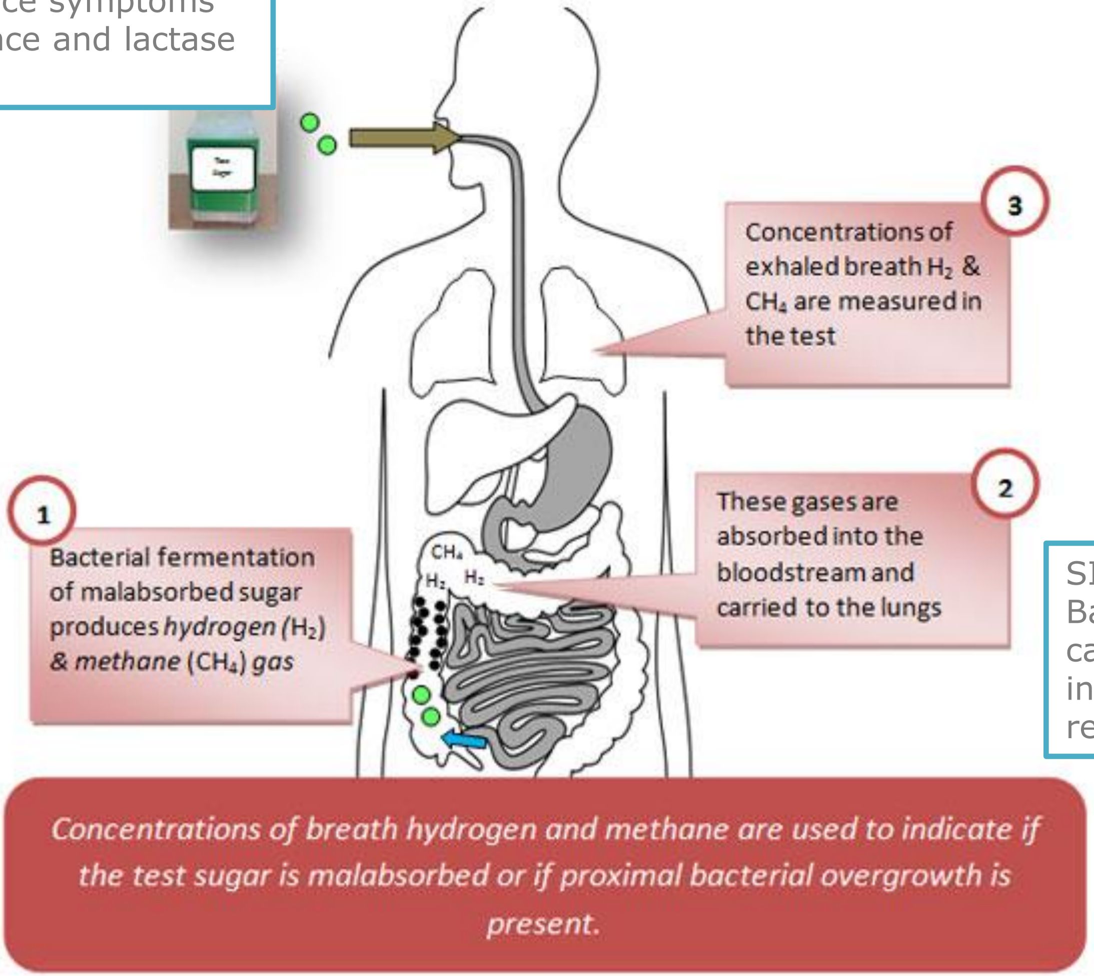
Breath samples at 15-30 minute intervals until 3 or 4 hours

Record symptoms

Protocols vary i.e. breath sampling intervals, diagnostic criteria, pre-test preparation, gases measured (H_2, CH_4)

Complexities within LI: false-positive LM test results

Single large doses or supra-threshold doses of lactose can generate lactose malabsorption-positive test results and induce lactose intolerance symptoms in lactase non-persistence and lactase persistence individuals



SIBO (Small Intestine Bacterial Overgrowth) can interfere with interpretation of test results

Bond & Levitt, 1976
Suarez et al., 1995, 1997
Vernia, Di Camillo, Foglietta, Avallone, & De Carolis, 2010
Paques, M. and Lindner, C. (2019). Lactose. 1st ed. Academic Press

Confirm diagnosis of lactose intolerance

Dietary lactose exclusion until symptom resolution

↓

Lactose re-challenge to induce symptoms

↓

Re-introduce lactose to personal tolerance level

Management of lactose intolerance

Only restrict lactose if necessary

Lactose (milk) exclusion 4 weeks

Monitor symptoms

Re-introduce lactose to tolerance increasing by 1g per day

Adjust dose gradually over time

Calcium still well absorbed from milk despite intolerance

Lactose: Dietary sources

Dietary sources

- Naturally-occurring in milk products
- Commercially added lactose
  - Bulking agent
  - Fillers in pharmaceuticals
  - Increases browning in baked goods

Average intake

- Sweden 12g/d in healthy individuals (Larsson et al., 2004)
- UK 7g/d in IBS patients (Staudacher et al., 2012)

Lactose Sources

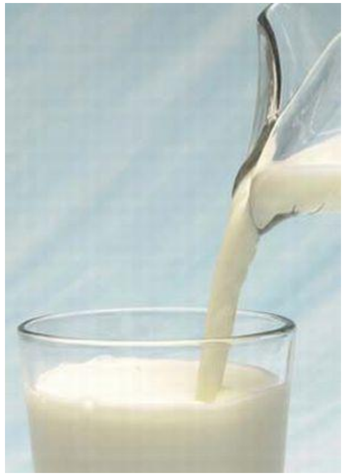
Food	Lactose content (g)
Milk (250ml)	15
Yoghurt (200g pot)	8
Custard (1/2 cup)	6
Ice cream (1 scoop)	5
Cheese - ricotta, cottage (3 tbs)	4
Chocolate (50g)	4
Cheese - cheddar, brie, stilton, edam, feta, goats, mozzarella (30g)	<1
Butter, cream, cream cheese	trace

Lactose sources from different milks

Milk	Lactose content (g/100g)
Semi-skimmed	4.7
Whole	4.6
Condensed, whole sweetened	12.3
Dried skimmed	52.9
Evaporated, whole	8.5
Goat	4.4
Human	7.2
Sheep	5.1

Suitable foods – lactose malabsorption

Milk & milk products
Usually 4g lactose at each sitting well tolerated



Lactose free milk
Plant-based alternatives to milk

- Soya
- Rice
- Oat
- Nut – almond, hazelnut, macadamia
- Hemp
- Coconut
- Quinoa

Lactose tolerance

Up to 250ml milk (12-15g lactose)

Dependent on lactase activity

No evidence for small intestinal adaptation

(Swallow Ann Rev Genet 2003)

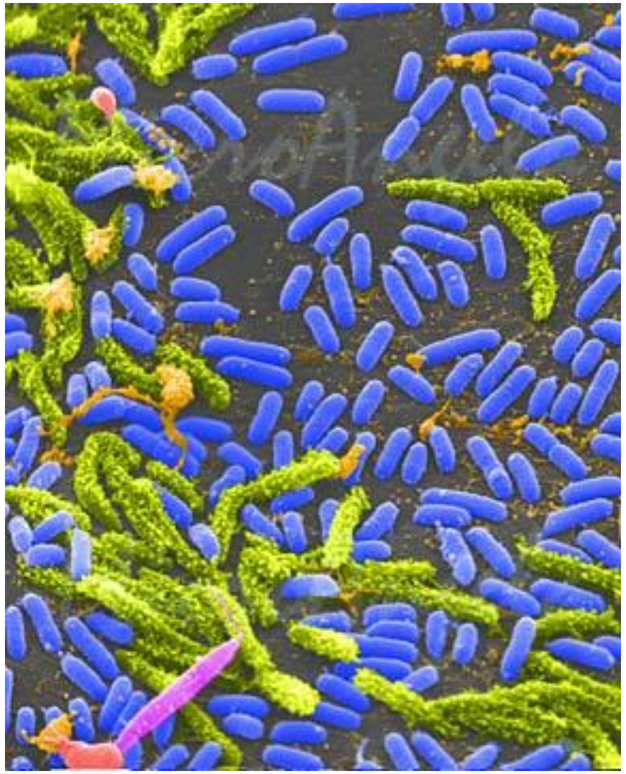
Intestinal microbiota

Transit time

Probiotics

Lactose as a prebiotic?

Individual perception of symptoms



Lactose tolerance

Mixed meals can improve tolerance

Cereals and increased energy content delay gastric emptying

Supplemental lactase not always effective

Food temperature may affect transit and tolerance

Other considerations

- Calcium and vitamin D - issues with bone mineral density
- Dairy free alternatives may be supplemented but often more expensive and less bioavailable
- Re-introduction and compliance
- Can the diet be nutritionally complete without lactose?
- Many people with lactose intolerance do not have lactose malabsorption

- Are the symptoms due to something else? Other fermentable carbohydrates
- Overlap with irritable bowel syndrome (IBS)
- Is milk avoidance really necessary? Prebiotic effect

Lactose intolerance symptoms

Abdominal pain

Bloating

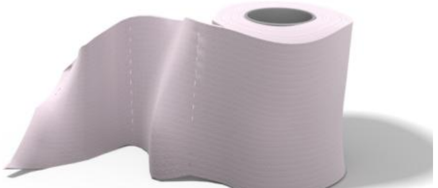
Flatus

Diarrhoea

Borborygmi

Nausea/vomiting

Constipation



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Abdominal pain

Bloating

Flatus

Diarrhoea

Borborygmi

Nausea/vomiting

Constipation

Overlap with irritable bowel syndrome

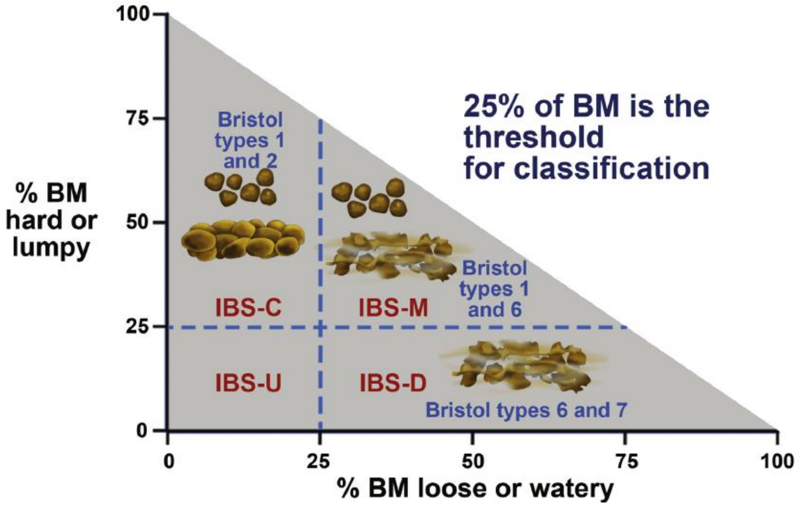
Lactose intolerance overlap with irritable bowel syndrome (IBS)

C1. Diagnostic Criteria[a] for Irritable Bowel Syndrome

Recurrent abdominal pain, on average, at least 1 day per week in the last 3 months, associated with 2 or more of the following criteria:

1. Related to defecation
2. Associated with a change in frequency of stool
3. Associated with a change in form (appearance) of stool

[a]Criteria fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis.



Rome IV IBS criteria
Lacy et al 2016

Dietary triggers in IBS

- Up to 90% report food induces symptoms (Hayes 2014, Lacy 2009, Heizer 2009)
- Two thirds patients initiate dietary restrictions (Monsbakken 2006)
- 45% IBS patients have lactose intolerance (Alpers 2006)
- Diet mainstay of treatment strategies

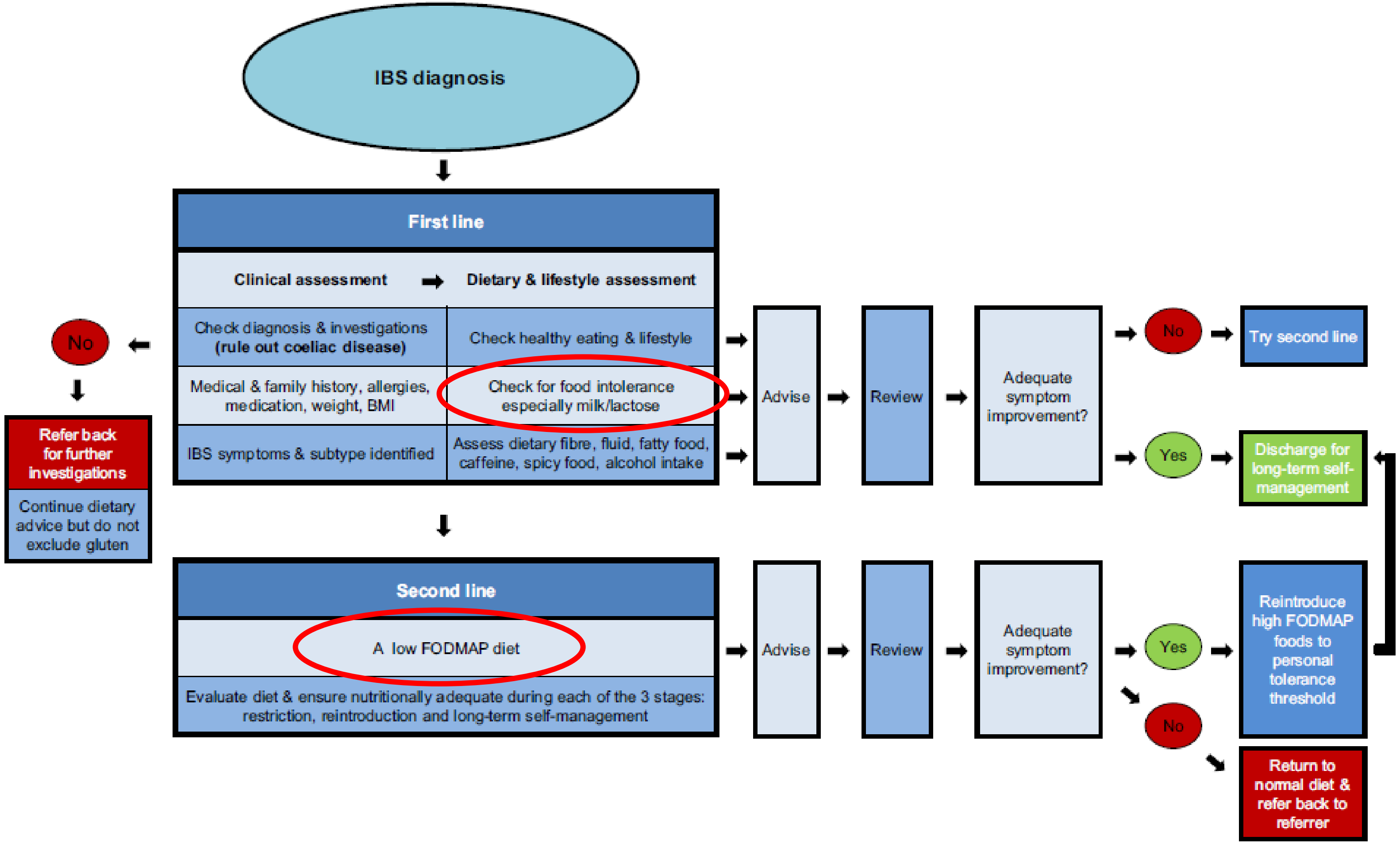
PROFESSIONAL GUIDELINE

doi: 10.1111/jhn.12385

The Association of UK Dietitians

British Dietetic Association systematic review and evidence-based practice guidelines for the dietary management of irritable bowel syndrome in adults (2016 update)

Y. A. McKenzie,[1] R. K. Bowyer,[2] H. Leach,[3] P. Gulia,[4] J. Horobin,[5] N. A. O'Sullivan,[6] C. Pettitt,[7] L. B. Reeves,[8] L. Seamark,[9] M. Williams,[9] J. Thompson,[10] M. C. E. Lomer[6,11] (IBS Dietetic Guideline Review Group on behalf of Gastroenterology Specialist Group of the British Dietetic Association)



What are FODMAPs

Fermentable

Oligosaccharides (fructans, galacto-oligosaccharides)

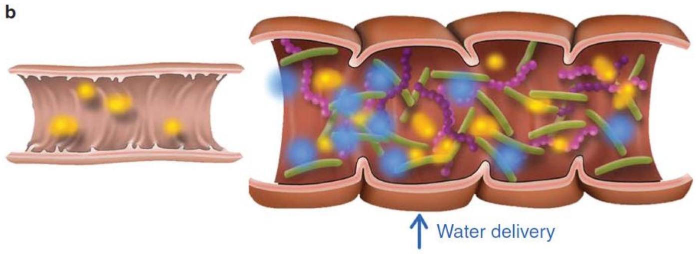
Disaccharides (lactose)

Monosaccharides (fructose)

And

Polyol**S** (sorbitol)

FODMAPs increase small intestinal water



Alimentary Pharmacology & Therapeutics

Dietary poorly absorbed, short-chain carbohydrates increase delivery of water and fermentable substrates to the proximal colon

J. S. BARRETT, R. B. GEARRY, J. G. MUIR, P. M. IRVING, R. ROSE, O. ROSELLA, M. L. HAINES, S. J. SHEPHERD & P. R. GIBSON

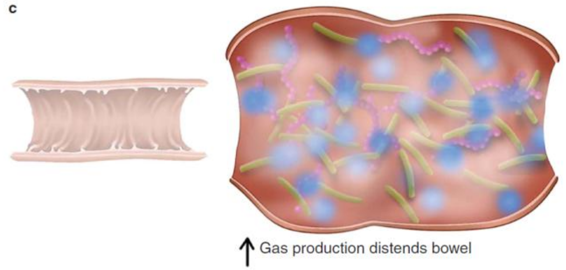
Barrett *et al,*
Alim Pharm Ther
2010; 31, 874–882

Differential Effects of FODMAPs (Fermentable Oligo-, Di-, Mono-Saccharides and Polyols) on Small and Large Intestinal Contents in Healthy Subjects Shown by MRI

Kathryn Murray, PhD[1], Victoria Wilkinson-Smith, BMedSci[2], Caroline Hoad, PhD[1], Carolyn Costigan, MSc[1], Eleanor Cox, PhD[1], Ching Lam, MB BCh[2], Luca Marciani, PhD[2], Penny Gowland, PhD[1] and Robin C. Spiller, MD, FRCP[2]

Murray et al,
Am J Gastro
2014; 109: 110-119

Fructans increase colonic gas production



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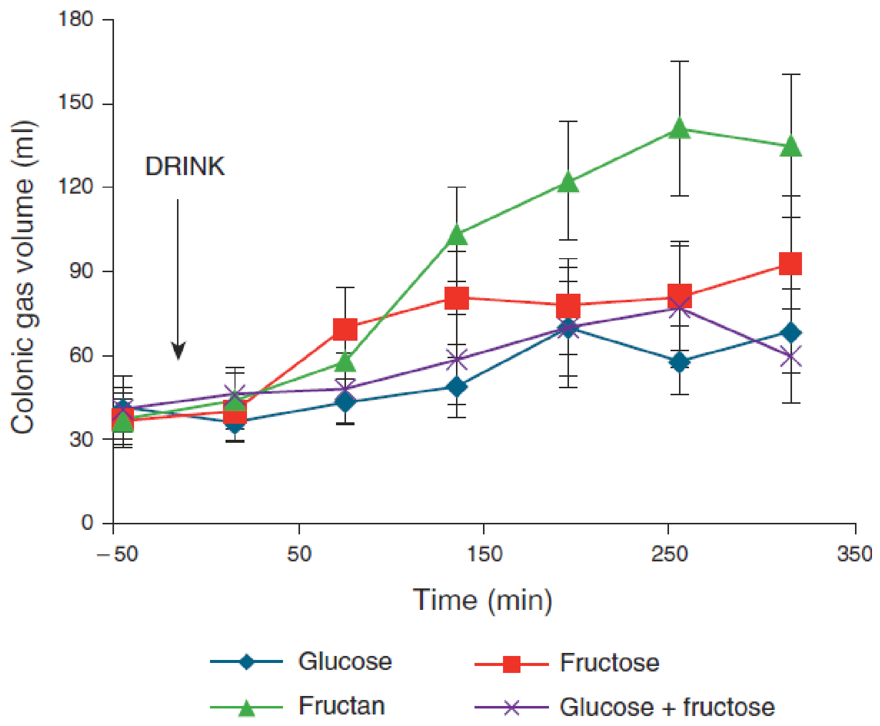


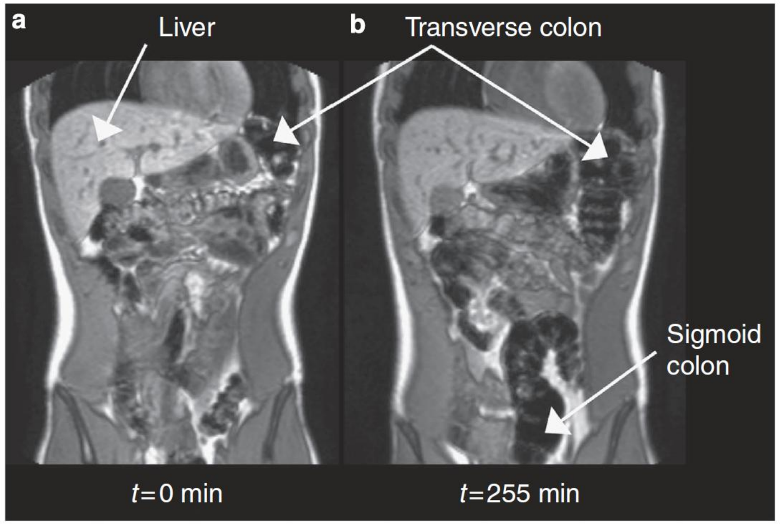


Figure 5. A representative example of coronal images through the large bowel of a single volunteer, comparing the visibility of gas in the colon at (**a**) baseline *t*= −45 min and (**b**) 255 min after drinking the fructan test meal.

Murray et al, Am J Gastroenterol. 2014; 109: 110-119.

Efficacy of a low-FODMAP diet in adult irritable bowel syndrome: a systematic review and meta-analysis

European Journal of Nutrition (2021) 60:3505–3522
https://doi.org/10.1007/s00394-020-02473-0

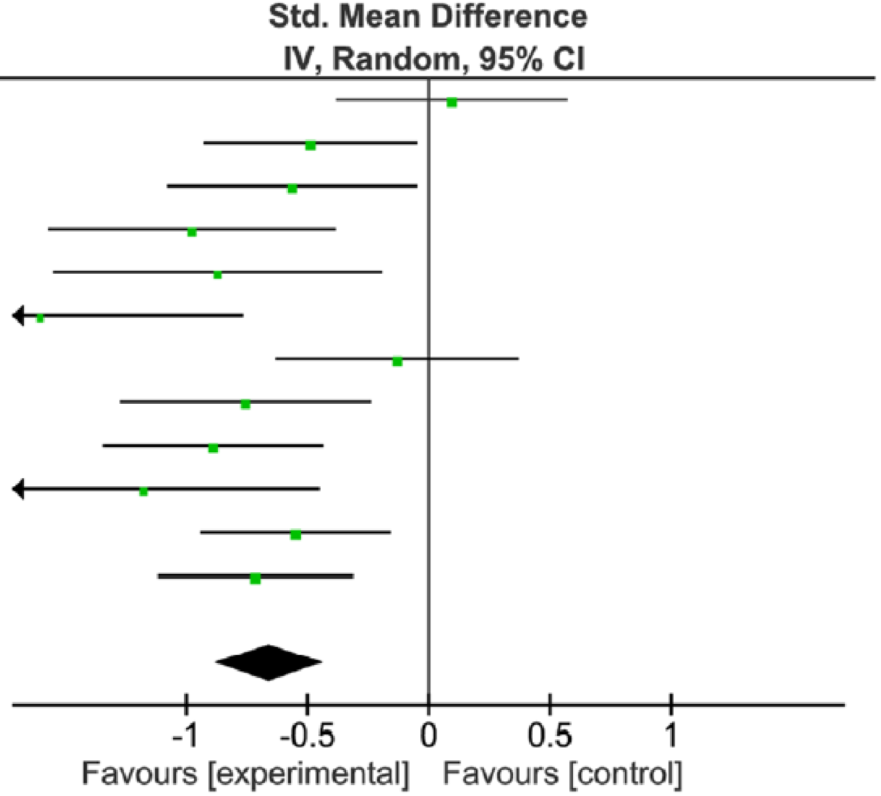
Anne-Sophie van Lanen[1,2] · Angelika de Bree[2] · Arno Greyling[2]

Standardized mean differences for IBS severity outcome measures

	LFD			Control				Std. Mean Difference
Study	**Mean**	**SD**	**n**	**Mean**	**SD**	**n**	**Weight**	**IV, Random, 95% CI**
Bohn 2015	246	127	33	236	78	34	9.1%	0.09 [-0.39, 0.57]
Eswaran 2016	3.38	2	43	4.41	2.2	39	9.8%	-0.49 [-0.93, -0.05]
Halmos 2014	22.8	32.4	30	44.9	44.19	30	8.5%	-0.56 [-1.08, -0.05]
Harvie 2017	128.47	87.75	23	206.31	69.59	27	7.5%	-0.98 [-1.57, -0.39]
McIntosh 2017	208	74.8	18	290	106	19	6.4%	-0.87 [-1.55, -0.19]
Ong 2010	2.52	2.01	15	5.83	2.01	15	4.9%	-1.60 [-2.44, -0.76]
Paduano 2019	16	8	34	17	7	28	8.8%	-0.13 [-0.63, 0.37]
Patcharatrakul 2019	38.5	20	30	53.5	19.2	32	8.5%	-0.76 [-1.27, -0.24]
Pedersen 2014	198.42	101.91	42	288.39	98.61	40	9.5%	-0.89 [-1.34, -0.43]
Staudacher 2012	1.1	0.47	16	1.7	0.52	19	5.9%	-1.18 [-1.90, -0.45]
Staudacher 2017	173	95	51	224	89	53	10.6%	-0.55 [-0.94, -0.16]
Zahedi 2018	108	63.82	50	149.75	51.39	51	10.4%	-0.72 [-1.12, -0.31]
Total (95% CI)			**385**			**387**	**100.0%**	**-0.66 [-0.88, -0.44]**

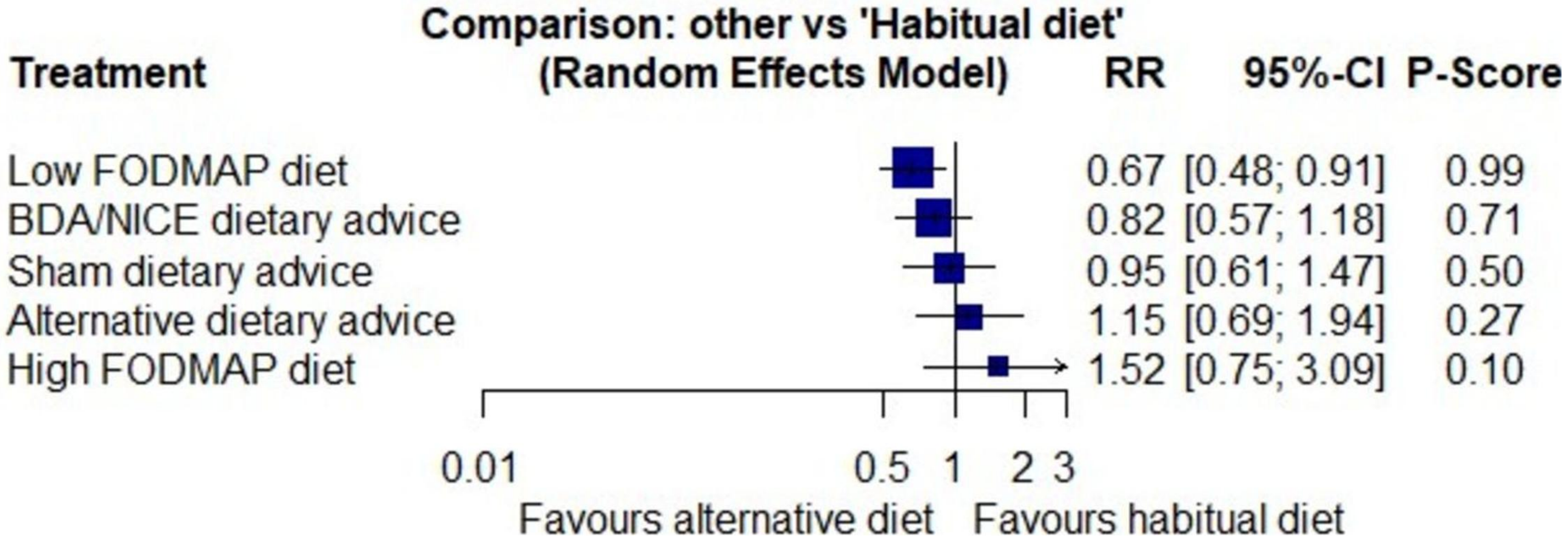
Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 24.01$, df = 11 ($P = 0.01$); $I^2 = 54\%$

Test for overall effect: $Z = 5.81$ ($P < 0.00001$)



Efficacy of a low FODMAP diet in irritable bowel syndrome: systematic review and network meta-analysis

Christopher J. Black [1,2] Heidi M. Staudacher [3] Alexander C. Ford [1,2]



Nutrient Intake, Diet Quality, and Diet Diversity in Irritable Bowel Syndrome and the Impact of the Low FODMAP Diet

JOURNAL OF THE ACADEMY OF NUTRITION AND DIETETICS

https://doi.org/10.1016/j.jand.2019.01.017

Heidi M. Staudacher, PhD, RD*; Frances S. E. Ralph, RD*; Peter M. Irving, MA, MD, FRCP; Kevin Whelan, PhD, RD*; Miranda C. E. Lomer, PhD, RD*

FODMAP	Habitual diet at baseline (n=130), mean (95% CI)	Low FODMAP diet (n=63)	Sham diet (n=48)	Habitual diet (n=19)	ANCOVA,[b] *P* value	FODMAP diet vs sham diet	FODMAP diet vs habitual diet
		←estimated marginal mean (95% CI)→					
Total FODMAP intake (g/d)	17.0 (5.4-18.5)	8.6 (6.9-10.4)	17.5 (15.6-19.5)	16.0 (12.8-19.1)	<0.001	<0.001	<0.001
Fructans (g/d)[c]	4.0 (3.3-4.8)	2.1 (1.5-2.6)	4.8 (4.1-5.5)	4.2 (3.2-5.2)	<0.001	<0.001	<0.001
Galacto-oligosaccharides (g/d)[c]	1.0 (0.9-1.2)	0.8 (0.7-1.0)	0.9 (0.7-1.2)	1.7 (1.4-2.0)	0.004	0.095	0.001
Lactose (g/d)	8.8 (7.5-10.1)	4.2 (2.8-5.6)	8.8 (7.1-10.4)	7.5 (4.9-10.1)	<0.001	<0.001	0.030
Excess fructose (g/d)[c]	1.6 (1.3-1.9)	12.6 (10.7-14.6)	16.4 (14.2-18.7)	19.5 (15.8-23.2)	0.009	0.011	0.015
Sorbitol (g/d)[c]	0.8 (0.6-0.9)	0.2 (0.1-0.4)	1.0 (0.8-1.2)	0.5 (0.2-0.8)	<0.001	<0.001	<0.001
Mannitol (g/d)[c]	0.4 (0.3-0.4)	0.1 (0.1-0.2)	0.3 (0.2-0.4)	0.3 (0.2-0.4)	0.007	0.011	0.100

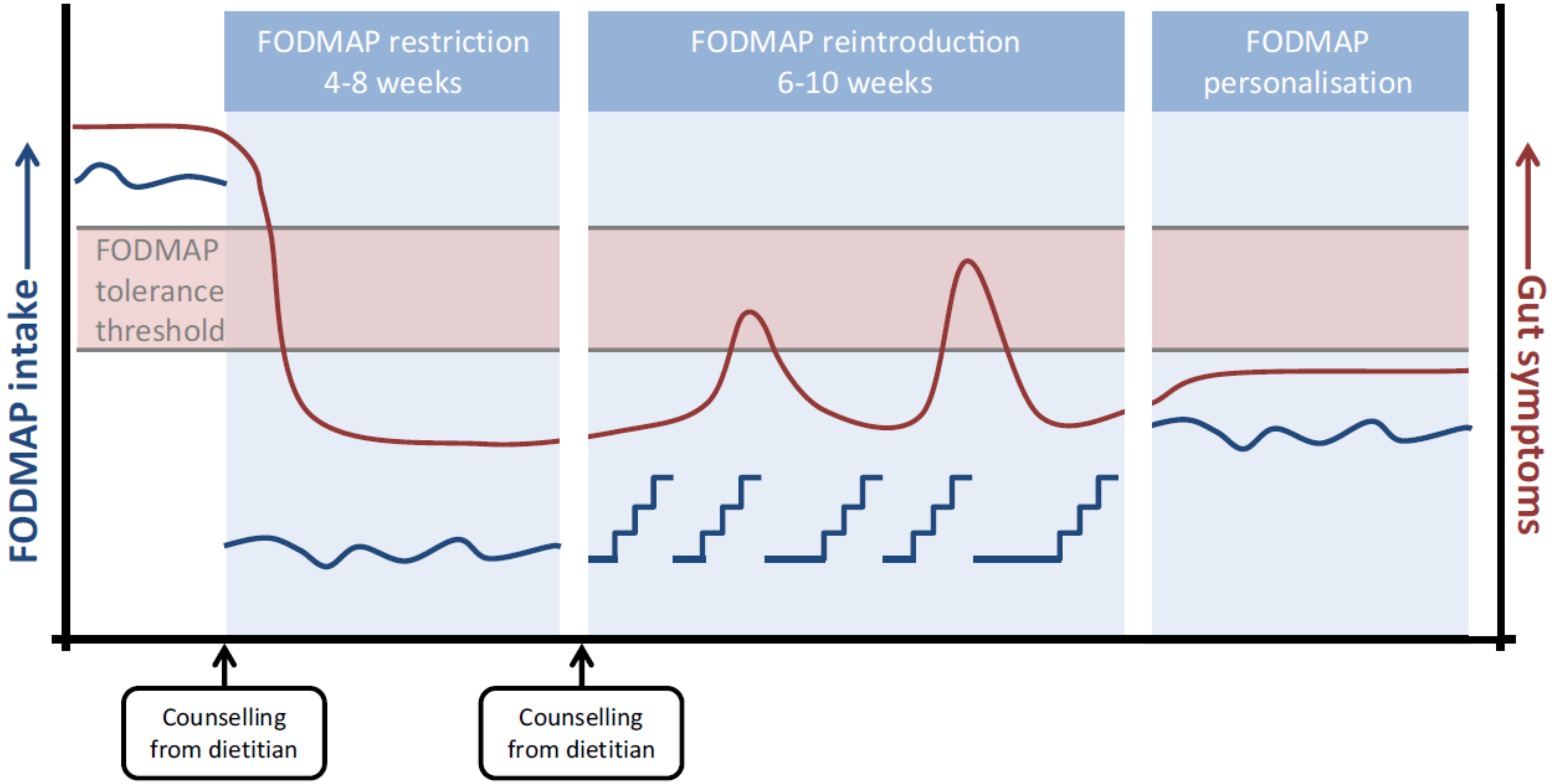
[a]FODMAP=fermentable oligosaccharides, disaccharides, monosaccharides, and polyols.
[b]ANCOVA=analysis of covariance with planned comparisons using simple planned contrasts.
[c]Log transformation required for ANCOVA.

The low FODMAP diet in practice

BDA The Association of UK Dietitians
THE OFFICIAL JOURNAL OF THE BRITISH DIETETIC ASSOCIATION
Journal of Human Nutrition and Dietetics

The low FODMAP diet in the management of irritable bowel syndrome: an evidence-based review of FODMAP restriction, reintroduction and personalisation in clinical practice

K. Whelan,[1] L. D. Martin,[1] H. M. Staudacher[1,2,3] & M. C. E. Lomer[1,2,4]



Whelan et al, J Hum Nutr Diet, 2018; 31: 239-255.

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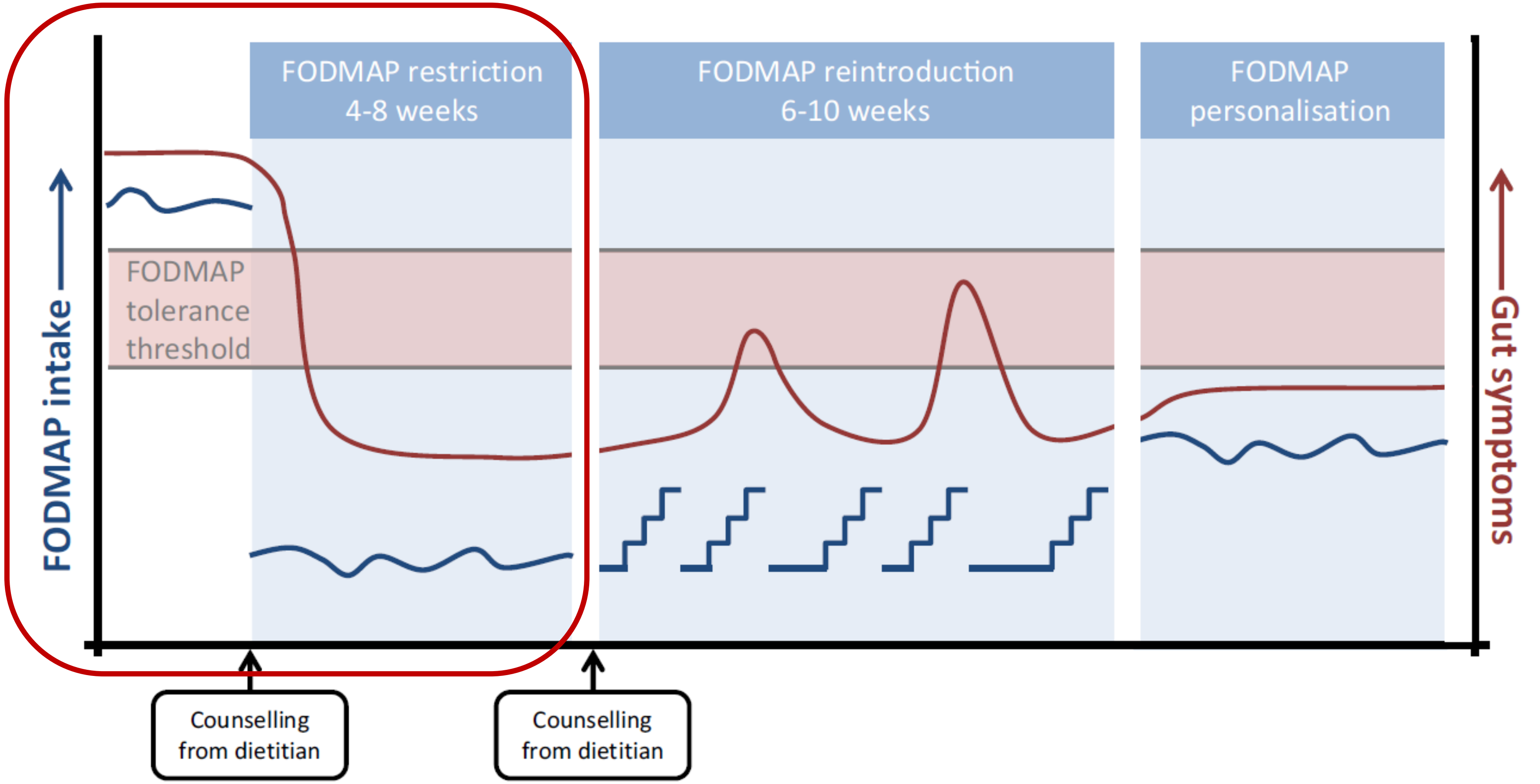

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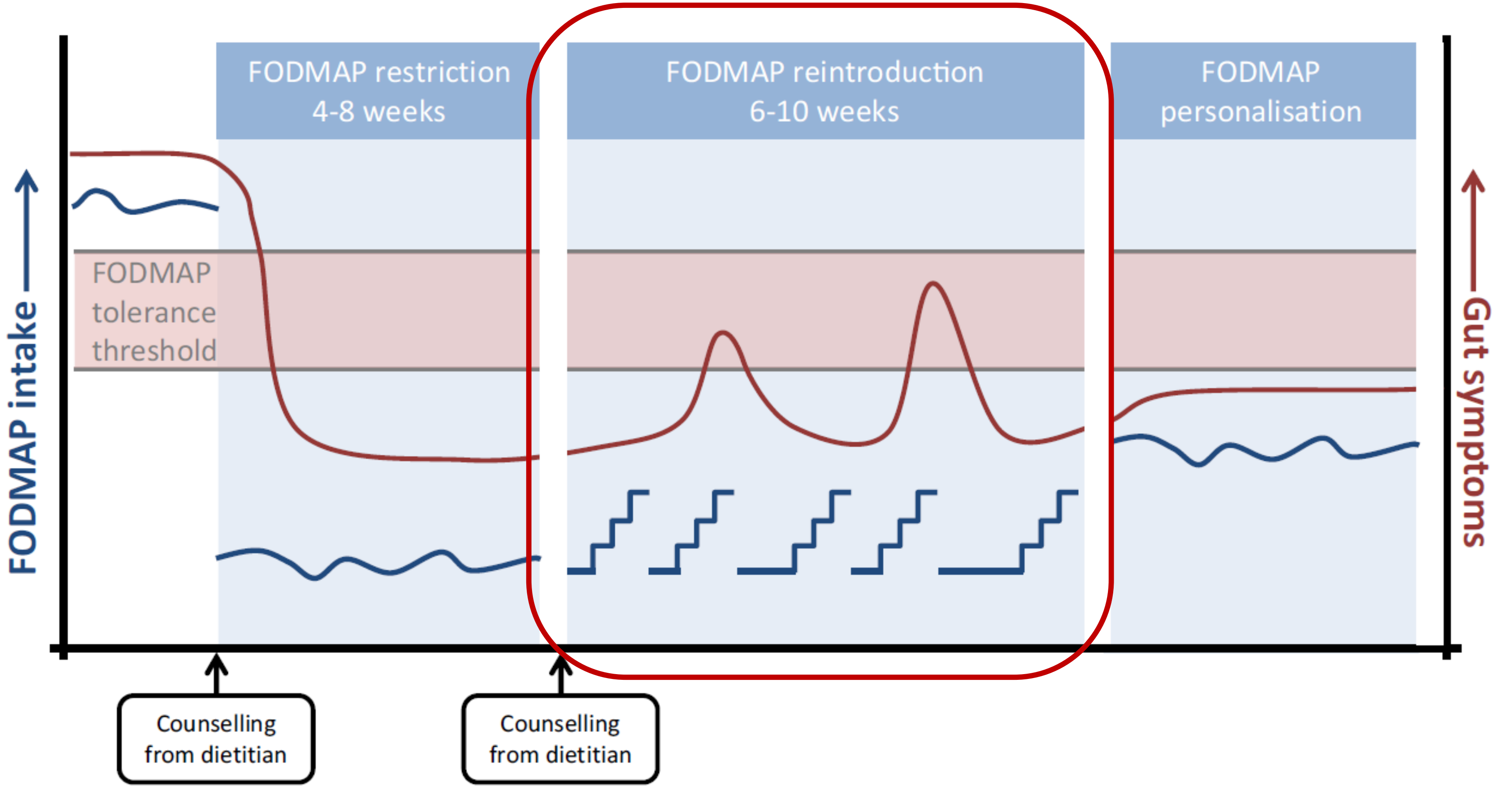

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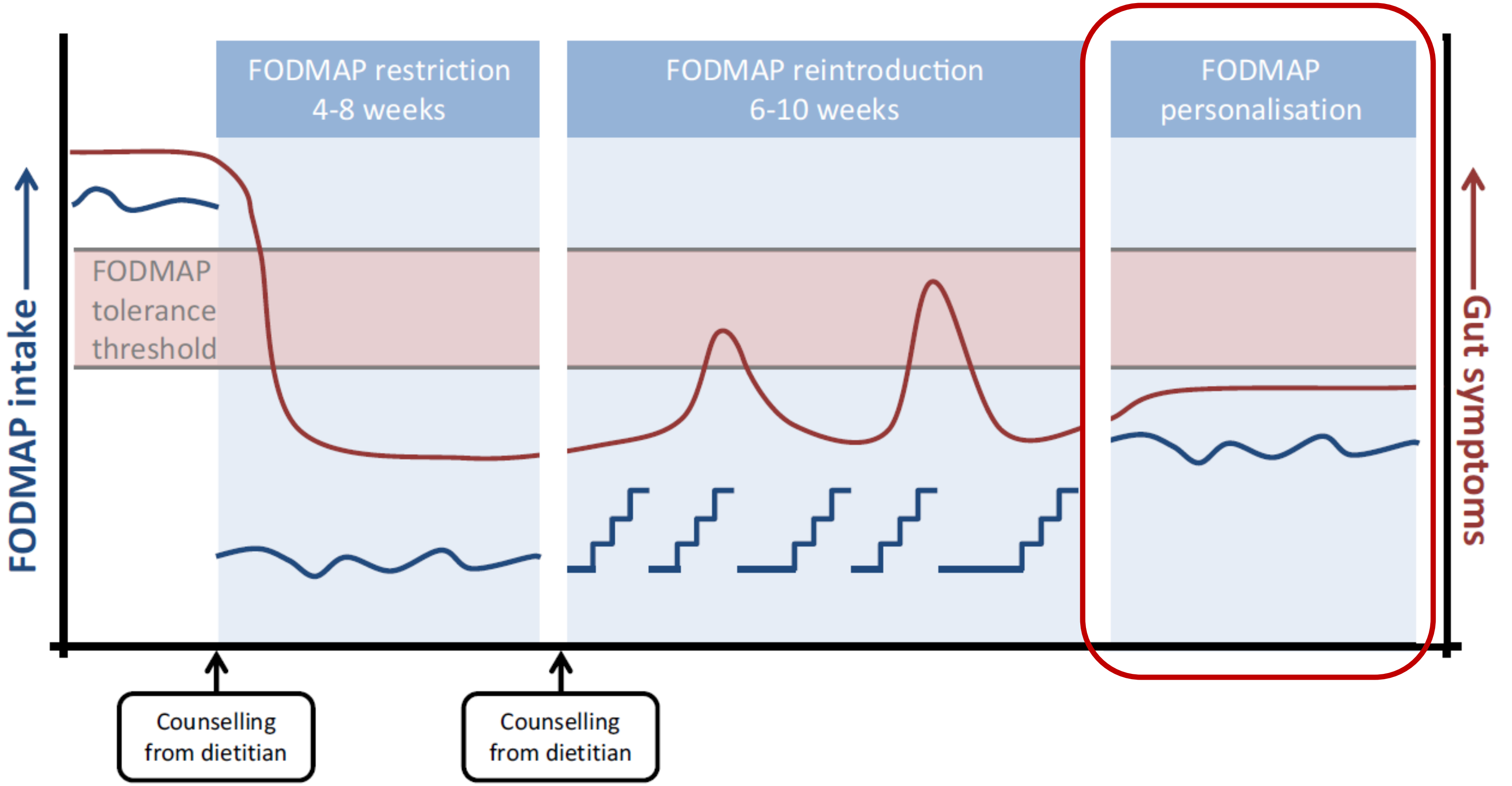

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Long-term personalised low FODMAP diet improves symptoms and maintains luminal Bifidobacteria abundance in irritable bowel syndrome

Staudacher et al 2022 Neurogastroenterol Motil. 2021; 00:e14241. DOI:10.1111/nmo.14241

FODMAP, energy and nutrient intake at baseline and after 12-months of low FODMAP diet

Dietary variable, median (IQR)	**Baseline (n=18)**	**Long-term personalised low FODMAP diet (n=18)**	**p***
Total FODMAPs, g/d	16.9 (14.4)	18.4 (9.7)	0.679
Fructans, g/d	4.8 (2.7)	4.0 (4.5)	0.557
GOS, g/d	0.6 (0.5)	0.6 (0.6)	0.112
Lactose, g/d	9.0 (11.8)	9.9 (8.4)	0.983
Excess fructose, g/d	1.3 (1.9)	1.0 (1.3)	0.500
Sorbitol, g/d	0.7 (1.1)	0.3 (0.4)	**0.028**
Mannitol, g/d	0.3 (0.4)	0.3 (0.3)	0.327
Energy, kcal/d	2052 (812)	1948 (603)	**0.043**
Carbohydrate, g/d	218 (85)	196 (79)	**0.039**
Total sugar, g/d	79 (27)	78 (62)	0.879
Starch, g/d	128 (71)	116 (48)	0.085
Total fibre, g/d	17.0 (5.6)	16.6 (5.7)	0.349
Protein, g/d	78 (47)	74 (27)	**0.011**
Fat, g/d	86 (31)	77 (41)	**0.048**
Calcium, mg/d	806 (308)	819 (424)	0.267
Iron, mg/d	11.4 (5.9)	9.4 (5.7)	**0.005**

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Prebiotic effect of lactose

Changes in gut microbiota and lactose intolerance symptoms before and after daily lactose supplementation in individuals with the lactase nonpersistent genotype

American Society for Nutrition
Excellence in Nutrition Research and Practice

The American Journal of CLINICAL NUTRITION

journal homepage: https://ajcn.nutrition.org/

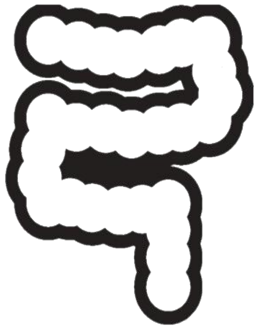
Lonneke JanssenDuijghuijsen [1,*], Ellen Looijesteijn [2], Maartje van den Belt [1], Beatrix Gerhard [3], Martin Ziegler [3], Renata Ariens [1], Reina Tjoelker [2], Jan Geurts [2]

[1] *Wageningen Food and Biobased Research, Wageningen University & Research, Wageningen, The Netherlands;* [2] *FrieslandCampina, Amersfoort, The Netherlands;* [3] *Biomax Labvantage, Planegg, Germany*

Lactastic study

To assess whether repetitive increasing doses of dietary lactose in LNP

- induces colonic microbial adaptation



- decreases symptoms of lactose intolerance

Study design - Lactastic study

25 Males and females of Asian ethnicity

18-50 years
Healthy

LNP genotype (13910C>T)
Based on buccal swab testing

Avoiding dietary lactose in habitual diet
Self-reported via questionnaire

Screening

3*4-week course of an increasing dose of lactose (3, 6 and 12 gram).
Twice a day

Dose-response single-blinded intervention study

2* 3 gr lactose + 9 gr dextrose

2* 6 gr lactose + 6 gr dextrose

2* 12 gr lactose

Intervention: 3 * 4 weeks

Microbiome: P
α-Diversity
β-Diversity
Microbial composition
Functional analysis

Gastrointestinal function: S
Hydrogen breath test
Fecal lactase activity
Gut comfort

Microbial activity: T
SCFAs

22 Participants in analysis

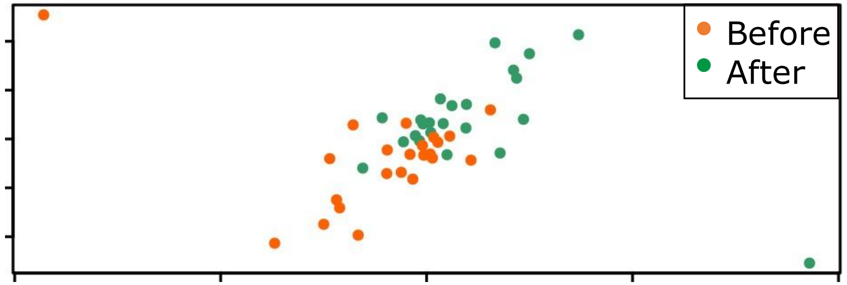
Outcomes

Lactose intervention increases relative abundance of *Bifidobacterium*

Alpha diversity (n=23)

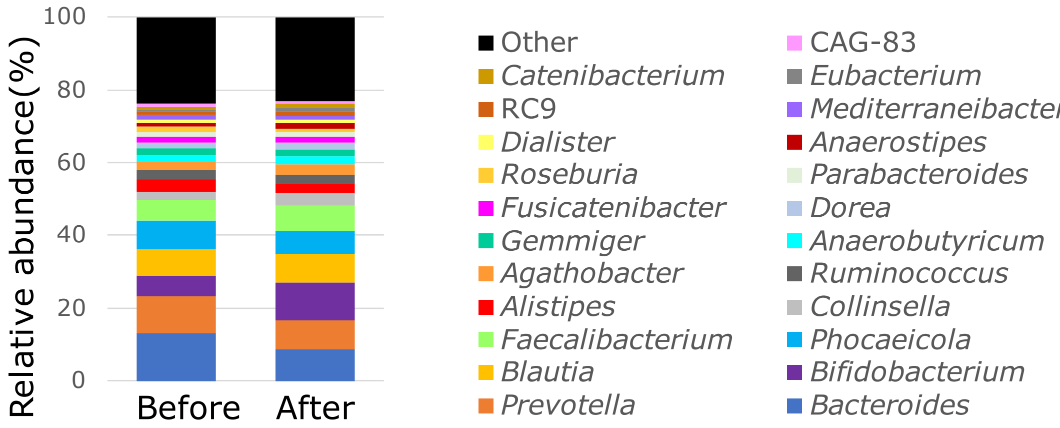
	Before	After	p-value
Shannon	4.54 (0.62)	4.51 (0.58)	0.687
Simpson	0.95 (0.04)	0.95 (0.05)	0.643

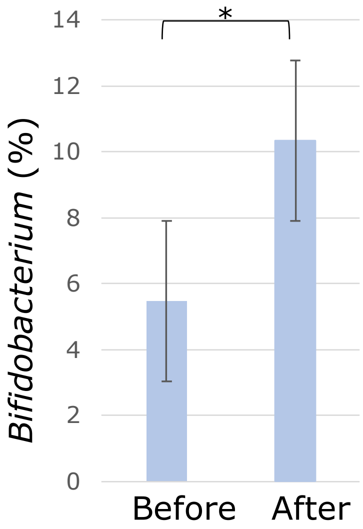
Beta diversity - Bray Curtis (n=23)

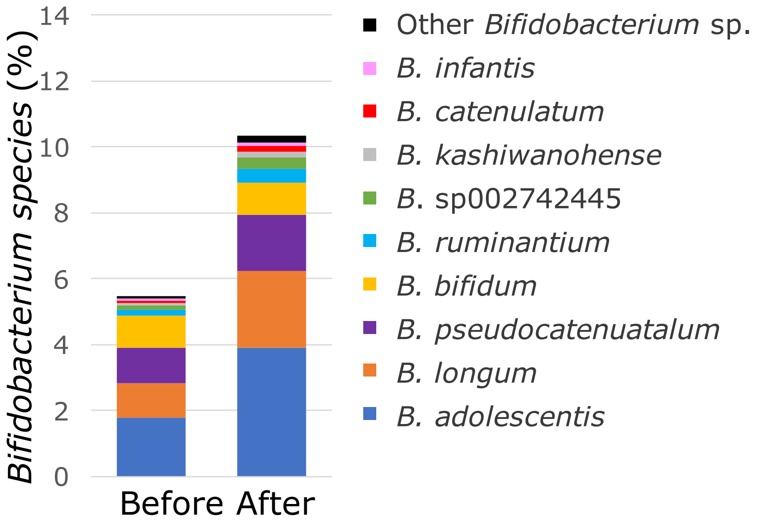


Significant shift of microbiota PERMANOVA (p=0.037)

Microbial composition (n=23)

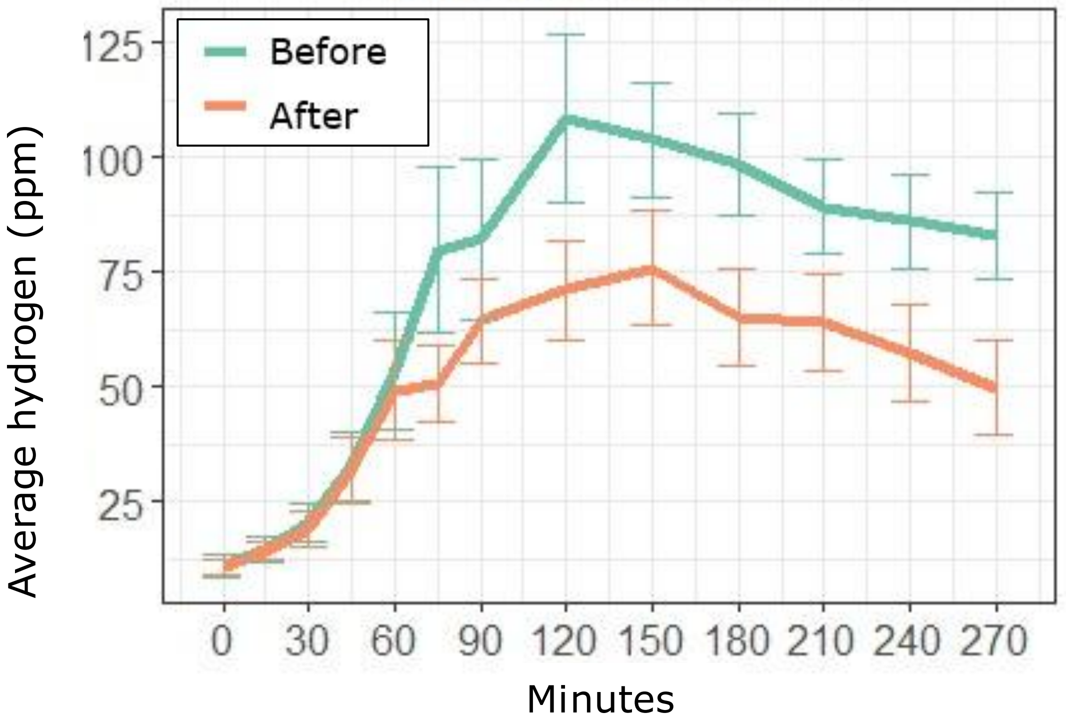




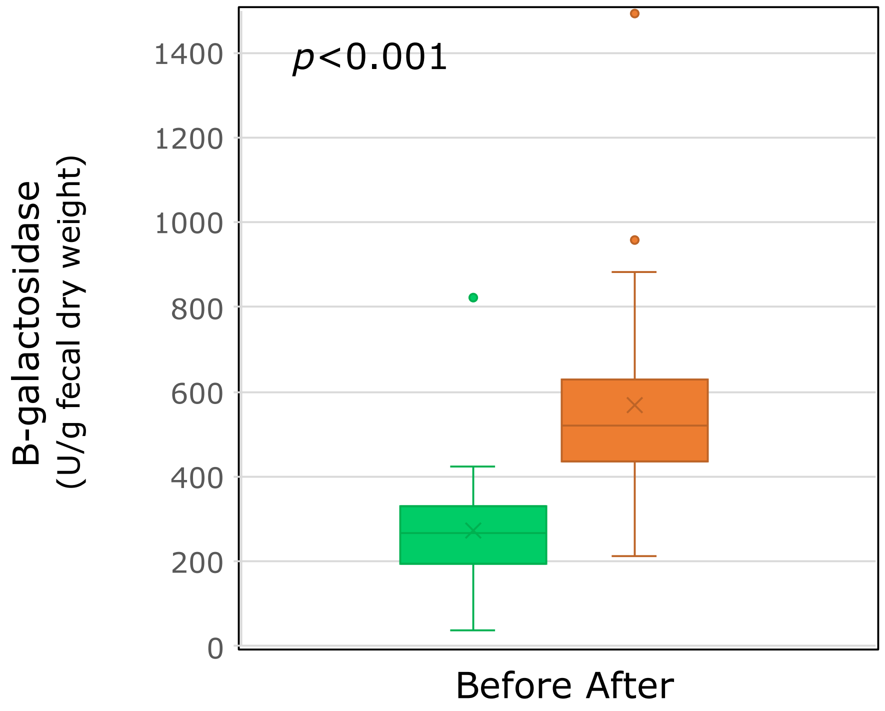


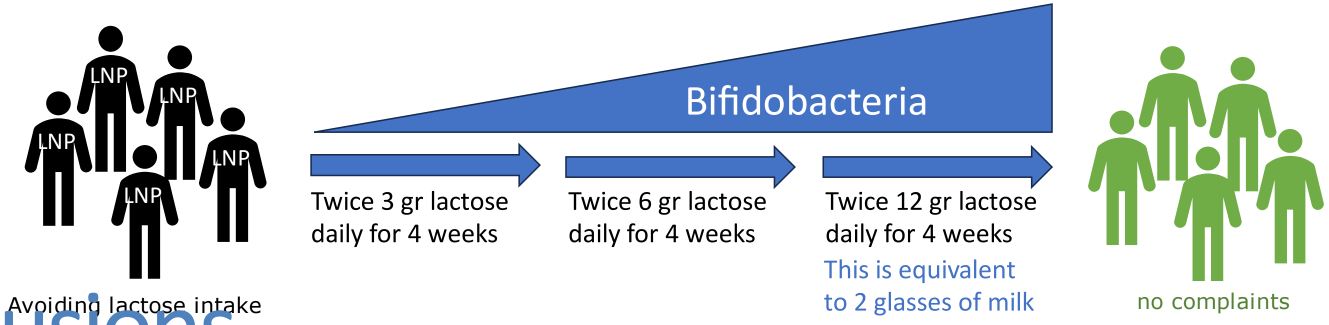
Lactose intervention increased lactose tolerance via adaptation of the gut microbiota

Hydrogen breath test (n=23)



Fecal β-galactosidase (n=23)





Lactastic conclusions

- Repetitive consumption of lactose increases beneficial bifidobacteria in the gut microbiome of LNP individuals - lactose acts as a dietary fibre
- This increase in bifidobacteria leads to an increased capacity to metabolize lactose without gas production
- Lactose consumption up to 24 grams per day is well-tolerated by LNP individuals and results in a reduction in expired breath hydrogen
- Regular consumption of lactose, whereby the amount of lactose is gradually increased, enables most LNP individuals to keep dairy products in their diet and thereby profit from the nutrient-richness of those foods

* JANSSEN DUIJGHUIJSEN, L. ET AL. (2023). AM J CLIN NUTR, S0002-9165(23)66349.

When to restrict lactose

Reported problem foods → Symptoms during breath test → Patient choice → Ability to comply → Re-test tolerance

Conclusions

Lactose is a unique and fascinating carbohydrate only found in mammalian milk

Lactose malabsorption is common and present in lactase non-persistence and lactase persistence

Diagnosis of lactose malabsorption is challenging

Lactose intolerance is clinically important

Management of lactose intolerance:

- Reduction in lactose dairy products, most people will tolerate some lactose
- Be aware of dietary calcium/vitamin D
- Mixed meals, gastric emptying, transit time improve tolerance
- Often associated with IBS – other dietary restrictions
- Prebiotic effects - gradual re-introduction helps colonic adaptation