STLO
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INRA SCIENCE & IMPACT

AGRO CAMPUS OUEST

Impact on health of dairy products

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Risk ?

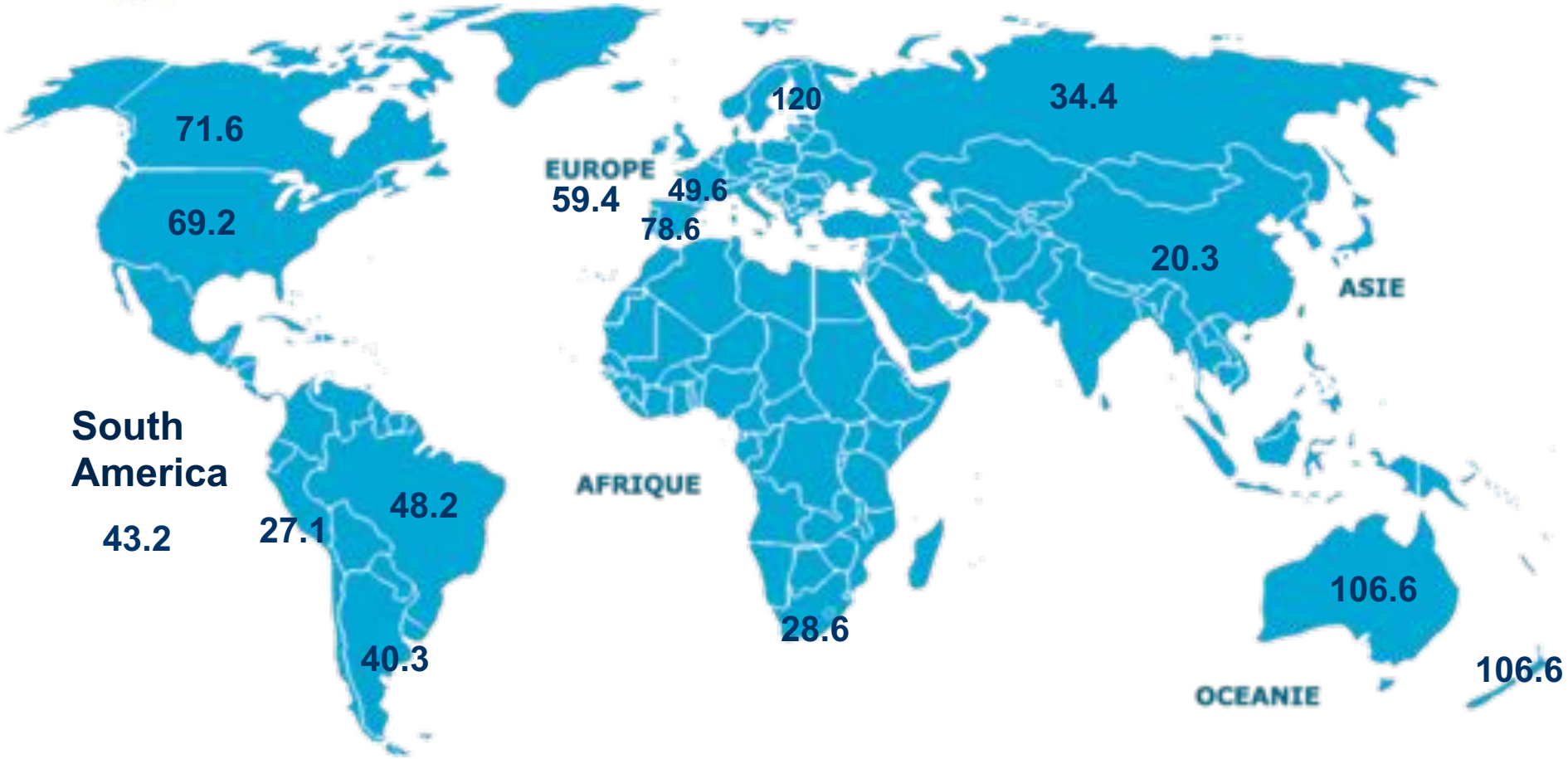
Benefit ?

HEALTH

Outline

- Dairy product consumption around the world
- Nutritional composition of milk
- Dairy products and impact of health

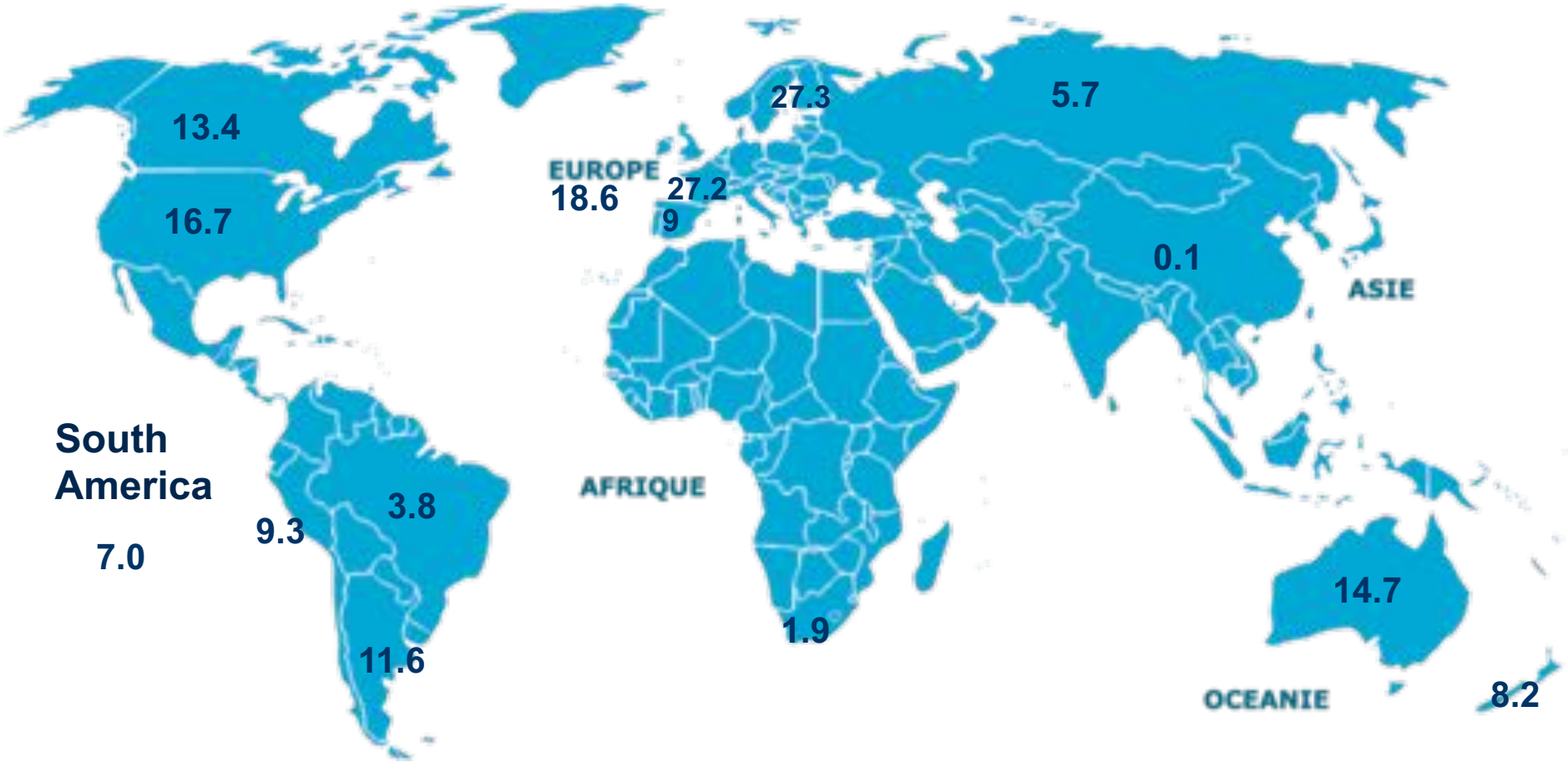
Fluid milk consumption around the world
L / capita / year



→ Chile : > 2 times less than in Europe
↗ 5 L in 5 years (↘ 8 L in France) from 2011 - 2016

Canadian dairy information centre, 2016

Cheese consumption around the world
Kg / capita / year

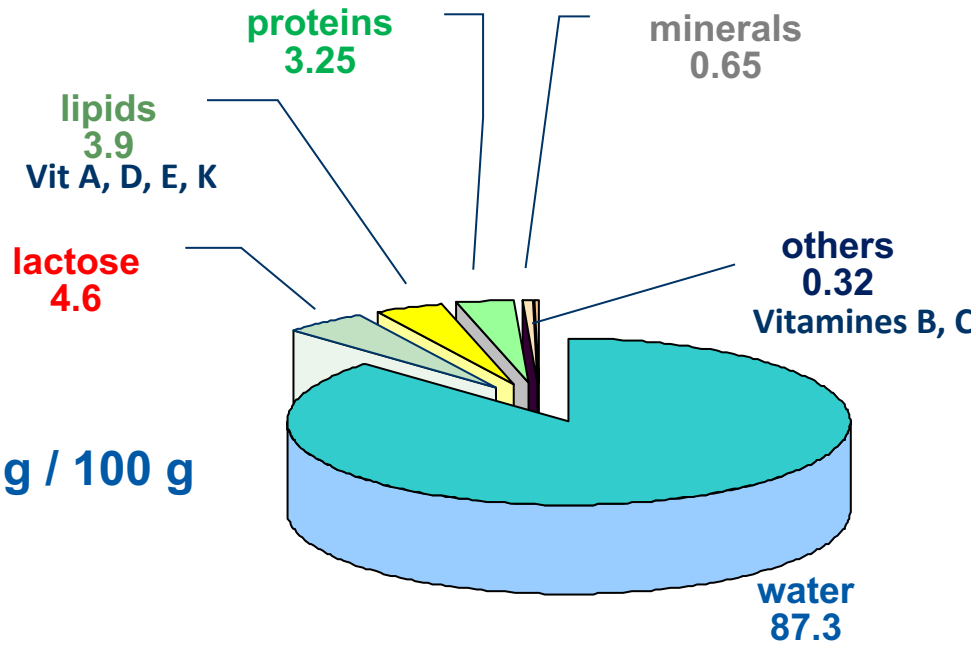


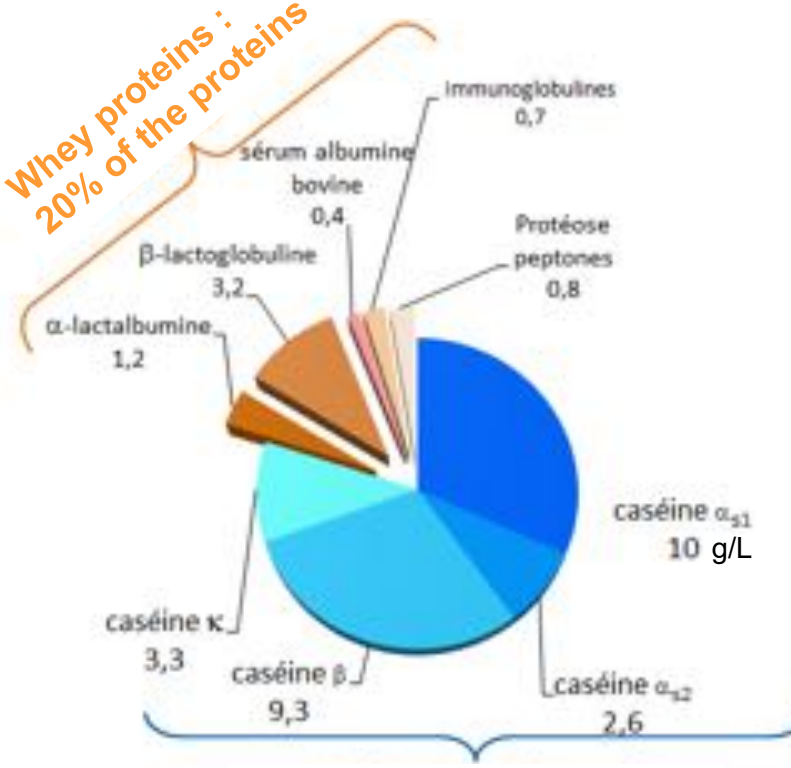
→ Chile : 2 times less than in Europe
↗ 2 kg in 5 years (↗1 kg in France) from 2011 - 2016

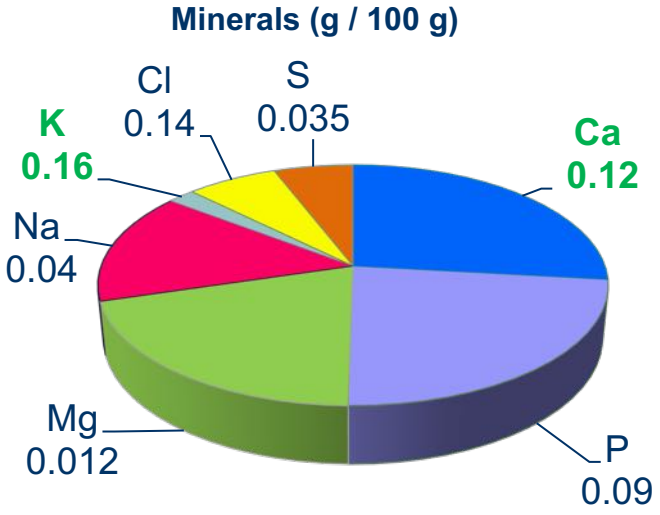
Butter consumption around the world
Kg / capita / year

→ Chile : > 2 times less than in Europe
↗ 0.4 kg in 5 years (↗ 0.6 kg in France) from 2011 - 2016

Nutritional composition of milk







Source : Joëlle Léonil

Whole milk

- A low energy food (65 kcal/100g)
- Great source of
  - high quality proteins
  - lipids (although mostly saturated fats)
  - mineral : calcium, phosphore
  - vitamines : D

… but low in iron

Nutritional quality of milk proteins

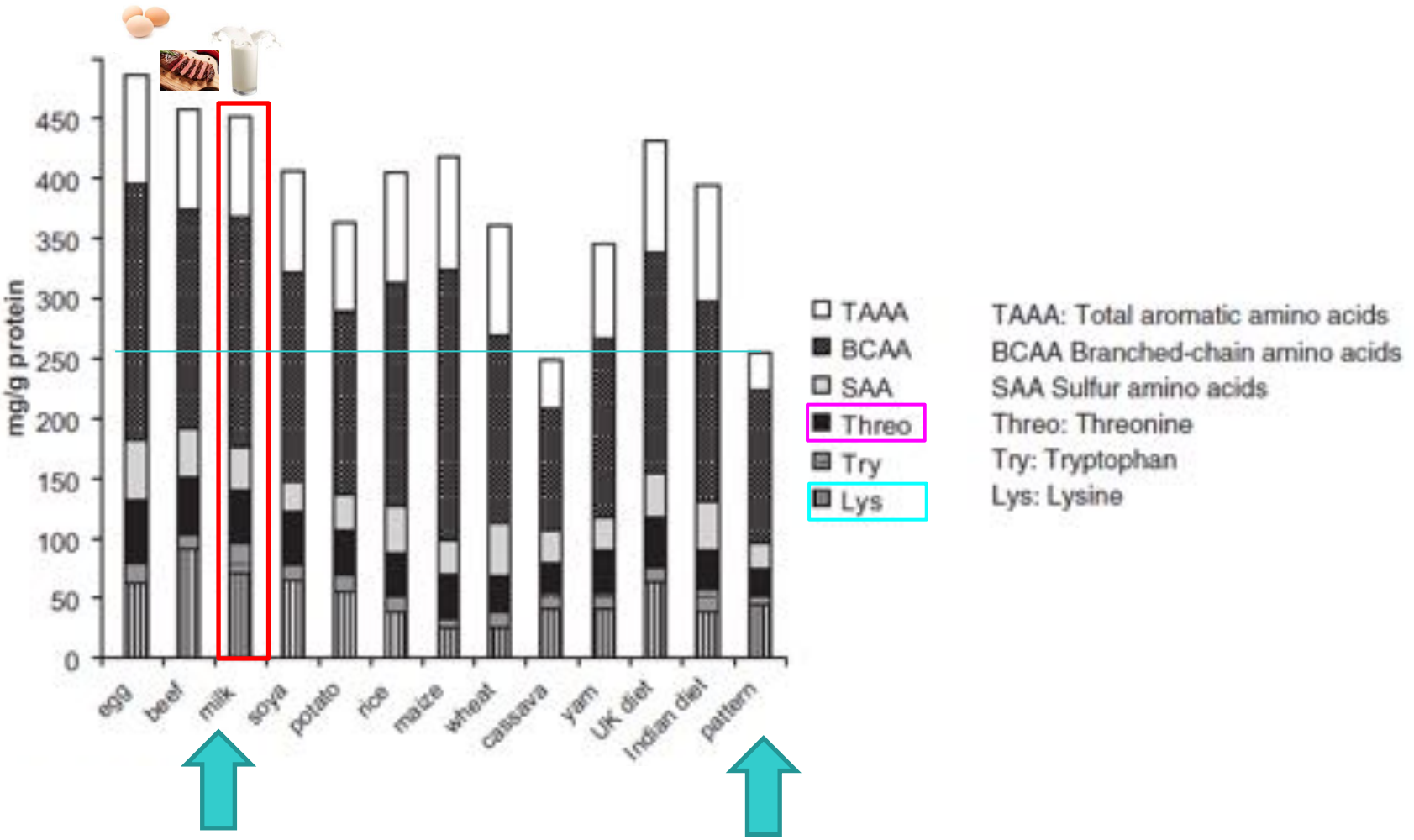
Proteins	True ileal digestibility	PDCAAS
	%	
Milk proteins	95	121
Caseins	*94*	*123*
Lactoserum	*96*	*111*
Egg	95 - 98	118
Beef	92	115
Soya	92 - 95	91 - 99
Lupin	91	-
Pea	90	73
Wheat	92	36 - 42
Rapeseed	84.0	-

World Health Organization

PDCAAS : protein-digestibility corrected amino acid score

Source : Schaafsma, J Nutr, 2000; Bos et al., 2003; Deglaire, 2009; FAO, 2013

Amino acid profile of milk and other protein sources compared to the reference pattern



Source : WHO/FAO/UNU, Technical Report Series, 2007

Milk fat

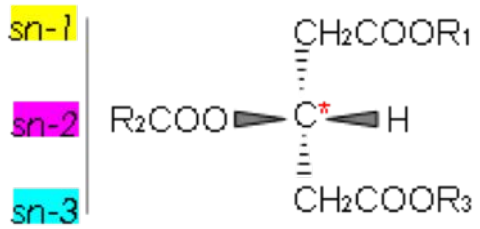
3.9 g of fat / 100 g of milk = 99.5% triglycerides + 0.5% liposoluble compounds (cholesterol max 13,8 mg/100 g; vitamins : A ,D ,E ,K; phospholipids)

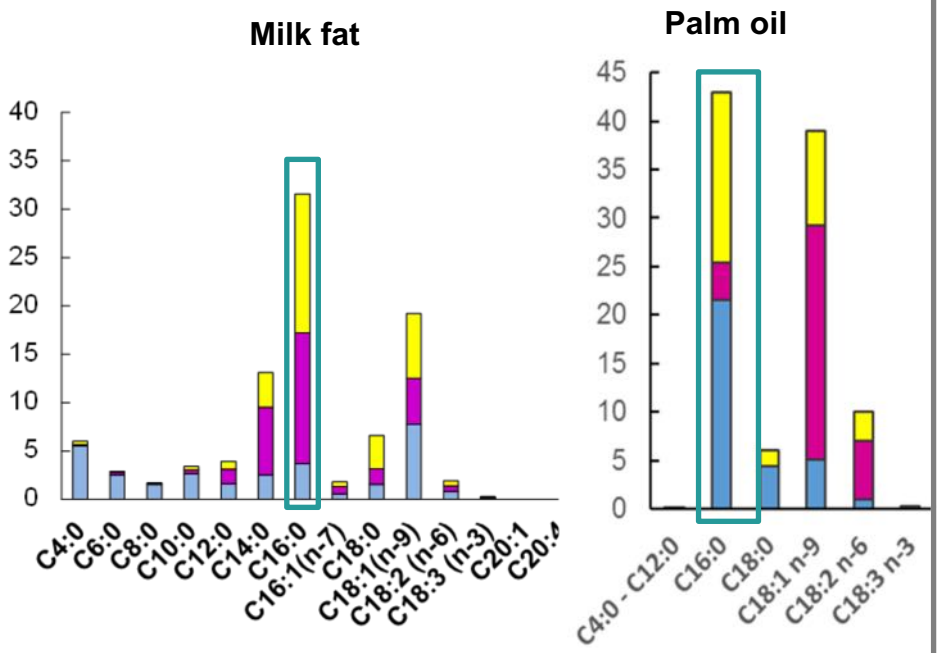
400 fatty acids

Fatty acid profile

	Milk	Palm oil
	%	
Staturated fatty acids	62	45-55
Lauric acid (C12:0)	3-4	<0.5
Myristic acid (C14:0)	9-12	0.5-2
Palmitic acid (C16:0)	23-32	39.5-47.5
Stearic acid (C18:0)	13	3.5-6
Mono-unsaturated fatty acids	29	38-45
Oleic acid (C18:1n-9)	29	36-44
Poly-unsaturated fatty acids	3	9-12
Linoleic acid (C18:2n-6)	2	9-12
Linolenic acid (C18:3n-3)	<1	<0.5

Stereo-distribution of the fatty acids





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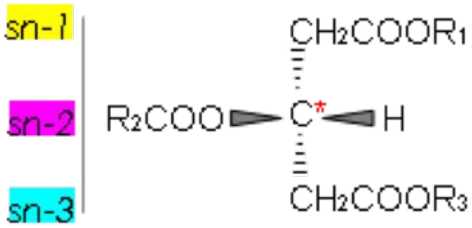
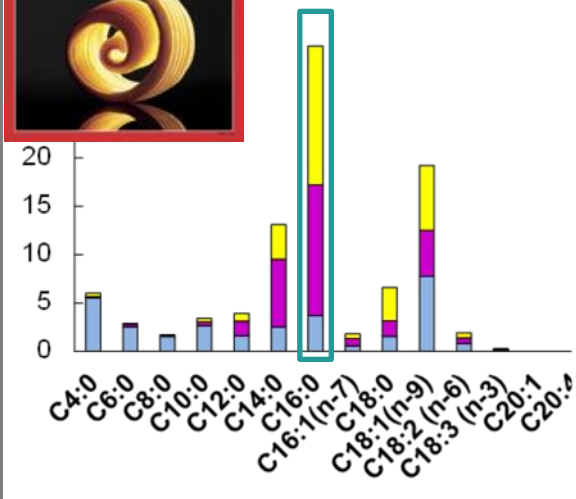
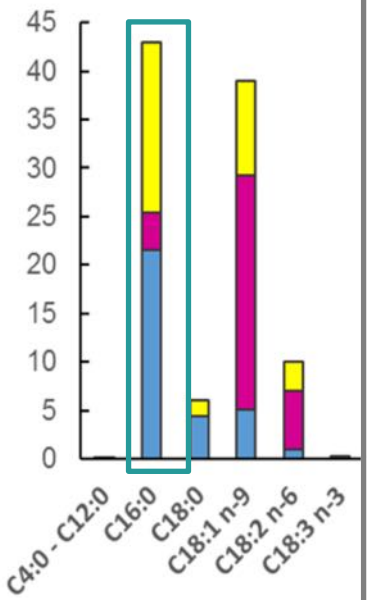


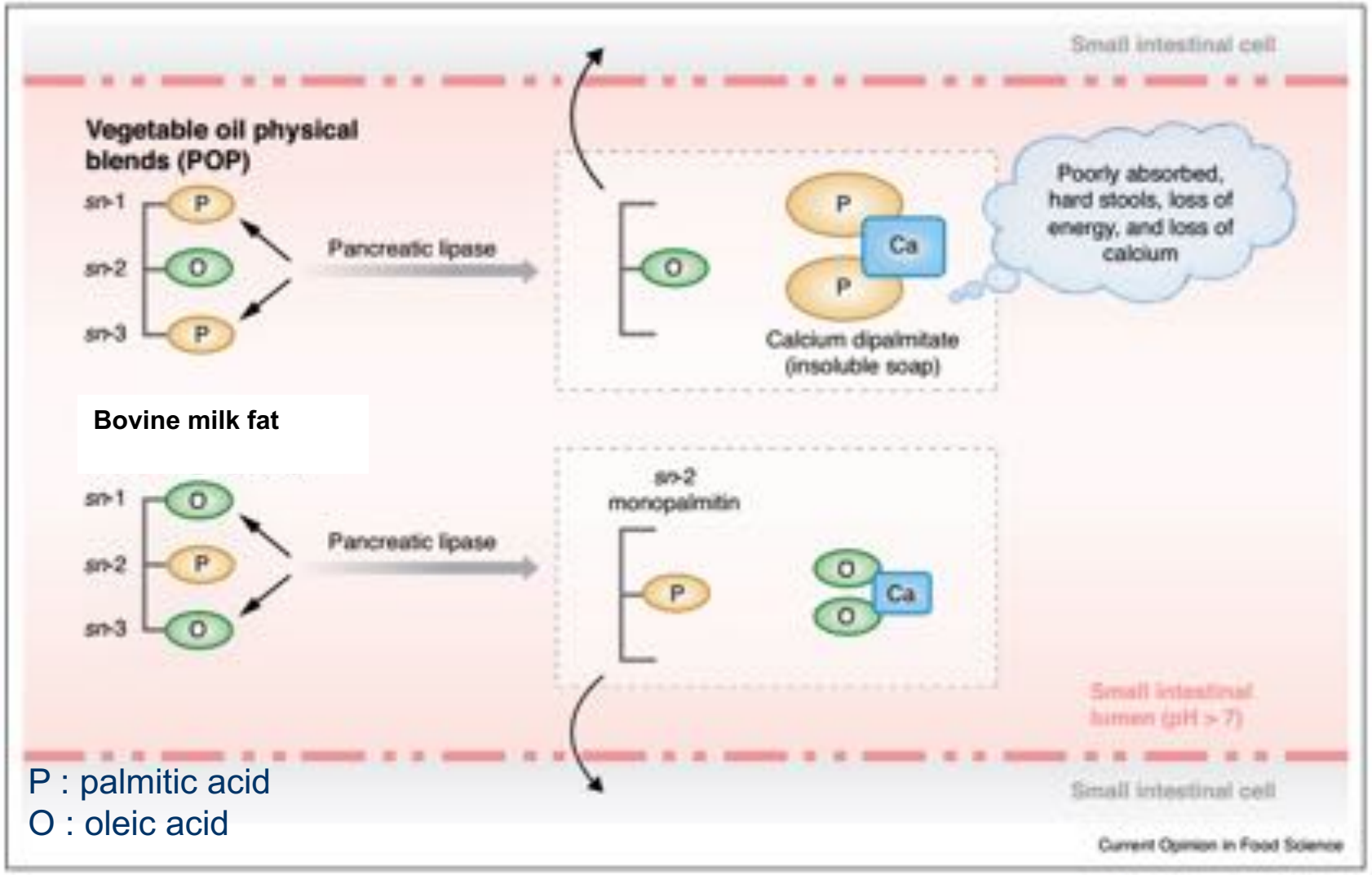
Milk fat



Palm oil



Sterodistribution of fatty acid and absorption



P : palmitic acid
O : oleic acid

Illustrate the importance of palmitic acid at sn-2 position for improved uptake of fat and minerals during lipid digestion [1].

Current Opinion in Food Science 2017, **16**:28–39 www.sciencedirect.com

Guo et al., 2017

Dairy products and health

Diabetes

Obesity

Cancer

Inflammatory disease

Cardiovascular disease

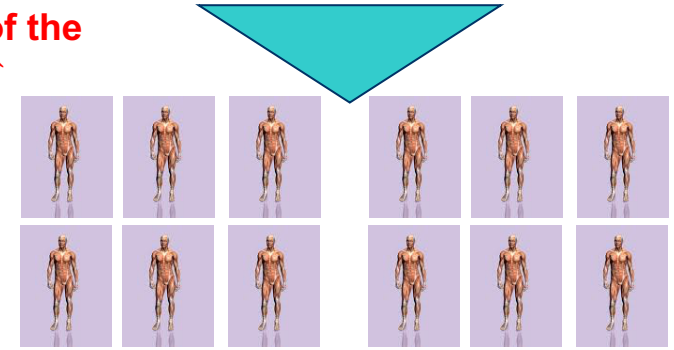
Osteroporosis

Allergy

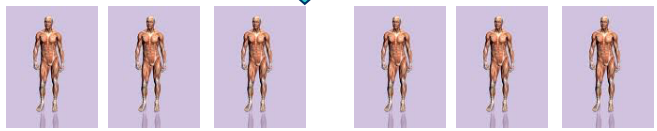
Food and Health ?

General recommandations

Strenght of the evidence ↑

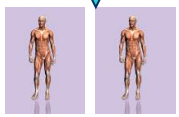


Several populations



One population or cohort

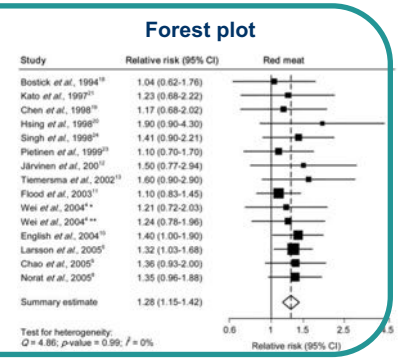
Group of individuals



Animals / Cell models

→ **Collaborative expert consultation**

→ **Meta-analyses**
May unravel strong and significant tendencies for **association** between food and health
→ **Relative Risk**
→ **Odds Ratio**



→ **Epidemiological studies**
Intervention
Observation prospective or retrospective
May identify risk factors, disease's prevalence and/or association

→ **Clinical studies**
may identify impaired physiological mechanisms at risk

→ **Mechanistic studies**

Source: Fardet, 2013

Risk of disease

Relative risk (RR) : ratio of disease incidence between exposed and unexposed populations.

	Sick	Healthy
Exposed	a	b
Non-exposed	c	d

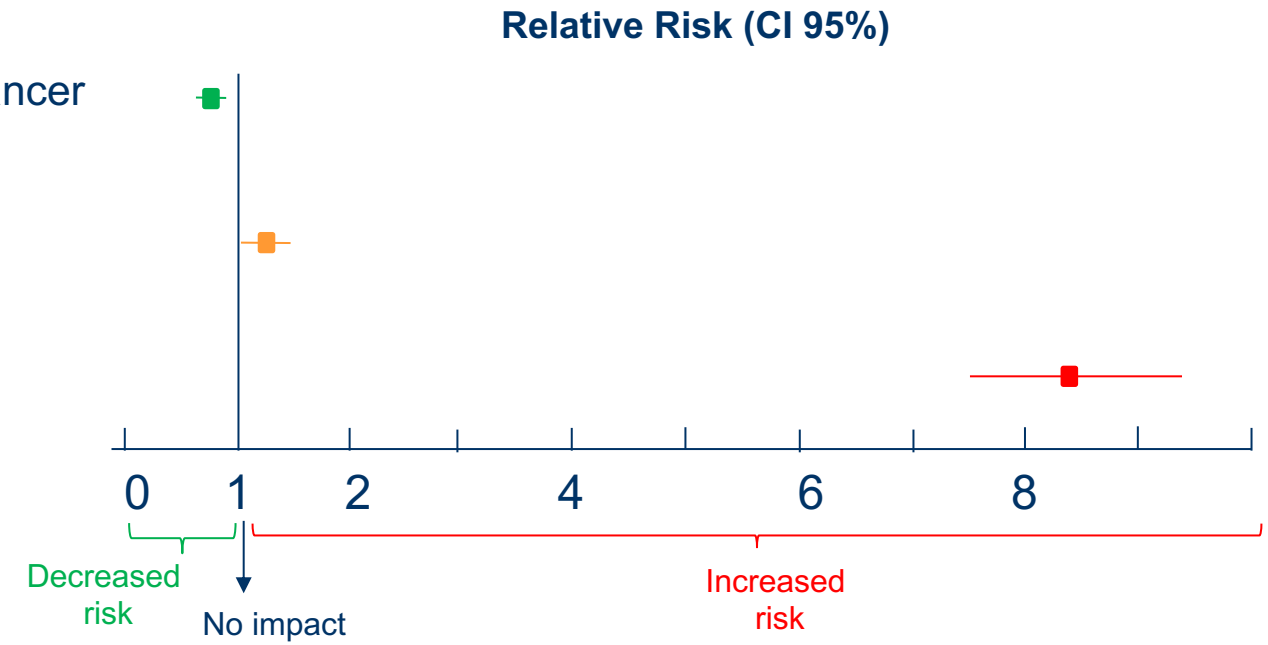
R_{expo} : Disease prevalence in exposed population = a/(a+b)
$R_{un\text{-}expo}$: Disease prevalence in unexposed population = c/(c+d)
→ **RR = R_{expo} / $R_{un\text{-}expo}$**

Odds Ratio : (a/b) / (c/d) → overestimates RR

Dairy products and colorectal cancer (WCRF, 2017)

Red meat and colorectal cancer (WCRF, 2017)

Smoking and lung cancer (Lee et al, 2012)



Different levels of nutritional studies

Diets and dietary pattern (several associated meals):
vegetarian, Mediterranean, Western, Okinawa, Nordic, low-sodium/GI, …

Holistic approach

Meals or food groups
(several associated foods):
breakfast, snacks, vegetables, fish, meat,…

Chronic metabolic effect,
i.e. after several months
or years

⊕ ⊖
Health

Health
⊕ ⊖

Foods (several associated ingredients)

Ingredients (several associated molecules):
resistant starch, fibre, polyphenols, protein, plant extract,…

Acute metabolic effect,
i.e. after several hour(s)
or day(s)

Molecules (isolated compounds):
Amino acids, fatty acids, vitamins, fructose,…

Reductionist approach

Source: Fardet, 2013

Dairy consumption and children bodyweight

Prospective study

Bigornia et al., 2012, The Journal of Nutrition : 2455 children (UK) between 10 and 13 y

- 88 vs 563 g / day of dairy products at 10 y (milk, cheese, yogurt, dairy products)

➢ Dairy consumption was **not associated with excess fat accumulation during early adolescence**

➢ Children consuming the most dairy products had a **30% reduced risk of excess body fat mass and overweight at 13y**

➢ **Full-fat dairy intake was more protective against excess weight** and limited gain in BMI, whereas reduced-fat dairy intake was unrelated to these outcomes

Dairy consumption on **childhood adiposity**

- **has no adverse effect**
- **may have a protective effect (full-fat)**

Dairy consumption and adult bodyweight

Meta-analyses

- Abargouei et al., 2012, Int J Obes (London) : 14 studies (1960-2011) – 883 adults
- Benatar et al., 2013, Plos One : 20 studies – 1677 adults
- Chen et al., 2012, AJCN : 29 studies (1966-2012) – 2101 adults
- Stonehouse et al., 2016, Nutrients : 18 studies – 864 adults

Similar CCL

Randomized controlled trial : dairy group (milk, yogurt, cheese) vs. control group

→ Increased dairy intake was associated with :

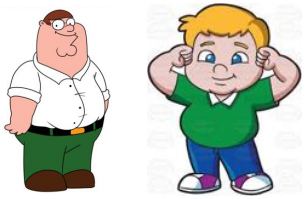
- a modest weight gain (+0.6 kg, CI : 0.3, 0.9 kg, p<0.0001) (Benatar et al., 2013)
- **no significant impact on body weight** and fat/lean mass **without energy restriction diets** (or long term studies)
- **modest benefits in facilitating weight loss with energy-restricted diets (or short-term studies)**

  Weight loss in dairy group :

  Chen et al., 2012 : BW : -0.79 kg; 95%CI: -1.35, -0.23 kg;

  Fat loss : -0.94 kg; 95% CI: -1.53, -0.34 kg

no major increase of bodyweight / body fat with dairy consumption in adults



Dairy consumption and obesity

- **Meta-analysis :** Wang et al., 2016, Annals of Epidemiology
  - 24 studies (n= 1209 to 75686 children or adults)
  - **Dairy product consumption : significant and reverse association with obesity (BMI, Waist circumference)**
    - Dairy products : odds Ratio for children / adults : 0.54 / 0.74 (non-linear association)
    - Milk: odds Ratio for children / adults : 0.81 / 0.77 (linear association)
      - **Risk obesity decreased of 16% for every 200g/d increment of milk consumption**

Dairy product consumption seems associated with a decreased risk of obesity both in children and adults

Dairy consumption and weight : hypotheses

Hypotheses (Chen et al., 2012)

→ **Calcium** :

- reduces lipogenesis and stimulates adipocyte lipolysis via the secretion of hormones (parathyoid/calciotropic) and suppresing formation of 1,25dihydroxyvitD
- Insoluble soaps in intestine and reduction of fat absorption
- Increase thermogenesis during enery restriction

→ **Conjugated linolenic acid** : regulation of adipogenesis, inflammation and lipid metabolism

→ **Medium chain fatty acids** : potential role in weight regulation

→ **Whey proteins** : muscle sparing, appetite regulation, lipid metabolism

Dairy consumption and type II diabetes

Meta-analyses

- Chen et al., 2014, BMC Medicine
  - 14 prospective cohort studies (n = 459 790)
- Gijsbers et al., 2016, AJCN
  - 22 prospective cohort studies (n = 579 832)
- Pimpin et al., 2016, Plos One
  - 11 prospective cohort studies (n = 201 628)
  - Butter only

✓ **total dairy consumption : not associated with incidence of type II diabetes**

RR: 0.99 [0.98 ; 1.01] for 1 serving/d

RR: 0.97 [0.95; 1.00] for 200 g/d increment

✓ **intake of yogurt (80-100g/day) associated with a reduced risk of T2D of ~ 15%**

RR: 0.82 [0.70; 0.96] for 1 yogurt/d

RR: 0.86 [0.83; 0.90] for 80 g/d

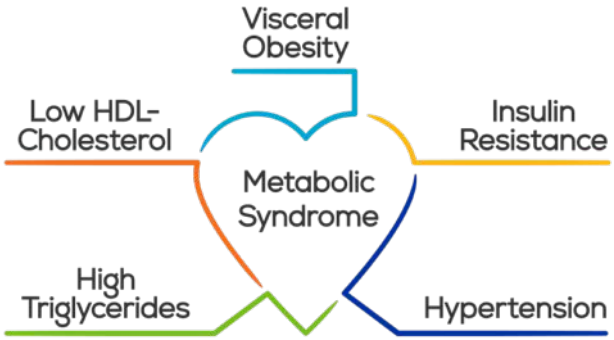
no added benefits with higher intake

✓ **intake of butter (14g/day) associated with a reduced risk of T2D of 4%**

RR: 0.96 [0.93;0.99] for 14g /d (Pimpin et al.)

✓ **Other dairy types not associated with type II diabete risk** (including butter for Chen and Gijsbers)

Dairy consumption and metabolic syndrome



Three meta-analyses

- Kim and Je, 2016, Diabetic medicine
  - 9 prospective cohort
  - 12 cross-sectional studies
- Chen et al., 2015, Scientific Reports
  - 7 prospective cohort
  - 15 cross-sectional studies
  - 1 case-control study

✓ higher dairy consumption **significantly reduced the risk** of Metabolic Syndrome **by about 15%**

✓ **Dose-response relationship** : 6-12% reduction of the risk for each additional serving/d

- Benatar et al., 2013, Plos One
  - 20 randomized controlled trials

✓ Dairy food consumption did not significantly impact cardio-metabolic risk factors although a slight significant increased in bodyweight (+0.6 kg)

Dairy consumption and cardiovascular diseases

Meta-analyses

- Guo et al., 2017, Eur J Epidemiol
  - 29 prospective cohort studies
- Pimpin et al., 2016, Plos One
  - 9 prospective cohort studies
  - Only on butter

✓ Virtually **no association** between total dairy intake or butter and all-cause of mortality, coronary heart or cardiovascular disease

✓ **Slight decreased risk (2%) of mortality and cardiovascular disease for total fermented dairy consumption** (cheese, yogurt, sour milk products)

RR: 0.98 [0.97-0.99] for increment of 20g/day

❖ **Food matrix** reducing lipid absorption ; Calcium, Vit D ?

❖ Heptadecanoic acid ?

Dairy consumption and bone health

Risk of hip fracture

Meta-analyses

- Bian et al., 2018, Eur J Epidemiol
  - 10 prospective cohort studies
  - 8 case-control studies
- Bischoff-Ferrari et al., 2011, J Bone Miner Res
  - 7 prospective cohort studies

- ✓ Total dairy or milk (high vs low) consumption not associated with incidence of hip fracture

- ✓ Unclear relation for milk consumption and hip fracture
  - eventual beneficial association in men (Bischoff-Ferrari et al., 2011) or for an intake of 200g / d (Bian et al., 2018)

- ✓ **intake of yogurt or cheese (80-100g/day) associated with a reduced risk of hip fracture of ~ 25-30%**

RR: 0.75 [0.66; 0.86] for yogurt
RR: 0.68 [0.61; 0.77] for cheese

- Huncharek et al. , 2008, Bone
  - 21 studies in children only

→ ✓ Increased dietary calcium/dairy products, with and without vitamin D, significantly increases total body and lumbar spine bone mineral content in children with low base-line intakes

Dairy products and inflammatory response

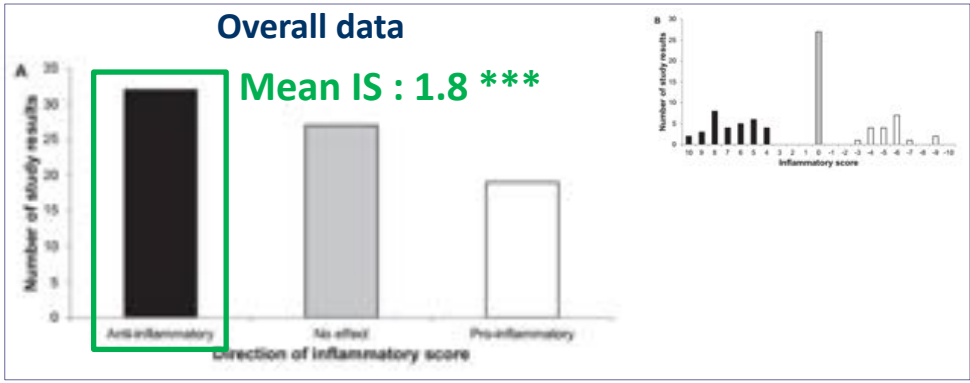
Inflammation

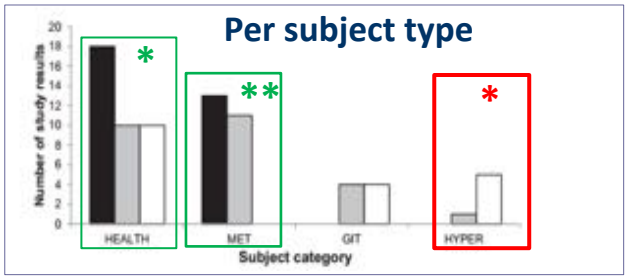
major biological process regulating the interaction between the organism and the environment such as diet

If sustained → chronic inflammatory diseases

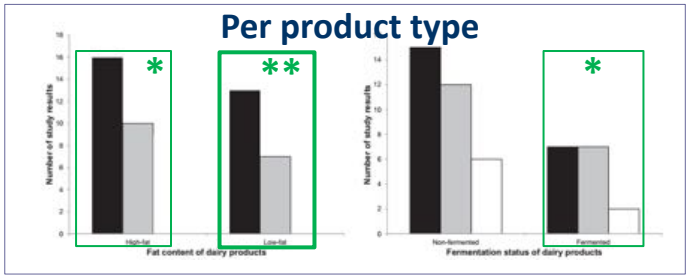
Systematic review

- Bordoni et al., 2016, CRFSN
  - 52 clinical studies → 78 study results
  - > 50 markers : CRP, IL-6, TNF-α, …
  - Inflammatory score





Test : median ≠ from 0
* <0.05
** < 0.01
*** <0.001



- ✓ In overall, dairy products exert an **anti-inflammatory activity** in humans
  - → subjects with metabolic disorders (unlike that for allergic subjects)
  - → Low-fat, high-fat and fermented products
- ✓ **In obese / overweight subjects** (Labonté et al., AJCN : review of 8 clinical trials)
  - → **No adverse effect** of dairy products on biomarkers of inflammation in these subjects

Dairy products and cancer

World Cancer Research Fund | American Institute for Cancer Research

Meat, fish and dairy products and the risk of cancer

2018

Strong evidence - probable

Cancer	Type of evidence	Total no. of studies	No. of studies in meta-analysis	No. of cases	Risk estimate (95% CI)	Increment	I^2 (%)	Conclusion[1]	Date of CUP cancer report[2]
Colorectum	Dairy products	14	10	14,859	0.87 (0.83–0.90)	400 g/day	18	Probable: Decreases risk	2017
	Milk	13	9	10,738	0.94 (0.92–0.96)	200 g/day	0		
	Cheese	9	7	6,462	0.94 (0.87–1.02)	50 g/day	10		
	Dietary calcium	20	13	11,519	0.94 (0.93–0.96)	200 mg/day	0		

Calcium

Lactic-acid producing bacteria

Lactoferrin
Vitamin D
Butyrate
} ?

Dairy products and colorectal cancer

Figure 5.4: CUP dose–response meta-analysis[1] for the risk of colorectal cancer, per 400 grams increase in dairy products consumed per day

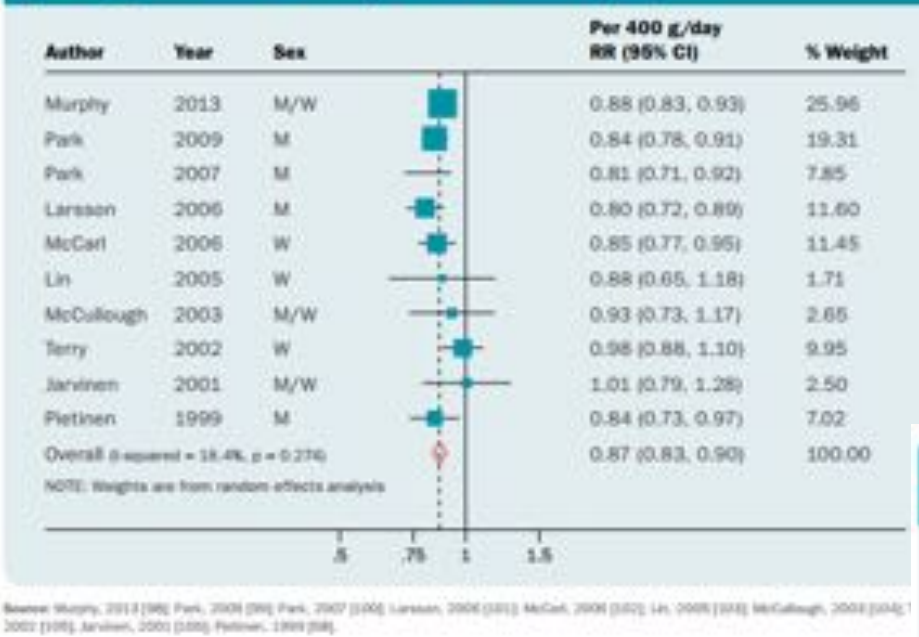
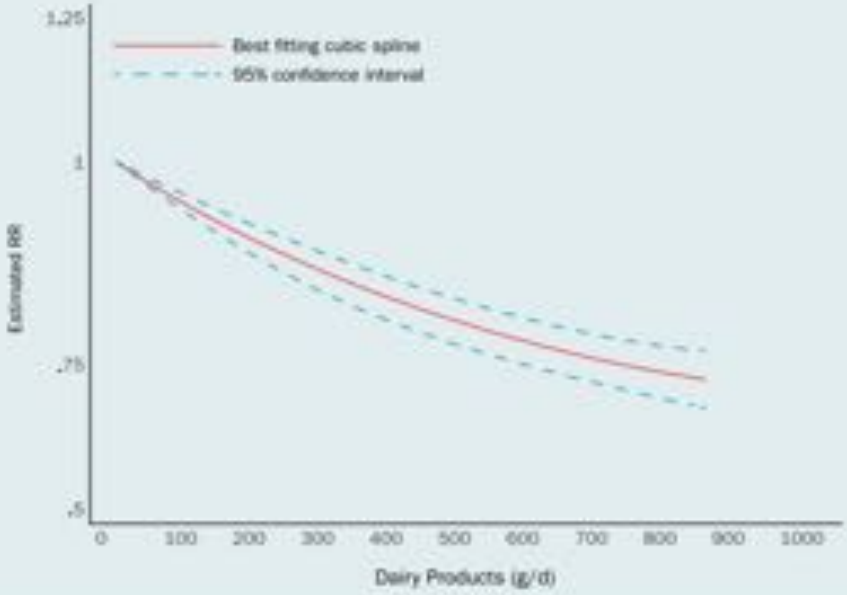


Figure 5.5: CUP non-linear dose–response association of dairy products intake and the risk of colorectal cancer



Dairy products and cancer

World Cancer Research Fund | American Institute for Cancer Research

Meat, fish and dairy products and the risk of cancer — 2018

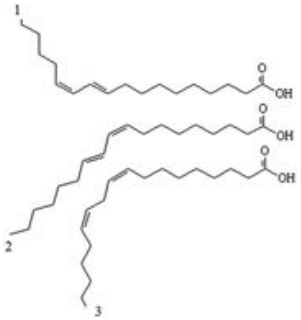
Limited evidence - suggestive

Cancer	Type of evidence	Total no. of studies	No. of studies in meta-analysis	No. of cases	Risk estimate (95% CI)	Increment	I^2 (%)	Conclusion[1]	Date of CUP cancer report[2]
Breast (premeno-pause)[3]	Dairy products	13	7	2,862	0.95 (0.92–0.99)	200 g/ day	0	Limited – suggestive: Decreases risk	2017

Further research required

Calcium

Conjugated linoleic acids



Vitamin D

Dairy products and cancer

World Cancer Research Fund | American Institute for Cancer Research

Meat, fish and dairy products and the risk of cancer 2018

Limited evidence - suggestive

Cancer	Type of evidence	Total no. of studies	No. of studies in meta-analysis	No. of cases	Risk estimate (95% CI)	Increment	I^2 (%)	Conclusion[1]	Date of CUP cancer report[2]
Prostate[4]	Dairy products	21	15	38,107	1.07 (1.02–1.12)	400 g/ day	0	Limited – suggestive: Increases risk	2014

Further research required

IGF-1

Calcium / vitamin D

Dairy products and cancer

Meat, fish and dairy products and the risk of cancer 2018

MEAT, FISH AND DAIRY PRODUCTS AND THE RISK OF CANCER

WCRF/AICR GRADING		DECREASES RISK		INCREASES RISK	
		Exposure	Cancer site	Exposure	Cancer site
STRONG EVIDENCE	Convincing			Processed meat[1]	Colorectum 2017
	Probable	Dairy products	Colorectum 2017[2]	Red meat[3] Cantonese-style salted fish[4]	Colorectum 2017 Nasopharynx 2017
LIMITED EVIDENCE	Limited – suggestive	Fish	Liver 2015 Colorectum 2017	Red meat[3]	Nasopharynx 2017 Lung 2017 Pancreas 2012
				Processed meat[1]	Nasopharynx 2017 Oesophagus (squamous cell carcinoma) 2016 Lung 2017 Stomach (non-cardia) 2016 Pancreas 2012
				Foods containing haem iron[5]	Colorectum 2017
				Grilled (broiled) or barbecued (charbroiled) meat and fish	Stomach 2016
		Dairy products	Breast (premenopause) 2017[6]	Dairy products	Prostate 2014[7]
		Diets high in calcium	Breast (premenopause) 2017 Breast (postmenopause) 2017	Diets high in calcium	Prostate 2014
STRONG EVIDENCE	Substantial effect on risk unlikely	None identified			

The Panel's Judgements:

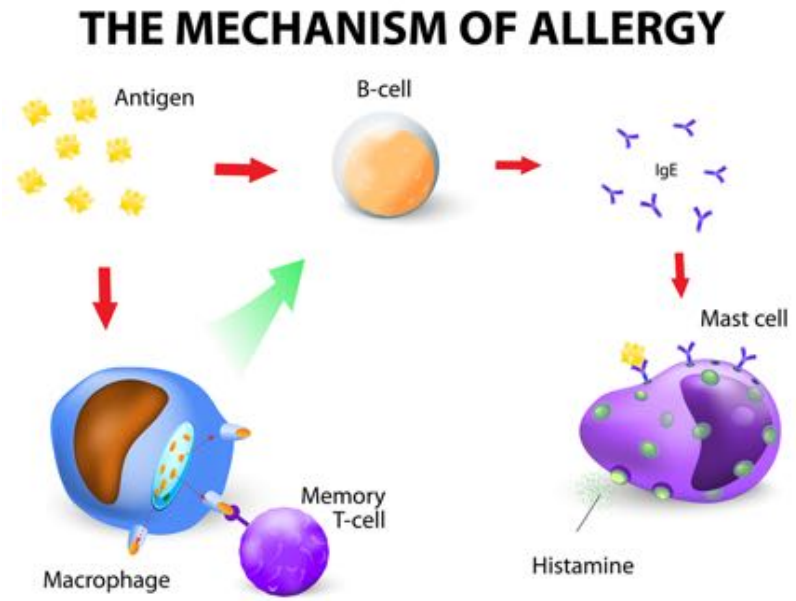
- Consumption of dairy products probably protects against colorectal cancer
- Consumption of calcium supplements probably protects against colorectal cancer.

NO recommendation

Dairy products and allergy

- Prevalence of milk protein allergy
  - 6-10% of children (Venter et al., 2008)
    - 80% are healthy at 3-year old
    - 90% at 16-year old
  - 3% of adults (Rona et al., 2007)

- Protein incriminated
  - **Caseins**
  - β-lactoglobulin
  - BSA



Summary

	Decreases risk	Neutral	Increases risk
Weight	- 0.8 kg BW for energy-restricted diets (Chen et al., 2012)	For all type of studies (with or without energy restriction) (Chen et al., 2012)	+0.4 kg for whole fat products +0.8 kg for low-fat products (Benatar et al., 2013)
Obesity	Bigornia et al., 2012 Wang et al., 2016		
Diabete II	**Butter / yogurt** Chen et al., 2014 Gijsbers et al., 2016 Pimpin et al., 2016	Total dairy Chen et al., 2014 Gijsbers et al., 2016	
Cardiovascular Disease	**Fermented products** Guo et al., 2017 Pimpin et al., 2016	Total dairy Guo et al., 2017 Pimpin et al., 2016	
Metabolic Syndrome	Kim & Je, 2016 Chen et al., 2015	Benatar et al., 2013	
Bone health (hip fracture)	**Yogurt / cheese** Bian et al., 2018 Bischoff-Ferrari et al., 2011	Total dairy Bian et al., 2018 Bischoff-Ferrari et al., 2011	
Inflammation	Total dairy (**Fermented** or High-/Low-fat products) Bordoni et al., 2016	Total dairy on overweight/obese subjects Labonté et al., 2013	
Cancer	Colorectal cancer (strong evidence) Breast cancer (limited evidence)		Prostate cancer (limited evidence)

CONCLUSION

- ✓ Dairy consumption does not increase the disease risk, except for prostate cancer (7% increased risk; limited-suggestive evidence)

- ✓ Regarding **bodyweight and obesity**, most studies suggest a protective effect, especially for energy-restricted diet. Only Benatar et al. found a small but significant BW increase (+0.6 kg)

- ✓ Total dairy consumption may be protective against :
  - ✓ **Metabolic syndrome**
  - ✓ **Inflammation**
  - ✓ **Colorectal or breast cancer**

- ✓ Fermented products may be protective against
  - ✓ **Diabetes type II**
  - ✓ **Cardiovascular disease**
  - ✓ **Bone health (hip fracture)**
  - ✓ **Inflammation**

- ✓ **Further randomized-control trial / intervention studies are necessary to confirm the causality and understand the mechanism beyond the observed relationship**