Milk’s sweet spot

Lactose: going beyond sweetness

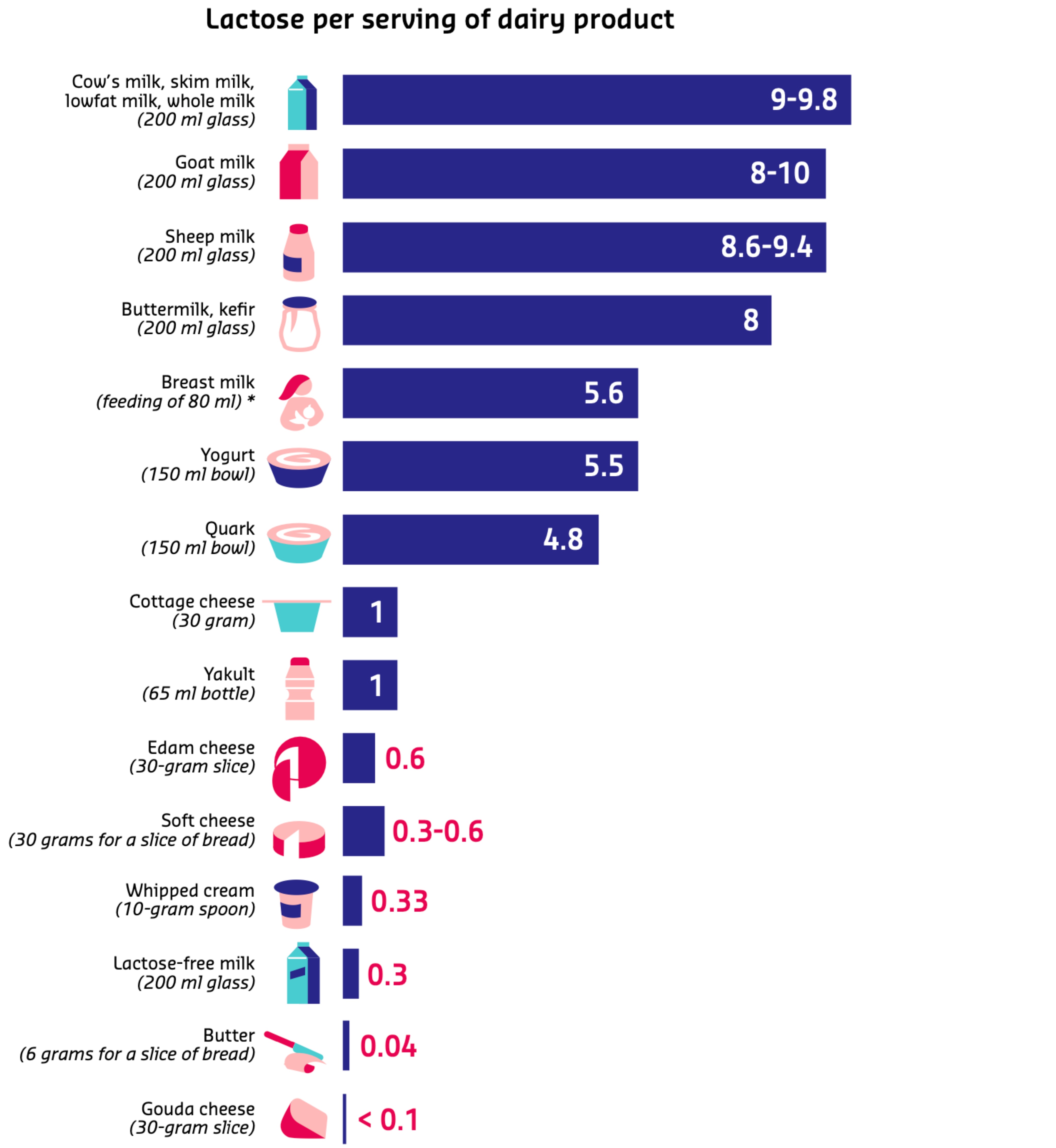
JAN GEURTS, MAY 2025

‘Milk is one of the only foods, that we are aware of, that is produced with the intention of being consumed. Most other foods generally want to avoid being eaten’

Prof. Dr. Mark Thomas, University College London

MOST

milks of placental mammals contain lactose as the principal carbohydrate

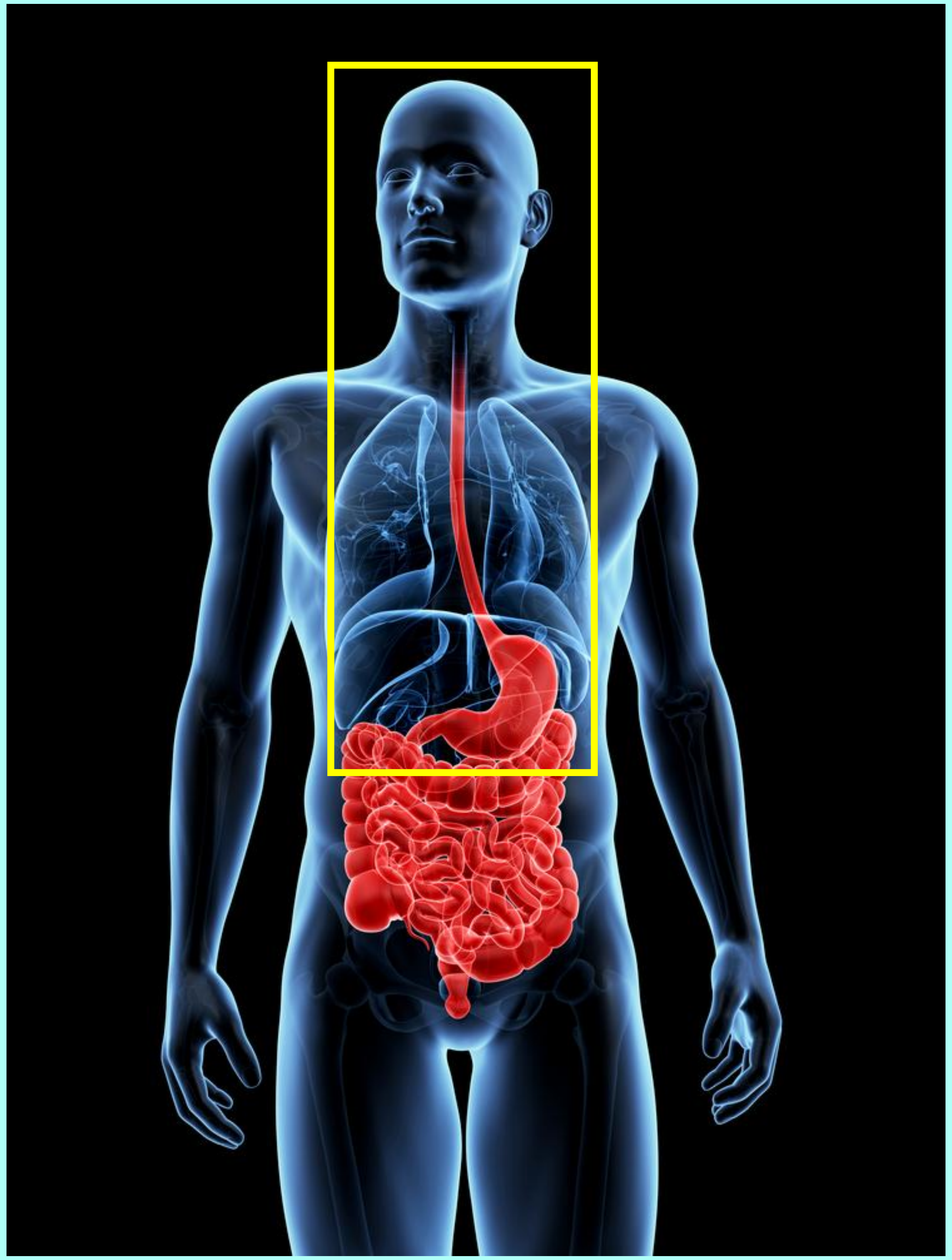


Lactose

Lactose is also known as 'milk sugar'

- Major milk component in most mammals
- Provides 40-50% of infant's energy needs
- Bovine milk contains ~46 g/L (~4.6%)
- Human milk contains ~70 g/L (~7%)

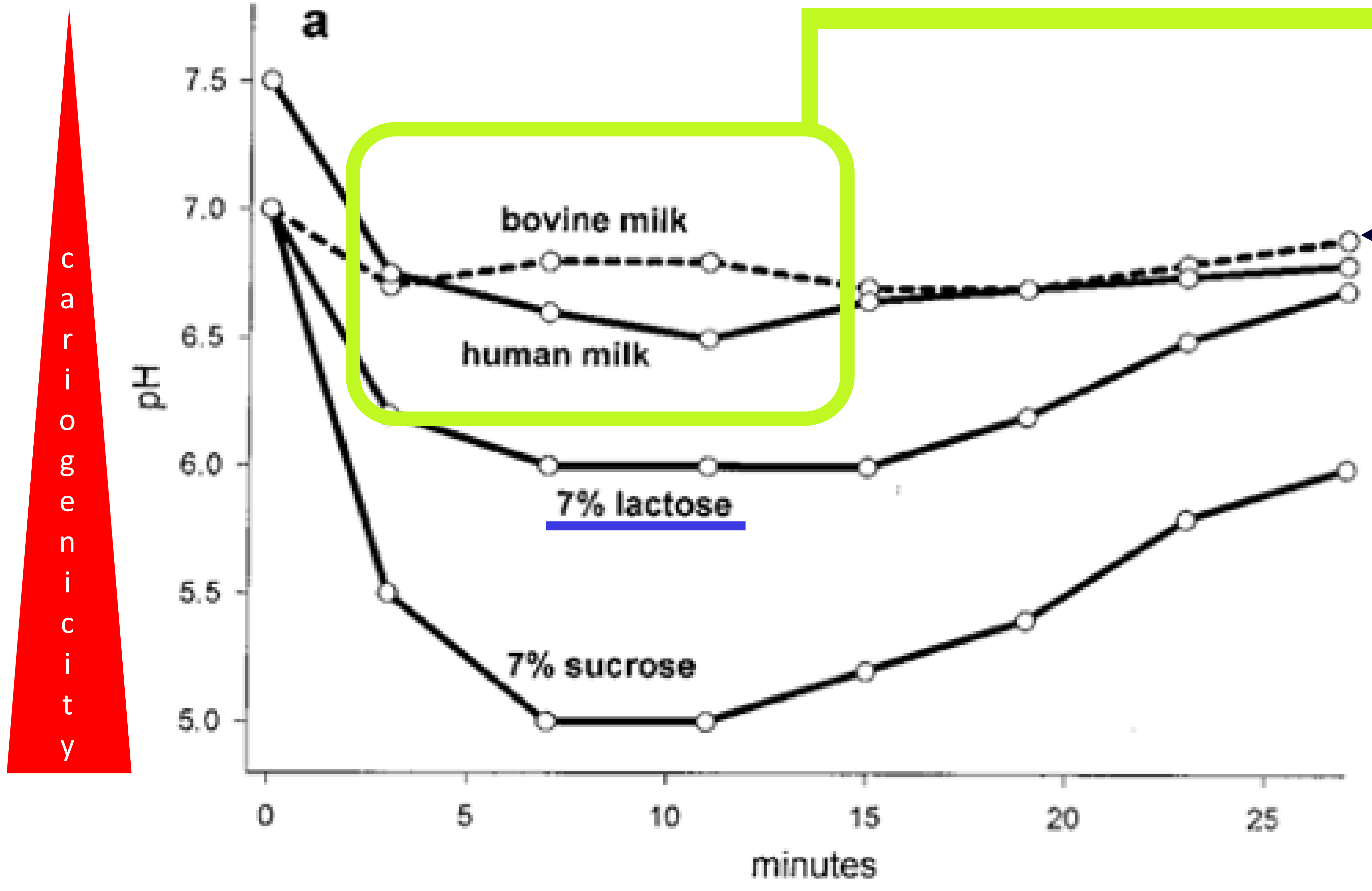
Peters, S, Geurts, JMW, Huupertz, T. Lactose maldigestion and intolerance: facts and figures. Voeding Magazine 2, 2025



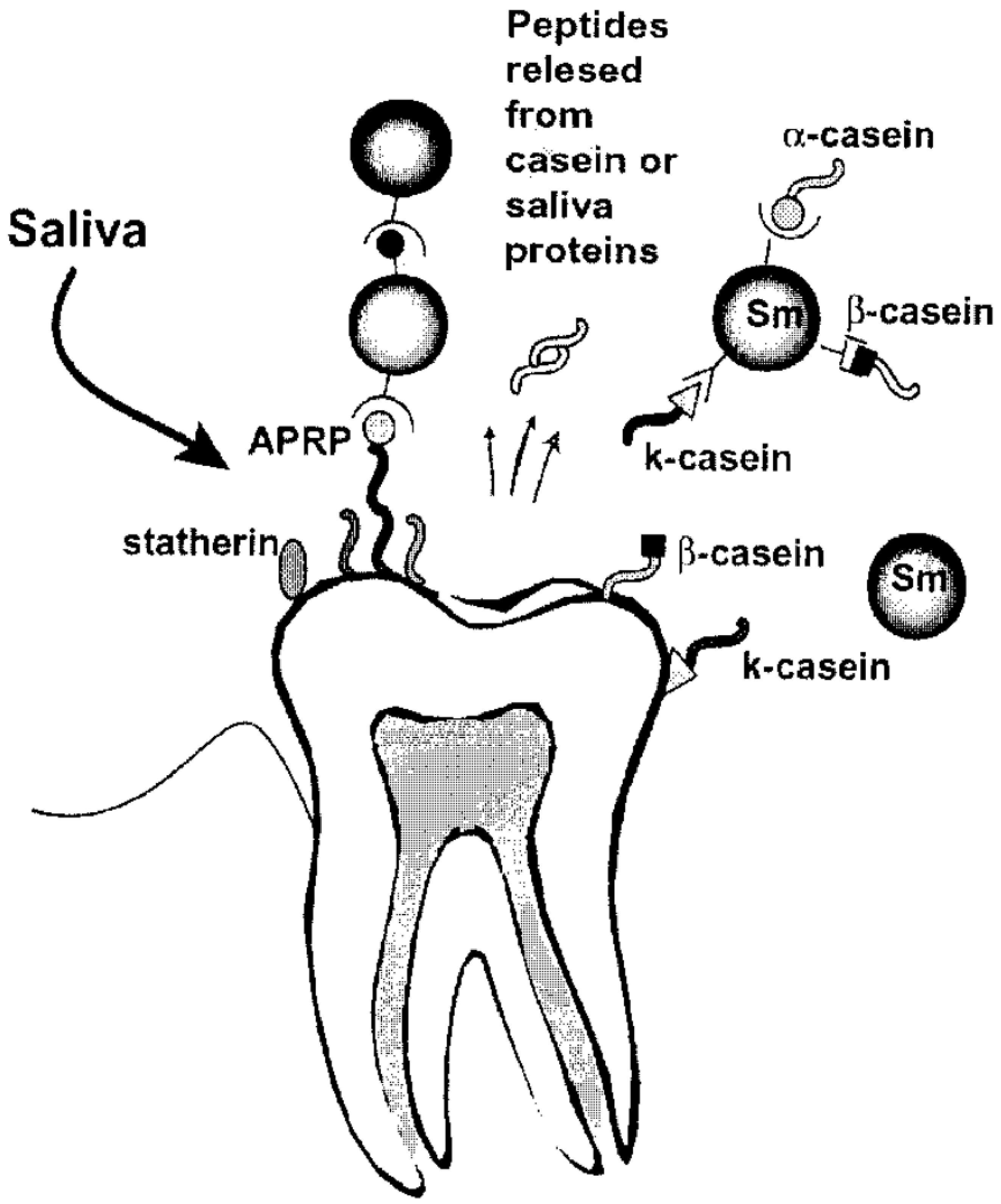
Benefits of intact lactose in the upper digestive tract

Lactose is less prone to cause dental caries

A DROP IN PH IS THE RESULT OF BACTERIAL FERMENTATION AND A PROXY FOR CARIOGENIC POTENTIAL



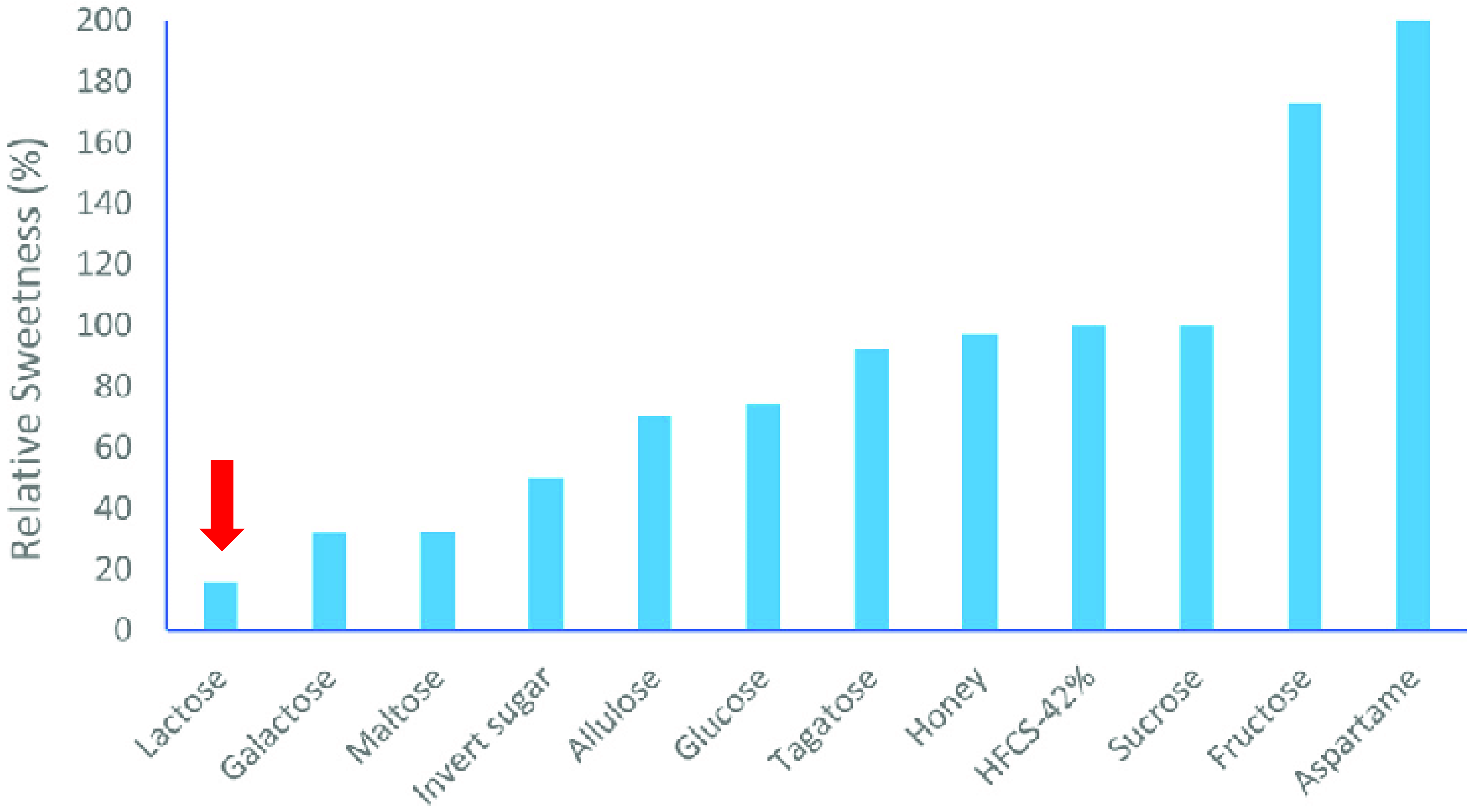
LACTOSE CAUSES A SMALLER DROP IN PH THAN SUCROSE BUT IS ALMOST NON-CARIOGENIC WHEN PART OF THE COMPLETE MILK MATRIX



Lactose is the least cariogenic sugar of all fermentable sugars.

KOULOURIDES ET AL. (1976). CARIOGENICITY OF NINE SUGARS TESTED WITH AN INTRAMURAL DEVICE IN MAN. CARIES RES 10:427-441
JOHANSSON, I. (2002). MILK AND DAIRY PRODUCTS: POSSIBLE EFFECTS ON DENTAL HEALTH. SCAN J NUTR 46(3):119-122

Lactose is less sweet than other sugars



Lactose does <u>not</u> elicit reward effects.

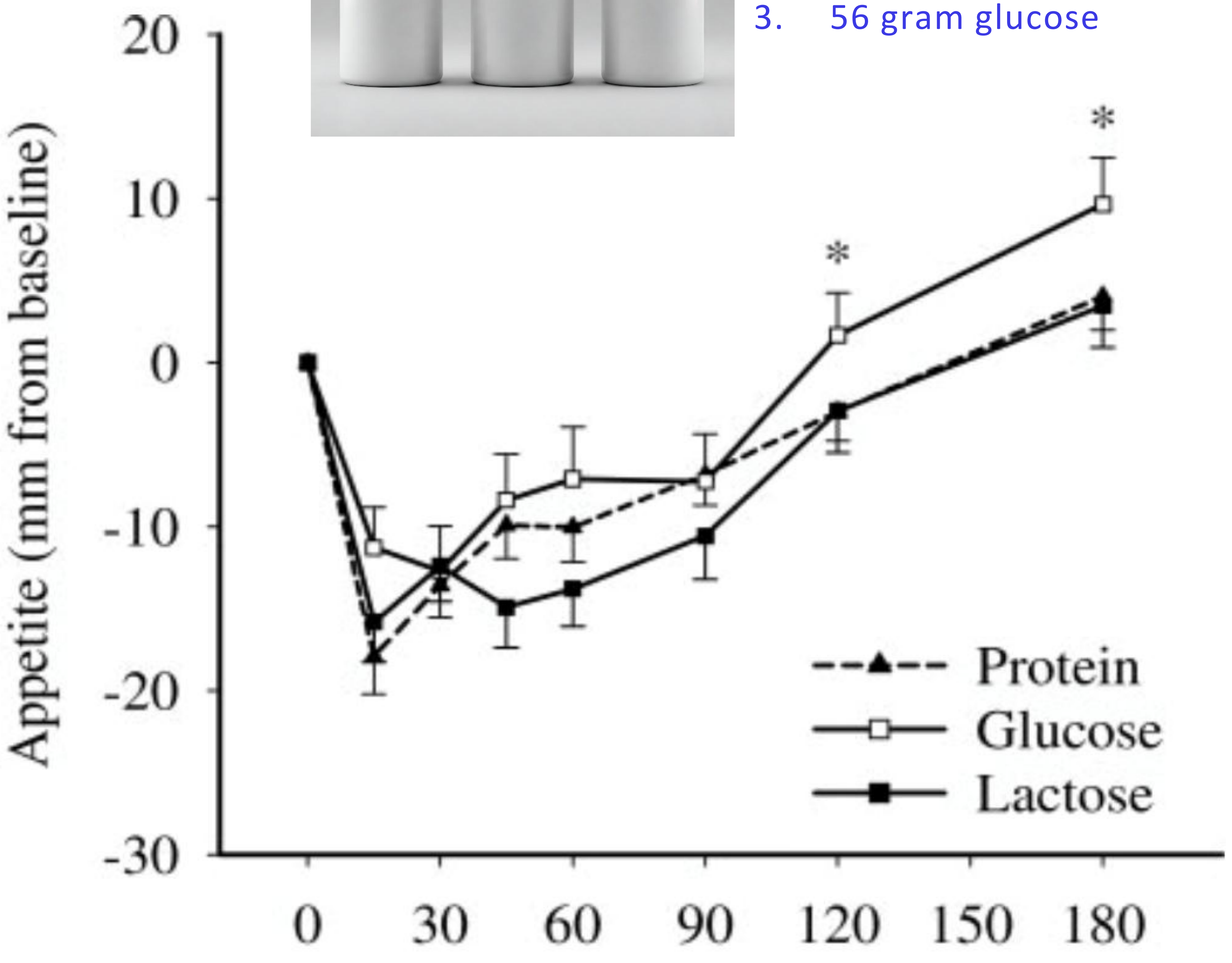
Important for taste preference and healthy body weight development in infants & young children?

PAQUES, M. AND LINDNER, C. (2019). LACTOSE. FIRST EDITION. ACADEMIC PRESS | DELAVEAU. (2002) LE LACTOSE DANS LA LAIT: HYPOTHÈSE SUR SON IMPORTANCE BIOLOGIQUE. ANN PHARM FR 61(5):340-342 | CLEMENS ET AL. (2016). FUNCTIONALITY OF SUGARS IN FOODS AND HEALTH. COMP REV FOOD SCI FOOD SAFETY 15(3):433-470 | TIMOFEEVA AND MITRA. (2013). THE EFFECTS OF SUCROSE ON NEURAL ACTIVITY. CHAPTER 5 IN SUCROSE. NOVA SCIENCE PUBLISHERS INC.

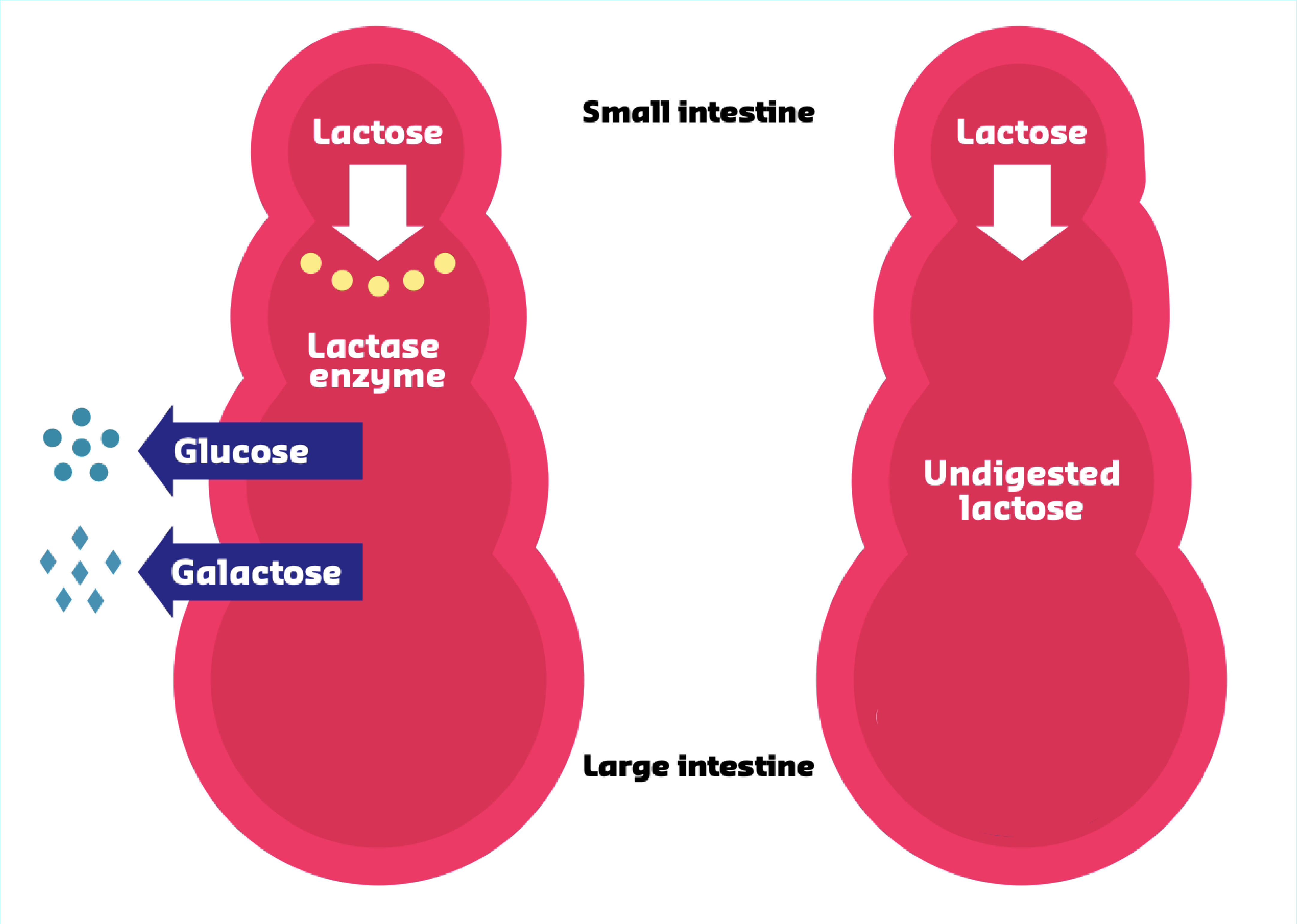
Under isocaloric conditions, consumption of lactose results in less acute appetite and reduced, second meal, energy intake compared with glucose

Iso-caloric liquid preloads

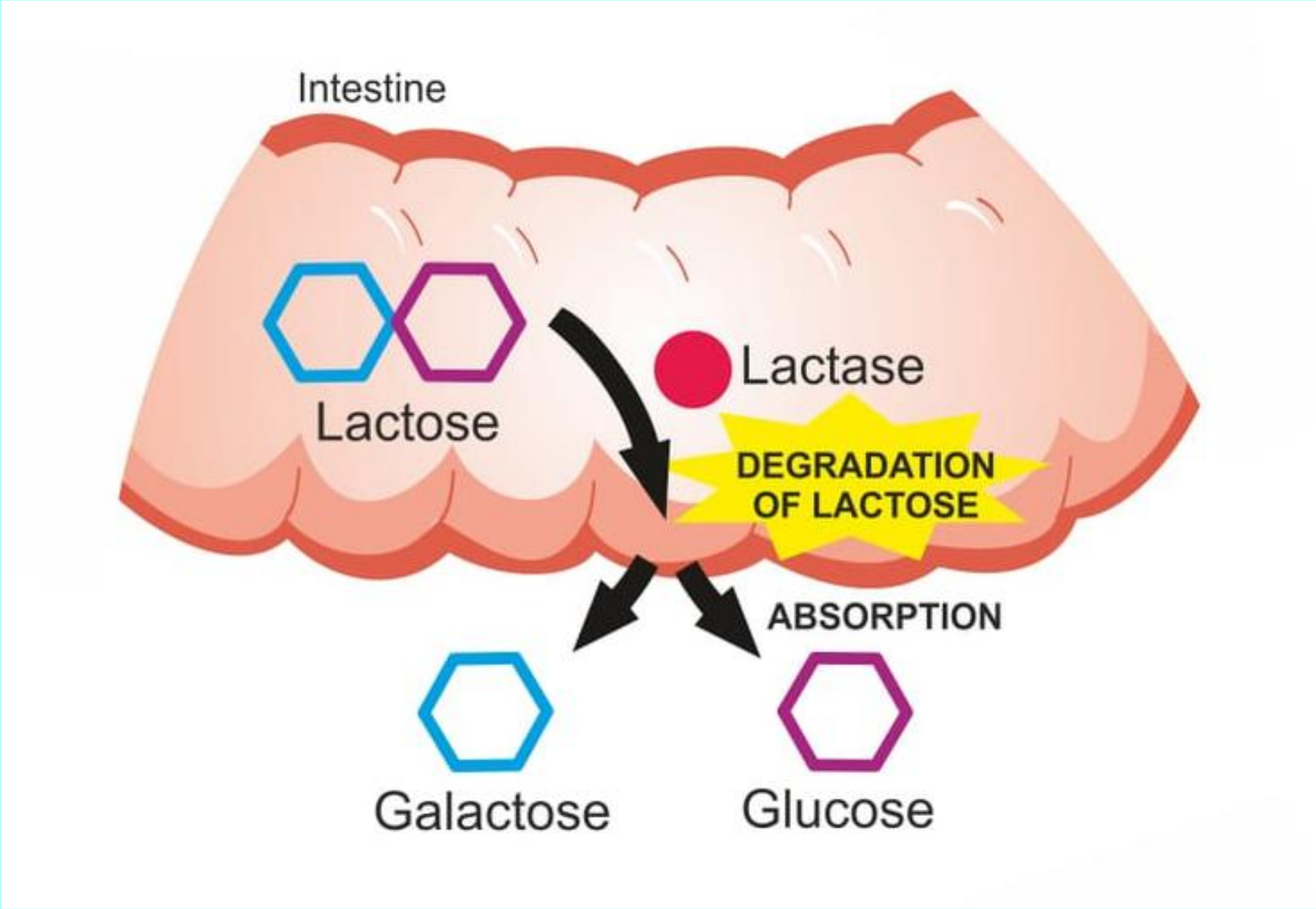
1. 55 gram protein
2. 56 gram lactose
3. 56 gram glucose



Three hours after consuming the lactose preload, *ad libitum* energy intake at a buffet lunch was reduced by **13%** compared to the glucose preload.

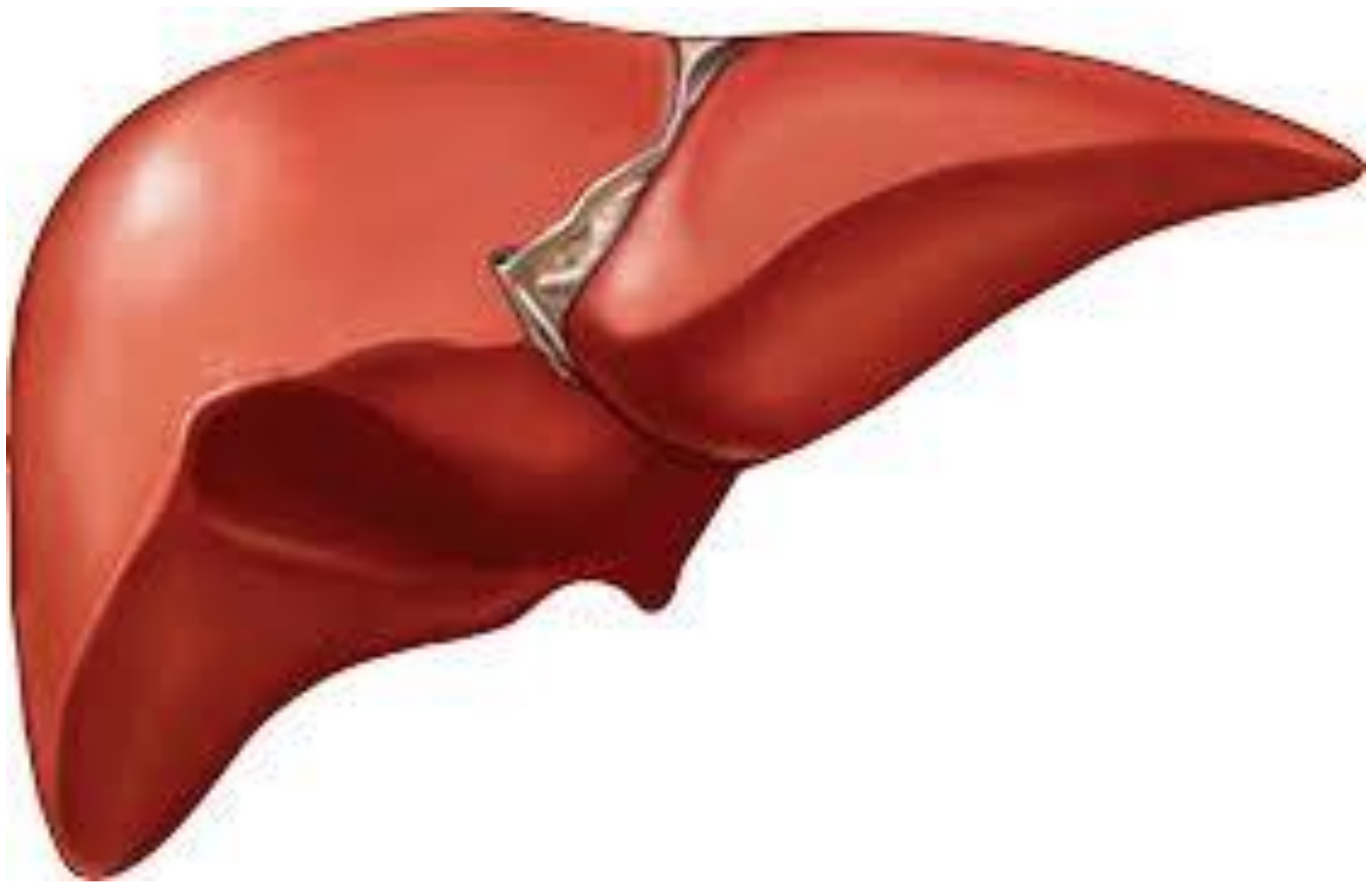


Health benefits of digested & undigested lactose in the lower parts of the GI-tract



Benefits of digested lactose (i.e., glucose and galactose)

Galactose from lactose is metabolized in the liver and largely converted to glycogen



- Liver glycogen represents a glucose reservoir, important for blood glucose homeostasis and energy provision.
- Lactose ingestion nearly **doubles** the rate of liver glycogen repletion compared to glucose alone:
  - During neonatal development, liver glycogen is an important source of energy.
  - For athletes, liver glycogen restoration is important for recovery and subsequent performance.
- Because of this galactose retention in the liver, lactose consumption results in a relatively low insulin response.

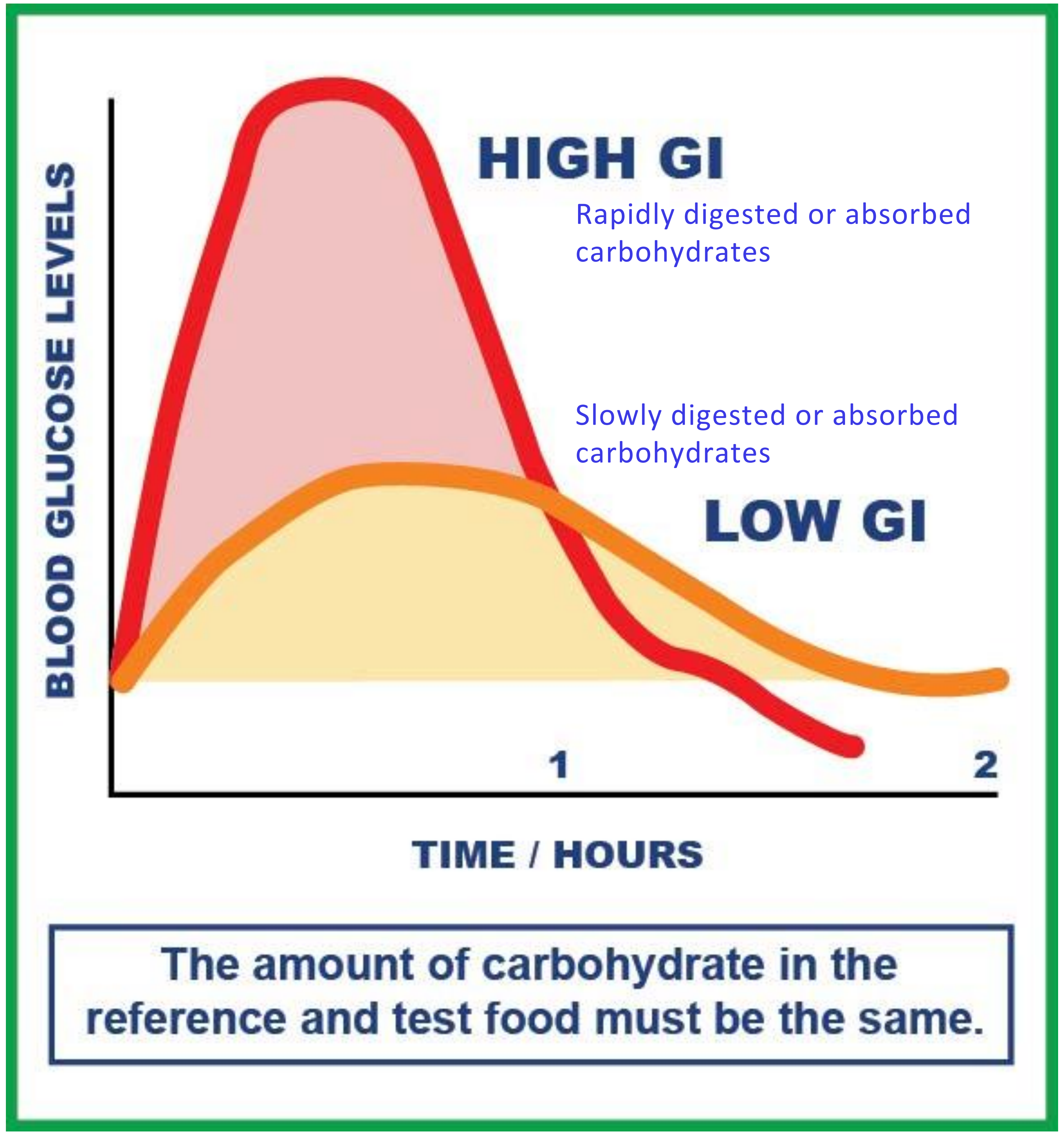
COELHO BERRY (2015). CURR OPEN CLIN NUTR METAB CARE | NUTTALL (2007). J AM COLL NUTR. | NUTSALL (1991). DIABETES CARE | BOUWMAN ET AL. (2019). J NUTR, 149:1140-1148 | STAHEL ET AL. (2017). PLOS ONE, 12:E172260

Glucose and galactose are important building blocks

Glucose and galactose are crucial building blocks for human milk oligo-saccharides (HMOs like 2'-fucosyllactose) and other complex macromolecules, especially in the **immune system** and **nervous system***

*GALACTOSE IS A KEY CONSTITUENT OF CEREBROSIDES, THE MAIN BUILDING BLOCKS OF MYELIN (WHITE MATTER)
LACTOSE IS THE PRIMARY SOURCE OF GALACTOSE IN THE DIET
ALTHOUGH GALACTOSE CAN BE PRODUCED IN THE BODY FROM GLUCOSE, THIS ENDOGENOUS ROUTE IS MOST LIKELY INSUFFICIENT FOR THE DEVELOPING IMMUNE AND NERVOUS SYSTMES

Lactose has a low glycemic index of 46



- Glycemic Index is a ranking of carbohydrates/foods based on their immediate effect on blood glucose levels.
- Low-GI is linked to improved management and/or prevention of diabetes, better weight loss management, reduced risk of development of heart disease and cardiovascular disease and mortality and reduced risk of development of specific cancers.
- GI is also linked to cognitive function and sports performance.

JENKINS ET AL. (1981). AM J CLIN NUTR, 34:362-366 | LIVESEY ET AL. (2019). NUTRIENTS, 11:1280 | LIVESEY ET AL. (2019). NUTRIENTS 11:1436 | THOMAS ET AL. (2009). COCHRANE DATABASE SYST REV, (1):CD006296 | LARSEN ET AL. (2010). N ENGL J MED, 363:2102-2113 | ZHU ET AL. (2021). DIABETES CARE, 2021. | LIVESEY & LIVESEY (2019). MAYO CLIN PROC INNOV QUAL OUTCOMES, 3:52–69 | JENKINS ET AL. (2021). MAYO CLIN PROC INNOV QUAL OUTCOMES, 3:52–69 | JENKINS ET AL. (2021). N ENGL J MED, 384:1312-22 | TURATI ET AL. (2019). NUTRIENTS, 11:2342 | PAPANIKOLAOU ET AL. (2006). DIABETOLOGICA, 49:855-62 | BENTON ET AL. (2003). PSYCHOPHARMACOL, 166:86-90 | STEVENSON ET AL. (2005). BR J NUTR, 93:885-93 | STEVENSON ET AL. (2006). AM J CLIN NUTR, 84:354-60 | STEVENSON ET AL. (2009). AM J PHYSIOL ENDOCRINOL METAB, 296:E1140-7

Mean and SD GI values of food categories and percentages of low-, medium-, and high-GI foods

Food category	*n*	Mean	SD	Proportion of products in each category: Low-GI foods	Medium-GI foods	High-GI foods
Bakery products	72	58	16	49%	31%	21%
Beverages	74	50	20	68%	18%	15%
Carbonated drinks	7	63	7	29%	43%	29%
Breads	214	64	14	29%	36%	35%
Breakfast cereals	148	61	15	37%	33%	30%
Cereal bars	20	54	14	45%	15%	20%
Cereal grains						
Rice	128	67	17	28%	34%	38%
Other cereal grains	60	47	20	73%	15%	12%
Cookies	135	49	9	84%	12%	4%
Cracker	43	55	17	47%	42%	12%
Dairy products	186	35	11	95%	5%	0%
Fruits and fruit products						
Fruits	105	51	11	72%	22%	6%
Fruit and vegetable juices	27	47	9	85%	15%	0%
Fruit spreads, jams	28	49	15	71%	25%	4%
Infant formula and weaning foods	43	48	17	65%	28%	7%
Legumes	32	34	14	94%	6%	0%
Meal replacement and weight management products	59	30	9	100%	0%	0%
Nutritional support products	62	42	20	90%	2%	8%
Nuts	3	22	1	100%	0%	0%
Pasta	77	52	12	64%	29%	8%
Snack food and confectionery						
Savory snack foods	35	60	15	46%	20%	34%
Sweet snacks and confectionery	53	48	16	68%	21%	11%
Fruit bars and snacks	41	45	21	76%	7%	17%
Snack bars	47	44	16	79%	15%	6%
Sports (energy) bars	35	32	13	94%	6%	0%
Soups	21	49	10	71%	29%	4%
Sugars and syrups	50	58	21	44%	32%	24%
Vegetables						
Potatoes and potato products	66	71	15	14%	29%	58%
Other vegetables	91	66	19	34%	14%	52%
Regional or traditional foods						
African	9	56	20	56%	0%	44%
Arabic and Turkish	28	61	11	32%	43%	25%
Asian	89	60	19	40%	34%	26%
Asian Indian	19	65	13	32%	32%	37%

The majority of dairy products are low-GI

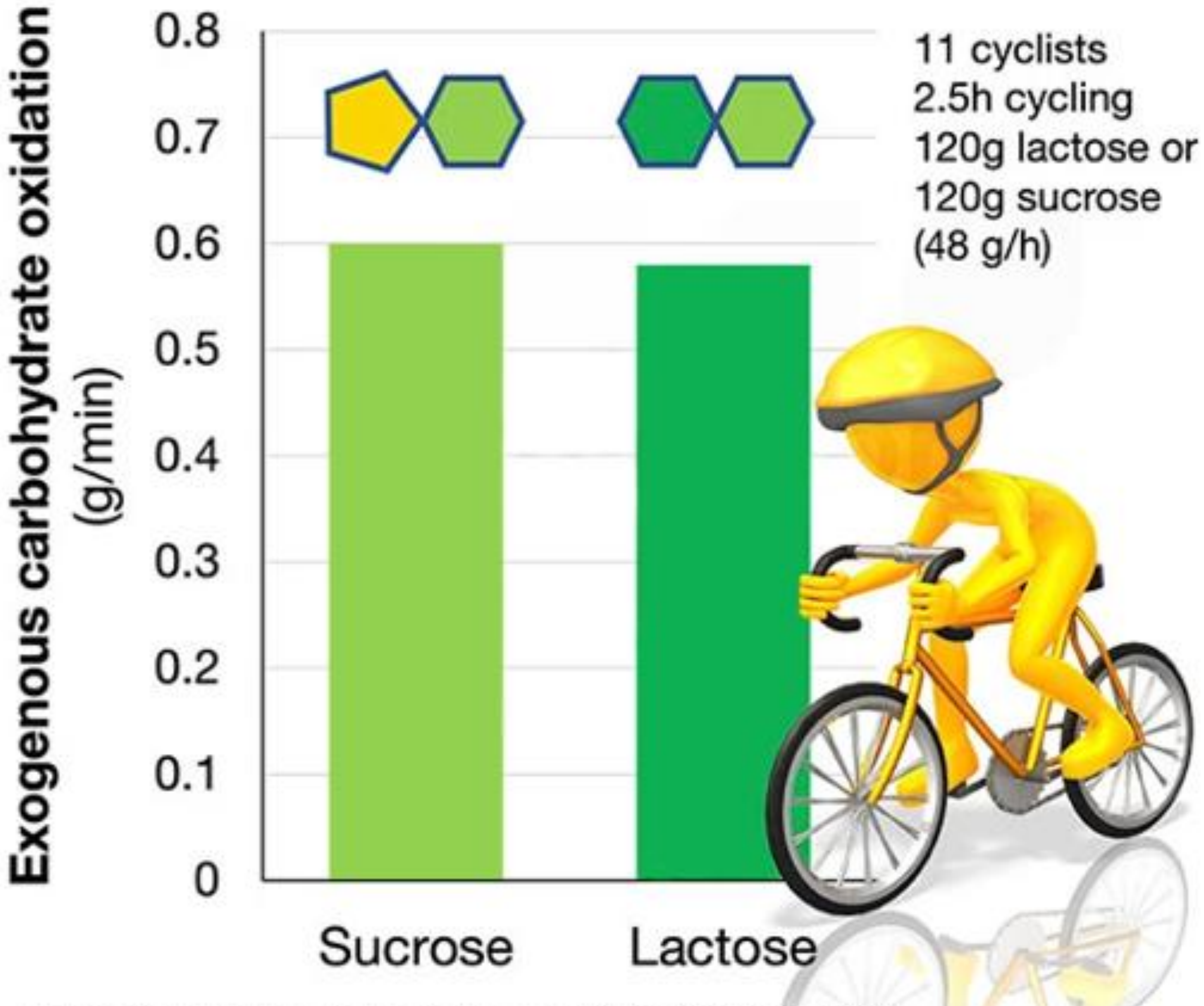
ATKINSON ET AL. (2021). AM J CLIN NUTR, 114:1625-1632

Replacement of lactose by corn- syrup-solids in infant formula is associated with an increased risk of unhealthy body weight development

	Lactose-based formula	CSS-based formula	Health implications
Carbohydrate source	Lactose	Corn syrup solids (i.e. glucose)	
Glycemic index	46	100	Higher GI is associated with increased insulin response and fat storage
Insulin/peptide-C response	Lower	Higher	Higher insulin may promote fat storage and weight gain
Gut microbiome	Closer to breast milk	More mature microbiome than lactose-based formula and breast milk (reduced *Bifidobacteriaceae*, increased *Lachnospiraceae and Acidaminococcaceae*)	Microbiome alterations may influence metabolic programming and weigh regulation
Obesity risk	Lower	Higher	Increased risk of obesity in infancy and early childhood (dose-dependent relationship). CSS-based formula associated with a 10% higher obesity risk at age 2, 8% at age 3, and 7% at age 4 compared to lactose-based formula
Eating behaviours	Healthier eating behaviours	Poorer eating behaviours (increased food fussiness, reduced enjoyment of food)	May contribute to poor diet quality and increased obesity risk

BRAND-MILLER ET AL. (2022). AM J CLIN NUTR, 116:853-854
ANDERSON ET AL. (2022). AM J CLIN NUTR, 116:1002-1009
JONES ET AL (2020). GUT MICROBES, 12:E1813534
HAMPSON ET AL (2022). NUTRIENTS, 14:1115

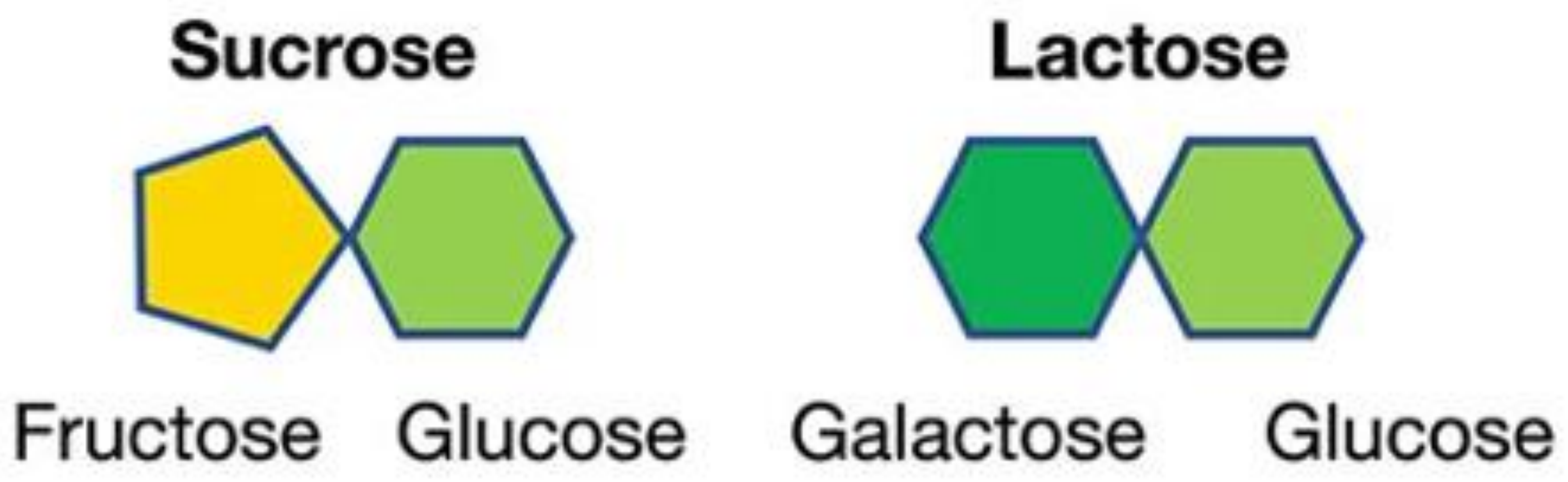
The application of lactose in sports nutrition



Odell et al Med Sci Sports Exerc. 52(12):2663-72, 2020

Sources of lactose (g/100g)

Milk	5.0
Yogurt	4.5-6.0
Ice cream	3.3-6.0
Whey protein concentrate	3.5



Lactose is an alternative energy source during exercise with oxidation rates, similar to sucrose (at least when ingested at moderate rates)

Interestingly, lactose permits fat burning during exercise

Sparing of glycogen

Lactose, being less insulinogenic than sucrose, permits fat oxidation

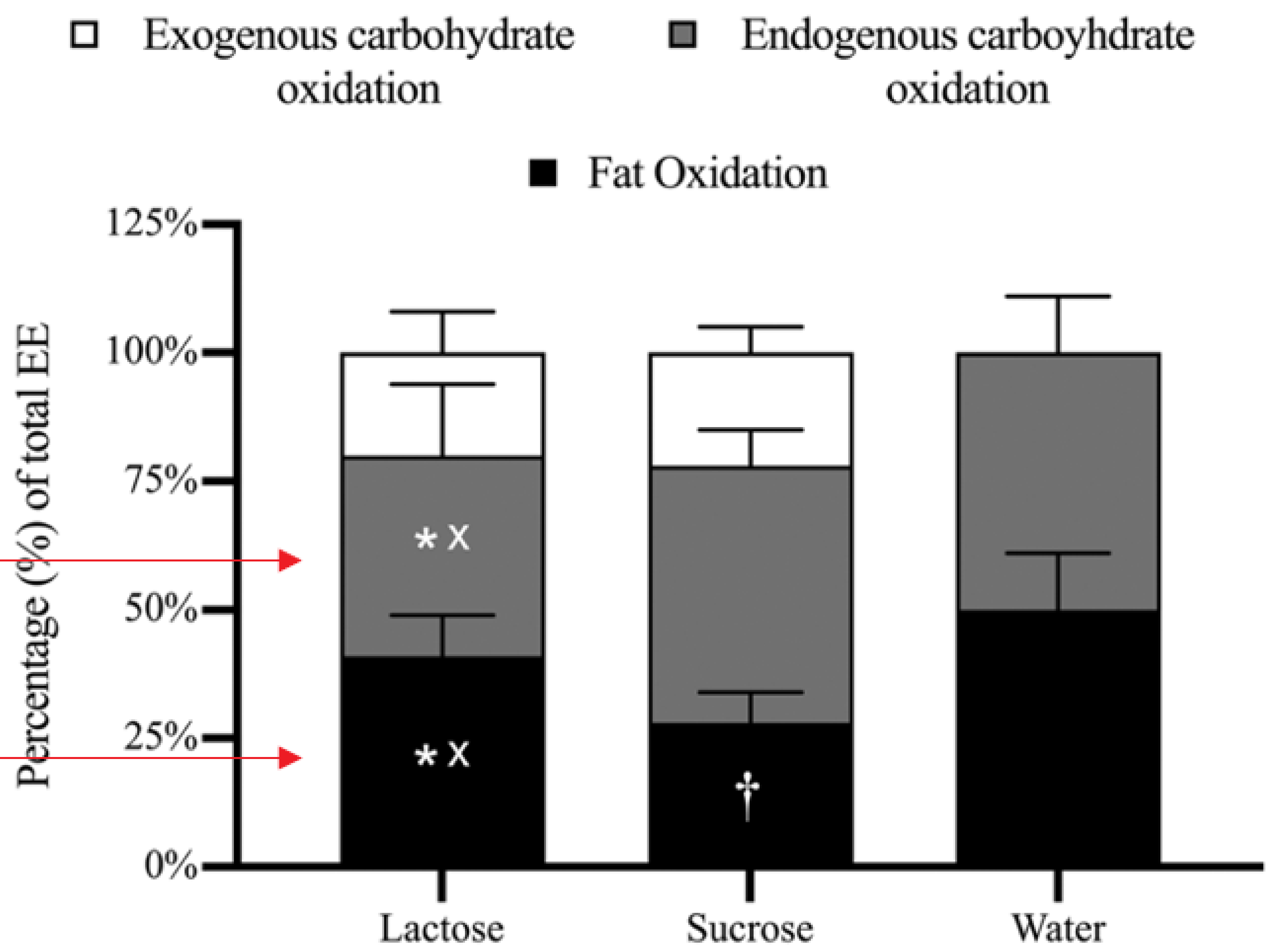
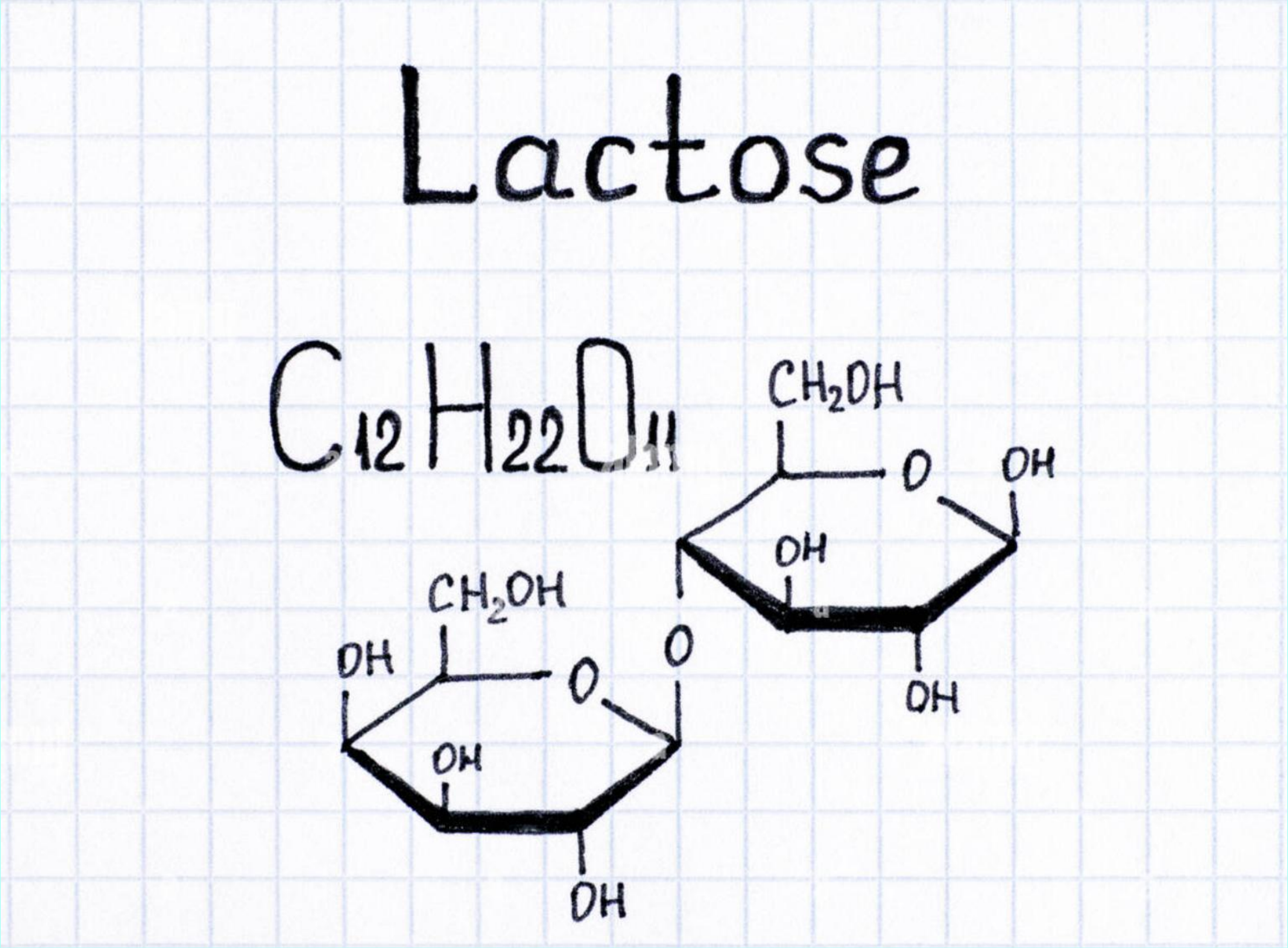


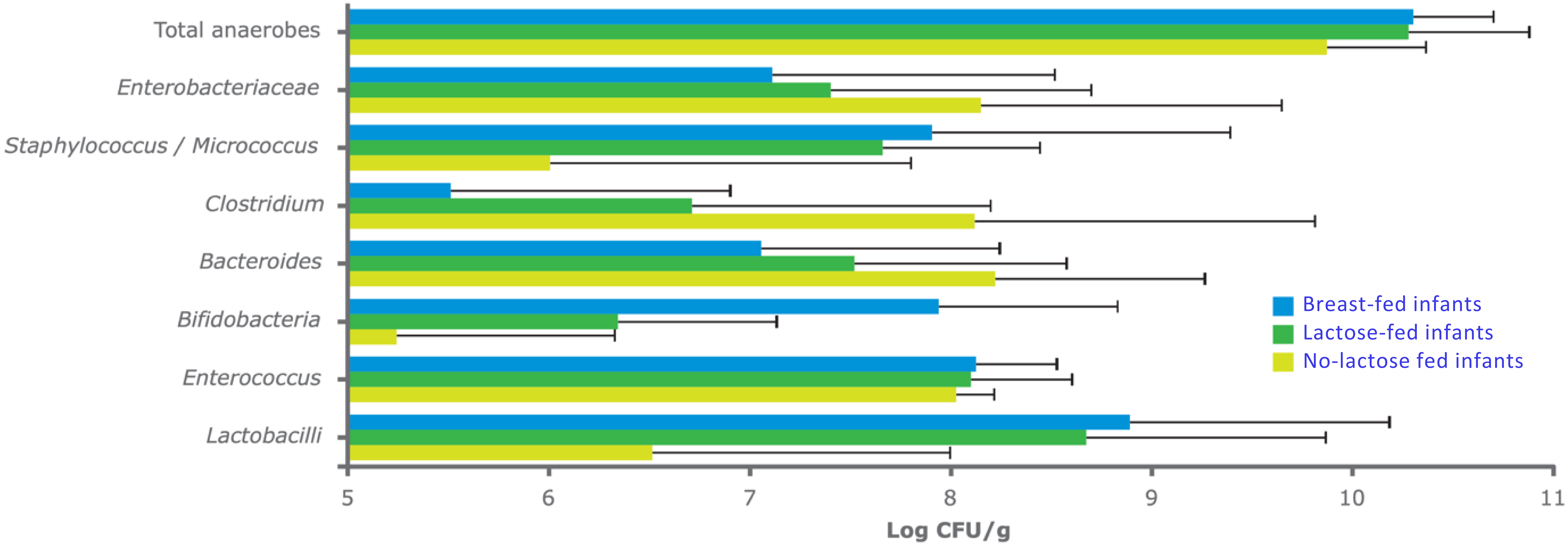
FIGURE 2—Substrate contributions to total EE from 60 to 150 min. *A significant difference ($P < 0.05$) between lactose and sucrose. [x]A significant difference ($P < 0.05$) between lactose and water. †A significant difference ($P < 0.05$) between sucrose and water.



Benefits of undigested lactose: a conditional prebiotic?

Undigested lactose can exert **microbiota shaping effects** that **improve gut microbiota composition** and activity

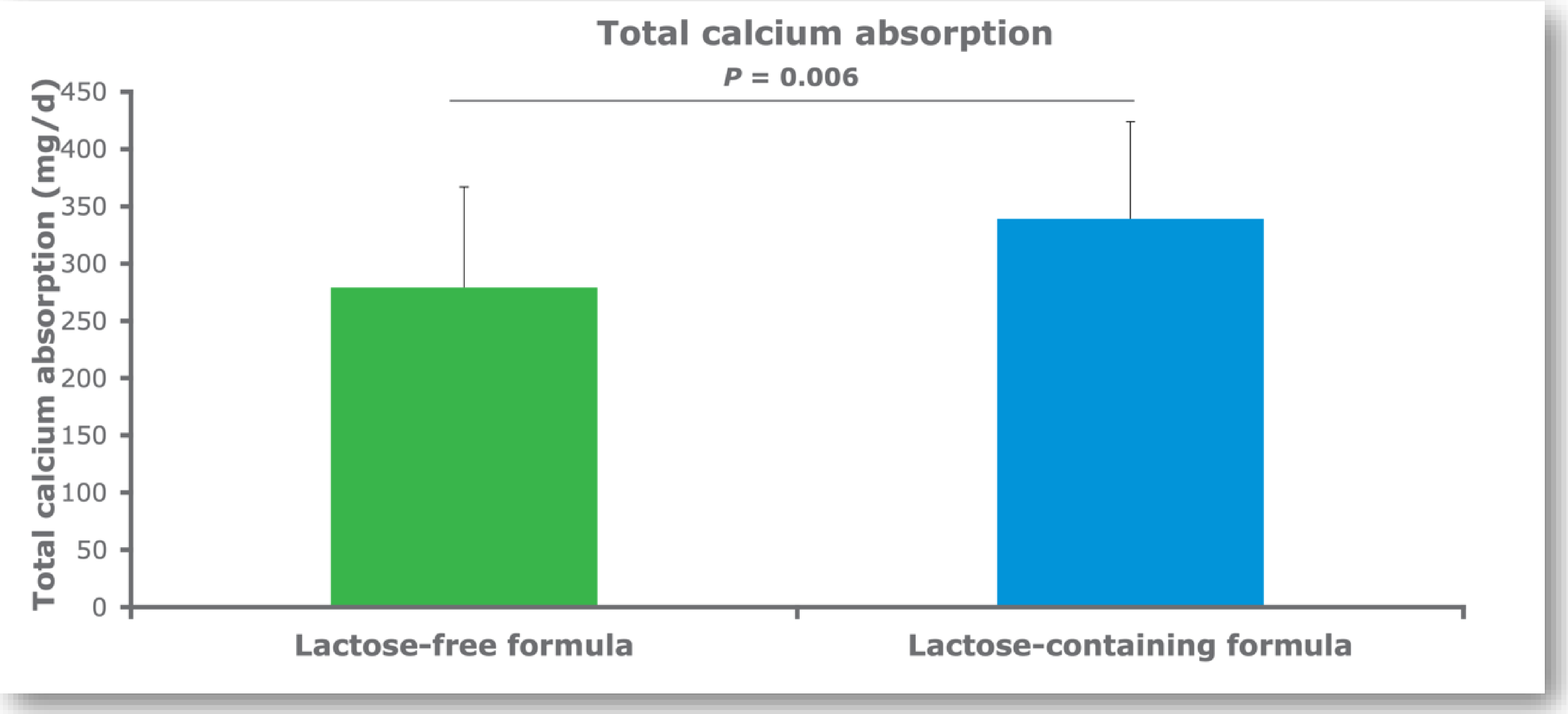
Lactose significantly increases the growth of *Bifidobacteria* and *Lactobacilli* in infants



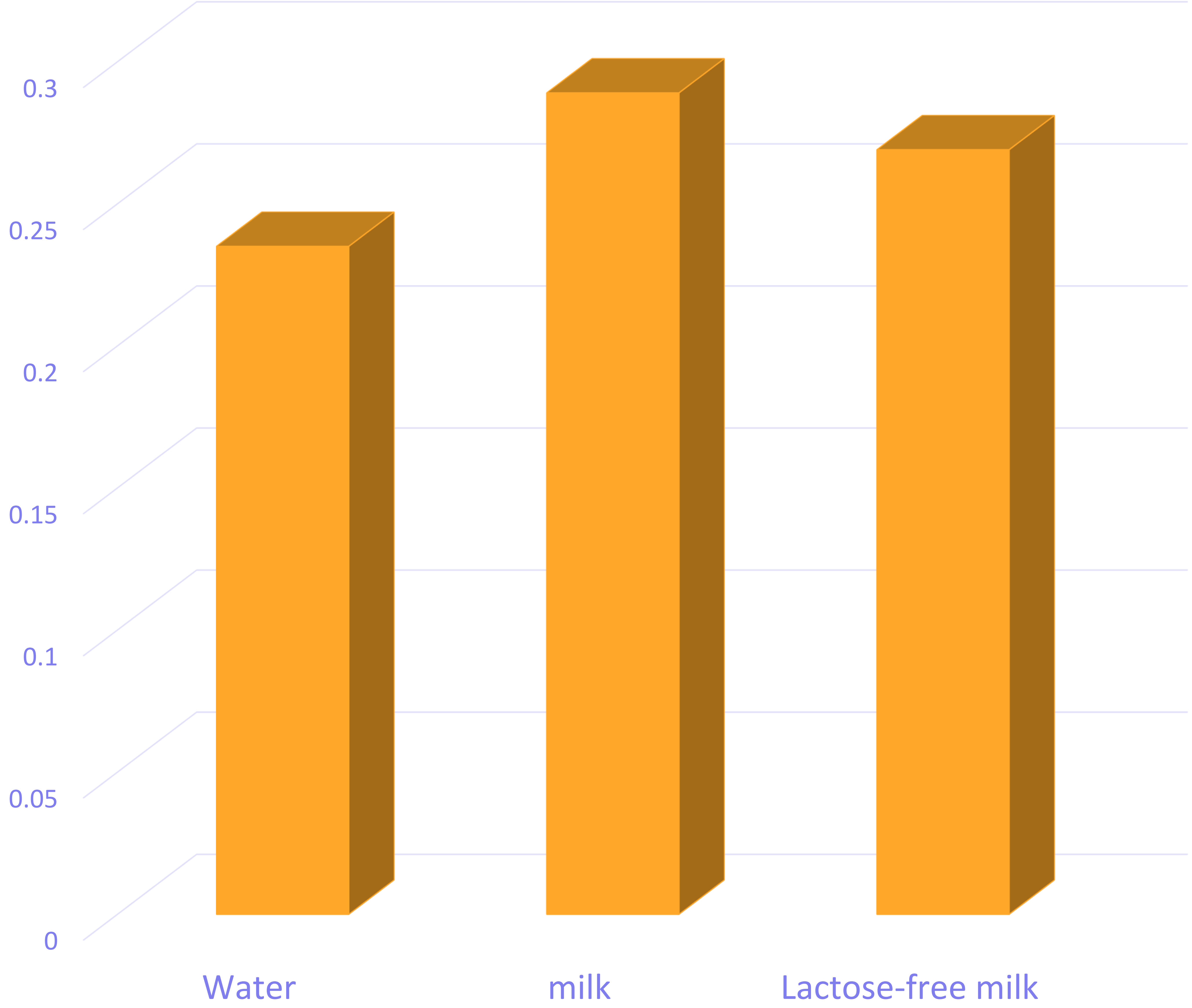
Also in adults (especially LNP), a phenomenon associated with increased lactose tolerance (i.e., colonic adaptation)

Francavilla et al, Pediatr Allergy Immunol, 2012

Undigested lactose enhances mineral absorption in the digestive tract, especially calcium and magnesium



Calcium absorption in infants



Calcium absorption in lactase-deficient adults

ANGUITA-RUIZ ET AL. (2025). CRIT REV FOOD SCI NUTR, 27:1-14
ROMERO-VELARDE ET AL. (2019). NUTRIENTS, 11:2737
ABRAMS ET AL. (2002). AM J CLIN NUTR, 76:442-446
GRIESSEN ET AL. (1989). AM J CLIN NUTR, 49:377–84

Milk intake variably influences risk of type 2 diabetes depending on lactase expression in the gut

nature metabolism

Article

https://doi.org/10.1038/s42255-023-00961-1

Variant of the lactase *LCT* gene explains association between milk intake and incident type 2 diabetes

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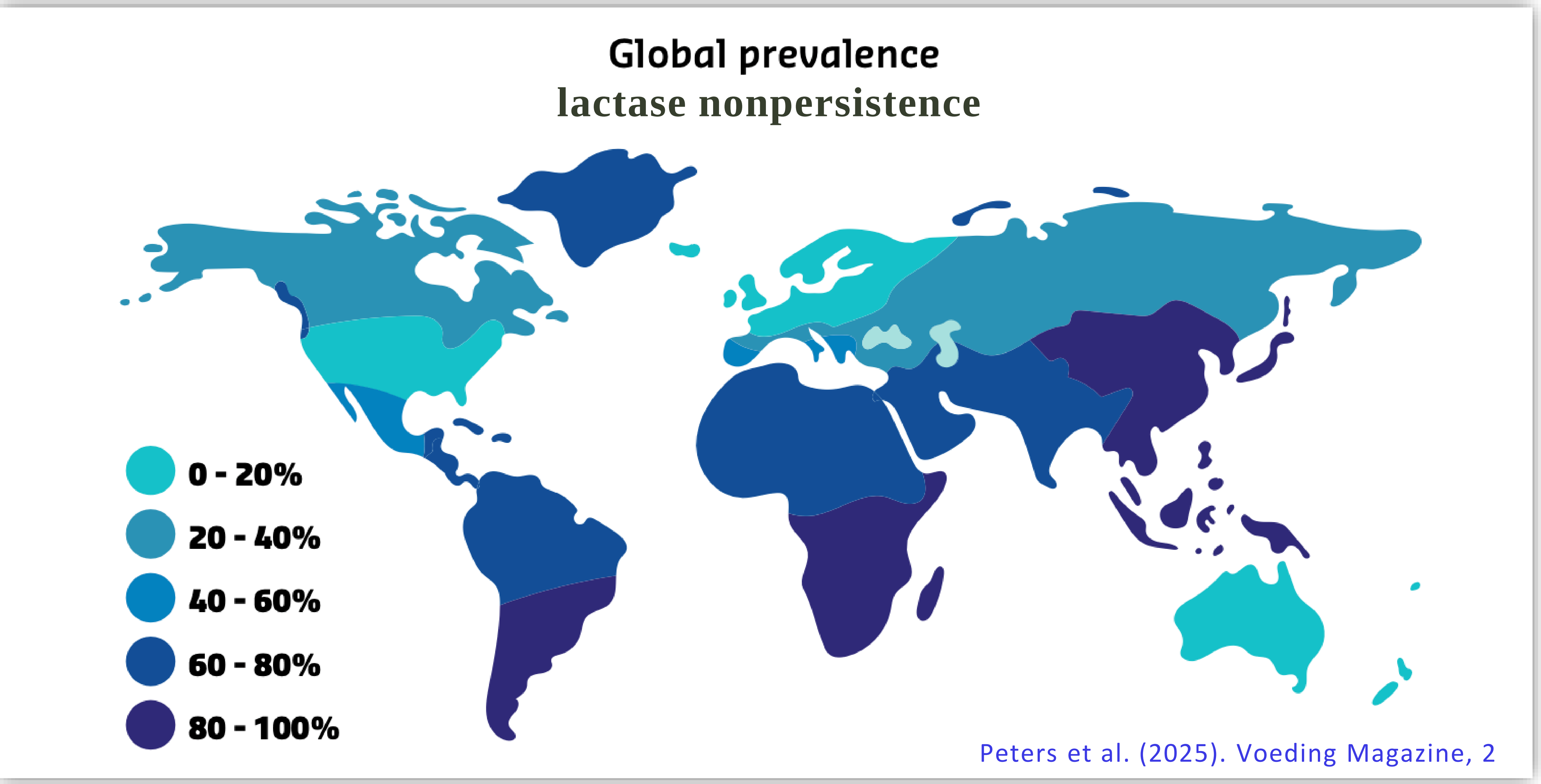
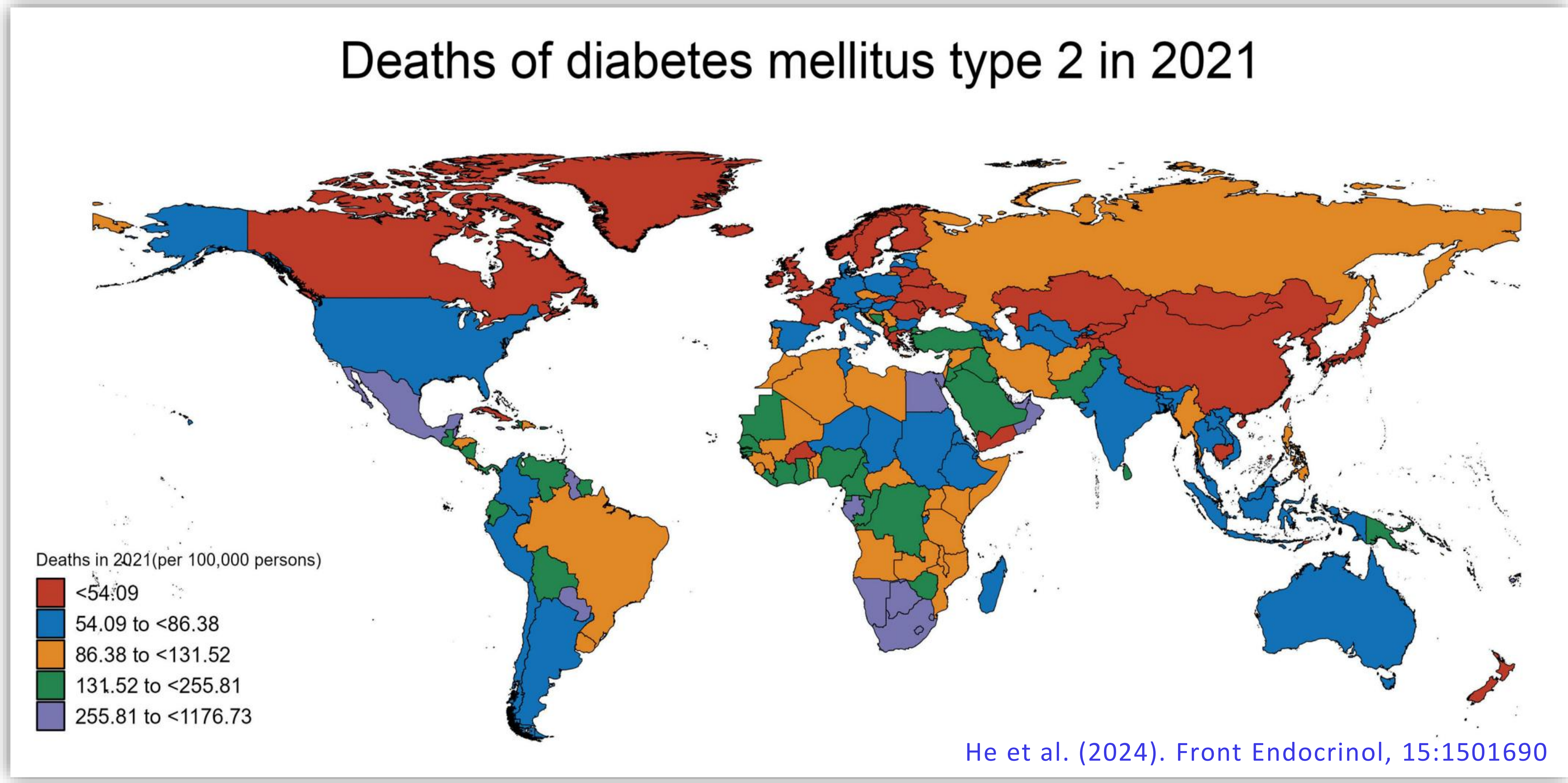
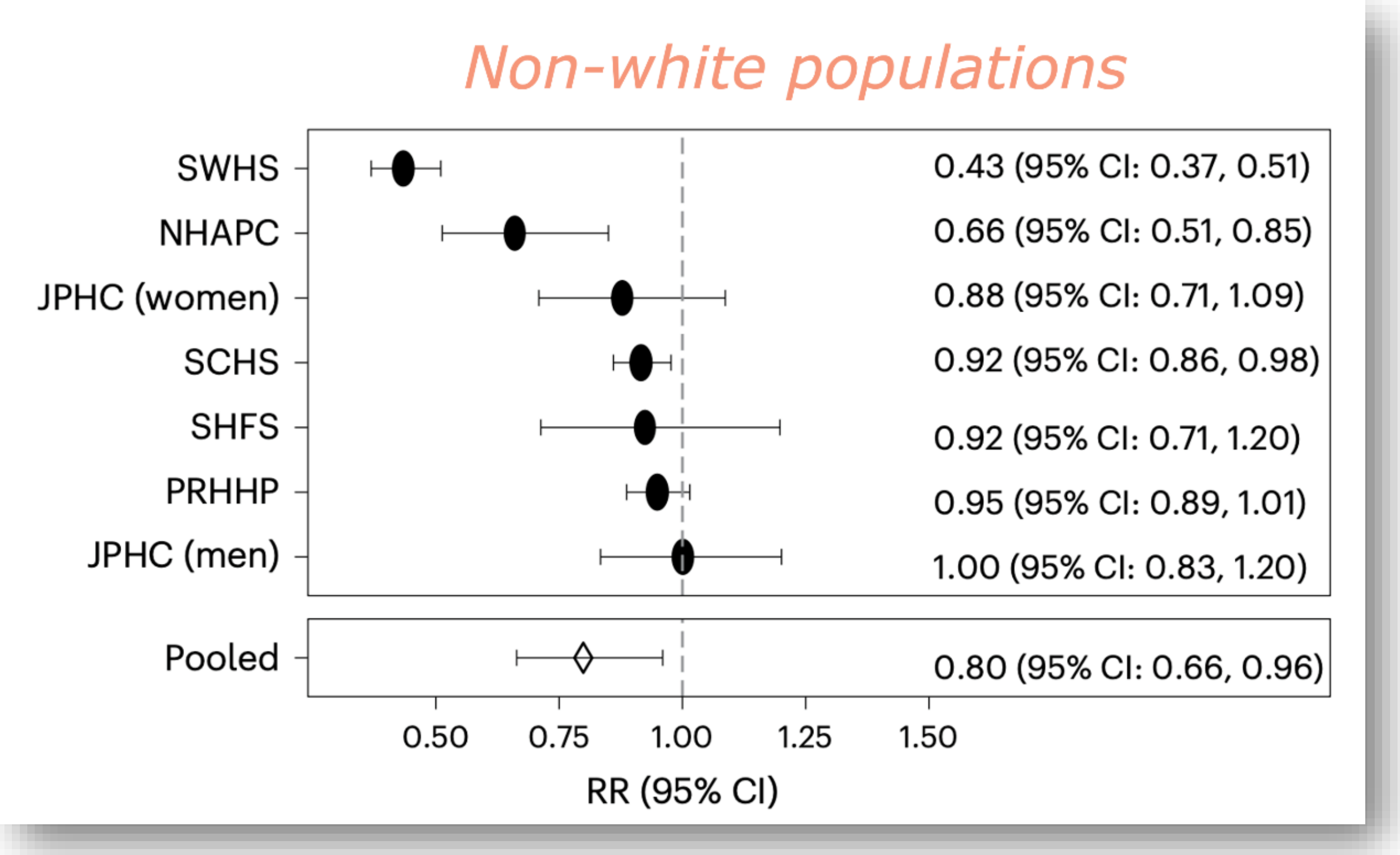
Check for updates

Kai Luo[1], Guo-Chong Chen[1,2], Yanbo Zhang[1], Jee-Young Moon[1], Jiaqian Xing[1], Brandilyn A. Peters[1], Mykhaylo Usyk[3,4], Zheng Wang[1], Gang Hu[5], Jun Li[6,7], Elizabeth Selvin[8], Casey M. Rebholz[8], Tao Wang[1], Carmen R. Isasi[1], Bing Yu[9], Rob Knight[10,11,12,13], Eric Boerwinkle[9], Robert D. Burk[1,3,4,14], Robert C. Kaplan[1,15] & Qibin Qi[1,7]

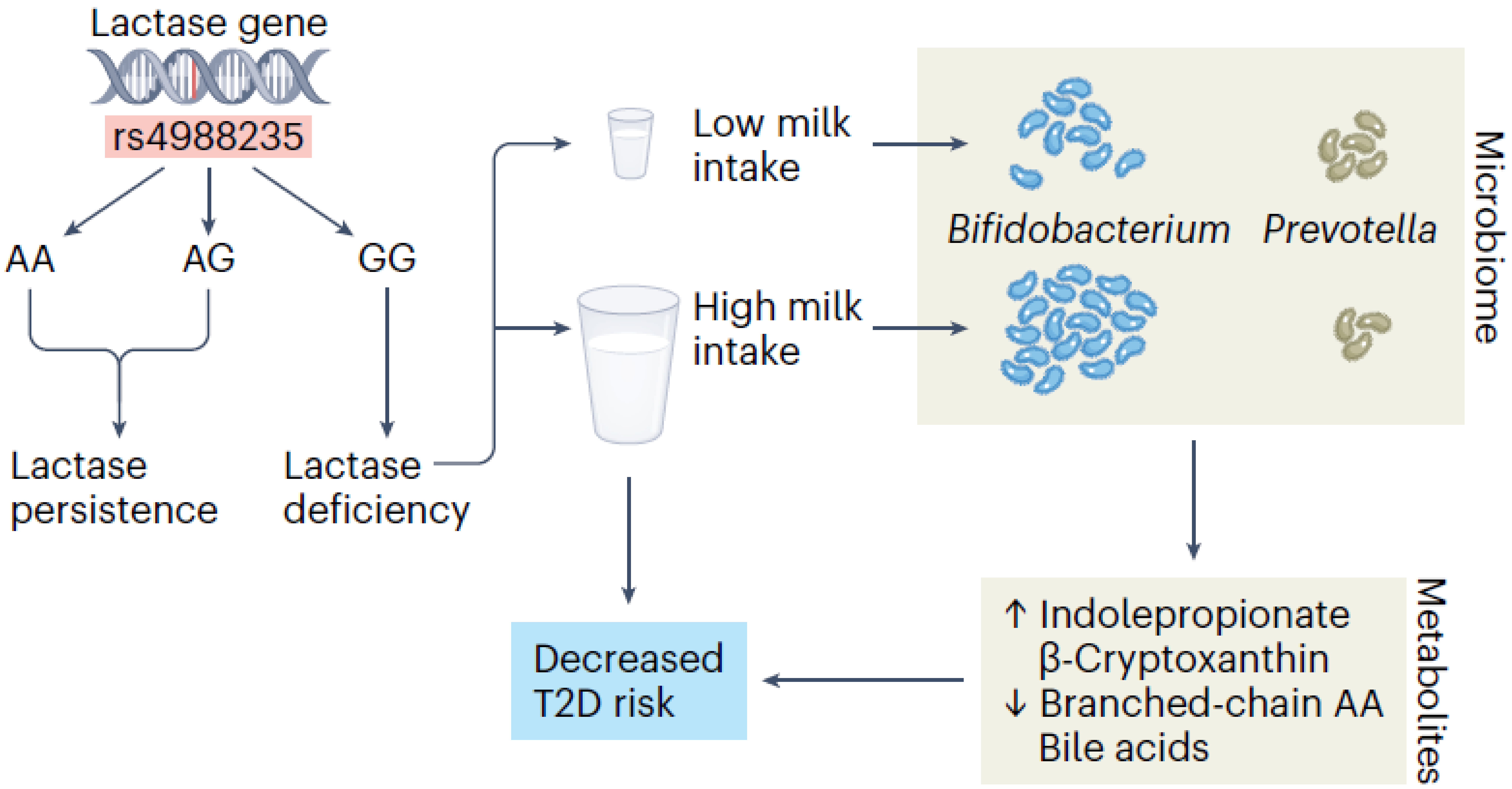
Cow's milk is frequently included in the human diet, but the relationship between milk intake and type 2 diabetes (T2D) remains controversial. Here, using data from the Hispanic Community Health Study/Study of Latinos, we show that in both sexes, higher milk intake is associated with lower risk of T2D in lactase non-persistent (LNP) individuals (determined by a variant of the lactase *LCT* gene, single nucleotide polymorphism rs4988235) but not in lactase persistent individuals. We validate this finding in the UK Biobank. Further analyses reveal that among LNP individuals, higher milk intake is associated with alterations in gut microbiota (for example, enriched *Bifidobacterium* and reduced *Prevotella*) and circulating metabolites (for example, increased indolepropionate and reduced branched-chain amino acid metabolites). Many of these metabolites are related to the identified milk-associated bacteria and partially mediate the association between milk intake and T2D in LNP individuals. Our study demonstrates a protective association between milk intake and T2D among LNP individuals and a potential involvement of gut microbiota and blood metabolites in this association.







Milk consumption has the strongest protective effect on T2DM in non-white populations; i.e. in lactase non-persistent individuals in whom lactose behaves as a prebiotic.


Lactase gene
rs4988235
AA
AG
GG
Lactase persistence
Lactase deficiency
Low milk intake
High milk intake
Bifidobacterium
Prevotella
Microbiome
↑ Indolepropionate
β-Cryptoxanthin
↓ Branched-chain AA
Bile acids
Metabolites
Decreased T2D risk

Fermentation of undigested lactose can lead to production of indole-propionate (IPA) from tryptophan. IPA is associated with a lower risk of T2D

X = no lactase

QI ET AL. (2022). GUT, 71:1095-1105
LUO, K. ET AL. (2024). NAT METAB, 6:169-186

But what about undigested lactose and lactose intolerance?

Lactase deficiency = lactase non-persistency (LNP) = lactose maldigestion = lactose malabsorption ≠ lactose intolerance

Lactase persistent – expressing lactase enzyme lifelong

Genetic changes
dominant trait

can digest lactose

33%
LP

but, after childhood

LNP
67%

No complaints

most can consume 12 g lactose (=± 1 glass of milk) in one sitting without complaints

Complaints

= lactose intolerant

cannot digest lactose
= lactose maldigestion

Lactase non-persistent – production of lactase enzyme significantly decreased

Lactose consumption leading to lactose tolerance

The American Journal of Clinical Nutrition 119 (2024) 702–710

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The American Journal of CLINICAL NUTRITION

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

Original Research Article

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

Check for updates

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]

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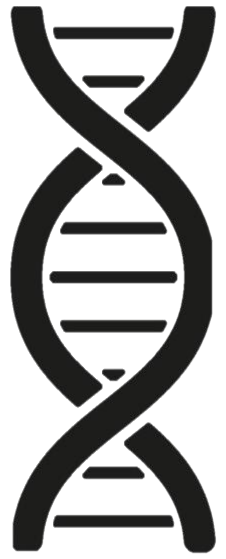
A B S T R A C T

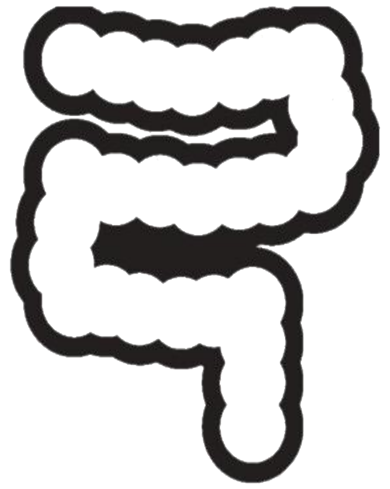
Background: Approximately 70%–100% of the Asian adult population is lactase nonpersistent (LNP). The literature shows that many individuals with the LNP-genotype can consume ≤12 g of lactose without experiencing gastrointestinal discomfort. Repetitive consumption of lactose may reduce intolerance symptoms via adaptation of the gut microbiota.
Objective: This study aimed to assess the effects of daily consumption of incremental lactose doses on microbiota composition and function, and intolerance symptoms.
Methods: Twenty-five healthy adults of Asian origin, carrying the LNP-genotype were included in this 12-wk before and after intervention trial. Participants consumed gradually increasing lactose doses from 3 to 6 g to 12 g twice daily, each daily dose of 6 g, 12 g, or 24 g being provided for 4 consecutive weeks. Participants handed-in repeated stool samples and underwent a 25 g lactose challenge hydrogen breath test (HBT) before and after the 12-wk intervention. Daily gastrointestinal symptoms and total symptom scores (TSSs) during the lactose challenge were recorded.
Results: A significant increase from 5.5% ± 7.6% to 10.4% ± 9.6% was observed in *Bifidobacterium* relative abundance after the intervention ($P =$ 0.009), accompanied by a 2-fold increase (570 ± 269 U/g; $P < 0.001$) in fecal β-galactosidase activity compared with baseline (272 ± 158 U/g). A 1.5-fold decrease (incremental area under the curve; $P = 0.01$) in expired hydrogen was observed during the second HBT (38 ± 35 ppm·min), compared with the baseline HBT (57 ± 38 ppm·min). There was a nonsignificant decrease in TSS (10.6 ± 8.3 before compared with 8.1 ± 7.2 after intervention; $P =$ 0.09). Daily consumption of lactose was well tolerated, with mild to no gastrointestinal complaints reported during the intervention.
Conclusions: Increased levels of *Bifidobacterium* indicate an adaptation of the gut microbiota upon repetitive consumption of incremental doses of lactose, which was well tolerated as demonstrated by reduced expired hydrogen concentrations during the second 25-g lactose HBT. Bifidobacteria metabolize lactose without gas production thereby potentially reducing intestinal gas formation in the gut of individuals with the LNP-genotype. This increased lactose tolerance possibly lifts the necessity to remove nutrient-rich dairy foods completely from the diet.
The trial is registered at the International Clinical Trials Registry Platform: NL9516. The effect of dietary lactose in lactase nonpersistent individuals on gut microbiota.

Keywords: lactose intolerance, lactase nonpersistence, microbiota, bifidobacteria, hydrogen breath test, fecal β-galactosidase activity, gut microbial adaptation, clinical trial

To assess whether repetitive consumption of an increasing dose of dietary lactose in lactase non-persistent individuals:

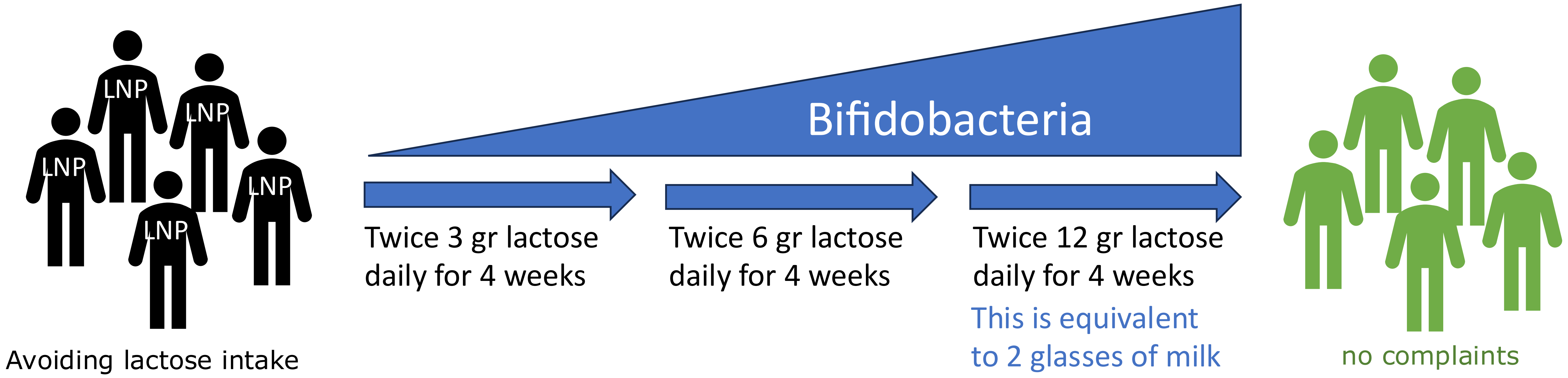


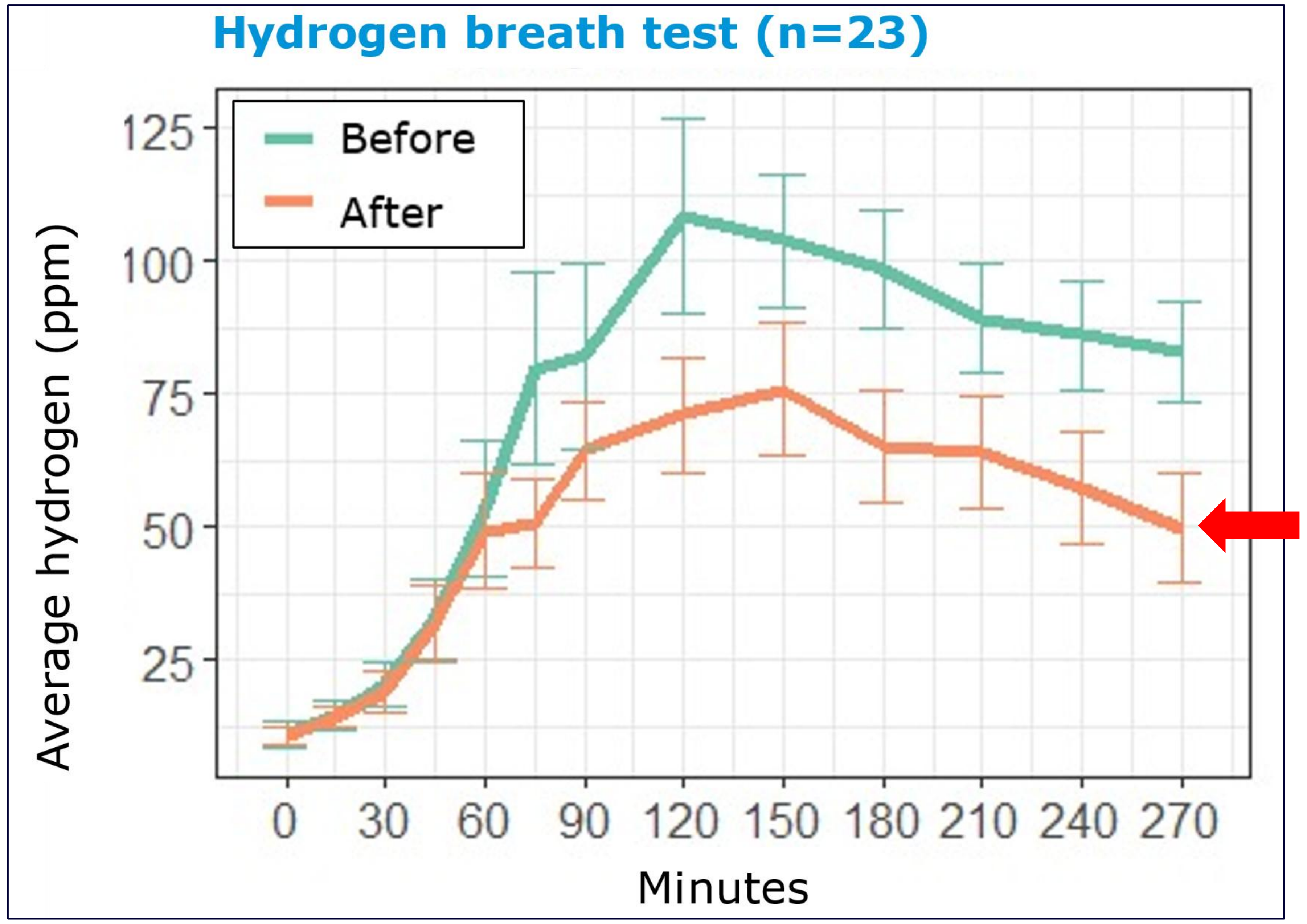
Changes the gut microbiota
('colonic microbial adaptation')

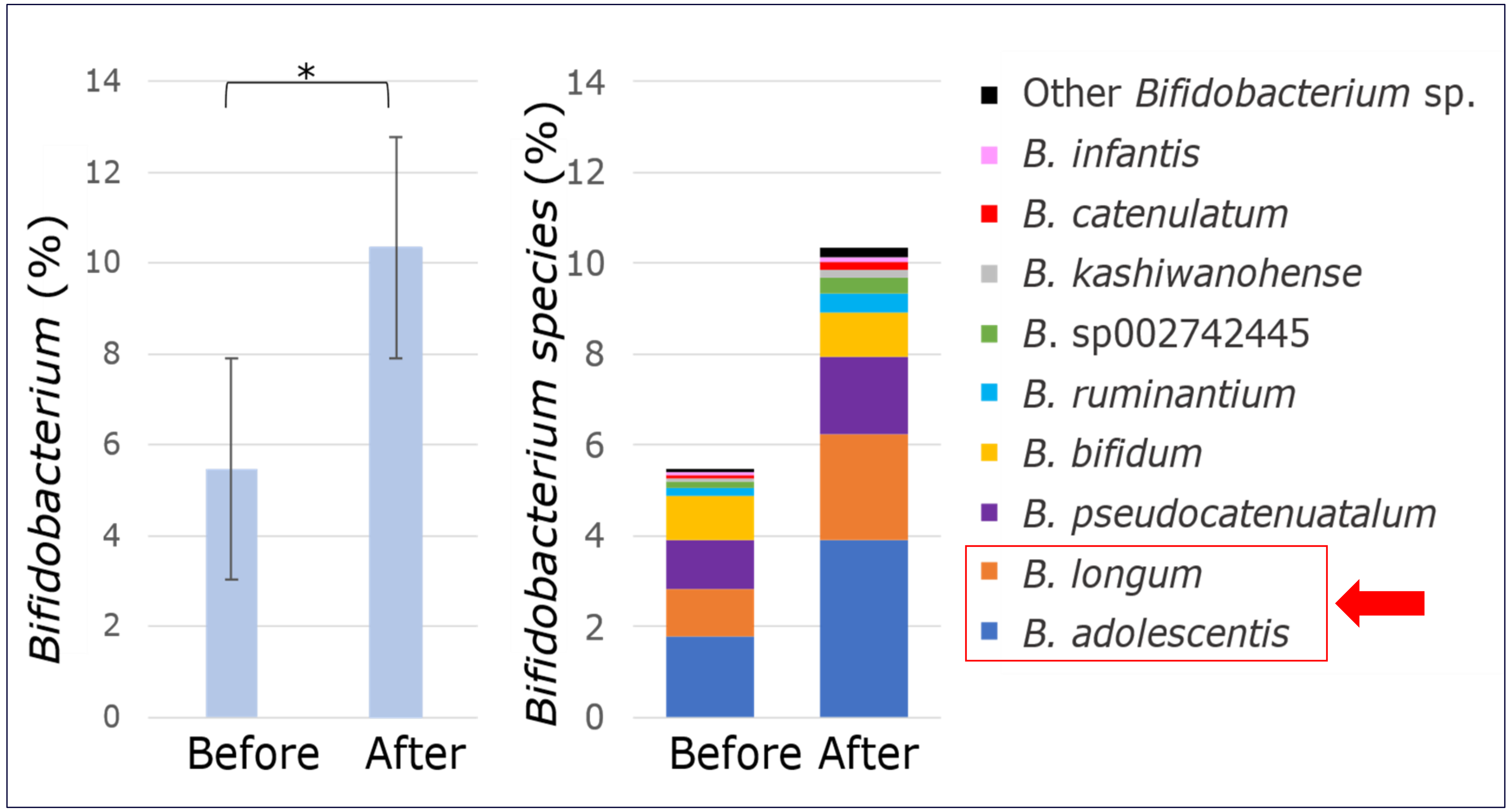


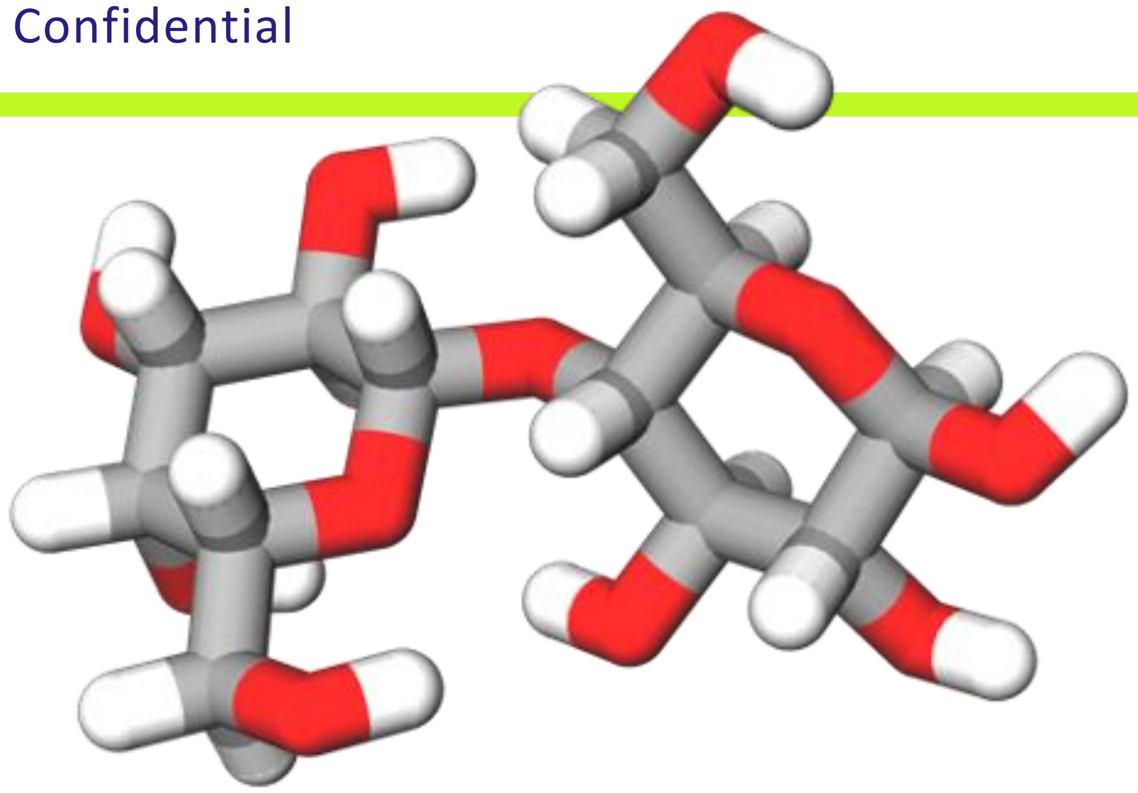
Decreases symptoms of lactose intolerance

Lactose intervention increased lactose tolerance via adaptation of the gut microbiota









- Lactose is the principal carbohydrate in the milk of most mammals.
- It is characterized by low sweetness, low cariogenicity and its satiating potential.
- Lactose gets digested in the small intestine by the enzyme lactase.
- In healthy infants and young children, lactose supports healthy growth and development by supplying energy, building blocks (glucose and galactose) and shaping the (developing) gut microbiota caused by some undigested lactose overflow in to the lower parts of the GI-tract.
- In all other age groups, physiological effects depend on the level of lactase in the small intestine:
  - ✓ *If lactase levels are sufficient (e.g., LP), lactose behaves as a low-GI sugar and provides energy and building blocks to the body.*
  - ✓ *If lactase levels are insufficient (e.g., LNP), lactose behaves as a prebiotic and interacts with the gut microbiota affecting microbial composition and activity resulting in various physiological benefits.*
  - ✓ *Lactose over-exposure can lead to intolerance complains but there are many influencing factors.*
- Because of these many health benefits of lactose, recent European and world recommendations have excluded lactose in dairy products from the definition of free sugars whose reduction is recommended against the development of metabolic diseases.*

*WORLD HEALTH ORGANIZATION (WHO) (2015). GUIDELINE: SUGARS INTAKE FOR ADULTS AND CHILDREN. ISBN: 978924154028


THANK
YOU!