

Evaluation of Benefit Claims: What evidence is sufficient and feasible ?

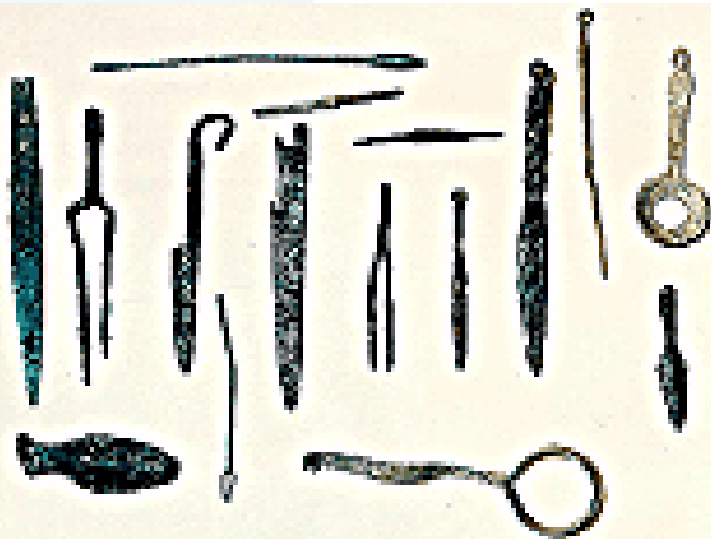
Dr. Jean Michel ANTOINE

Council for Responsible Nutrition International:
Geneva July 3rd 2010

Let food be your medicine and medicine be your food



ΑΝΙΣΤΑΤΕ ΤΑ ΑΡΧΑΙΑ
ΙΝΑ ΣΠΕΥΔΗΤΕ ΤΑ ΚΑΙΝΑ



Let food be your medicine and medicine be your food

PODALIRIUS:
Healer

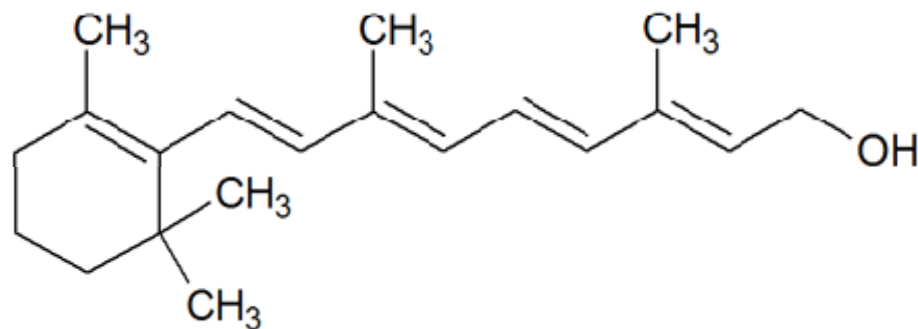
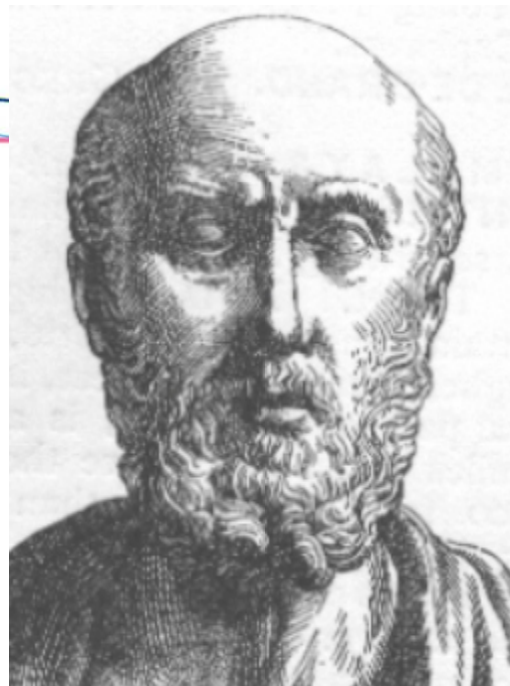
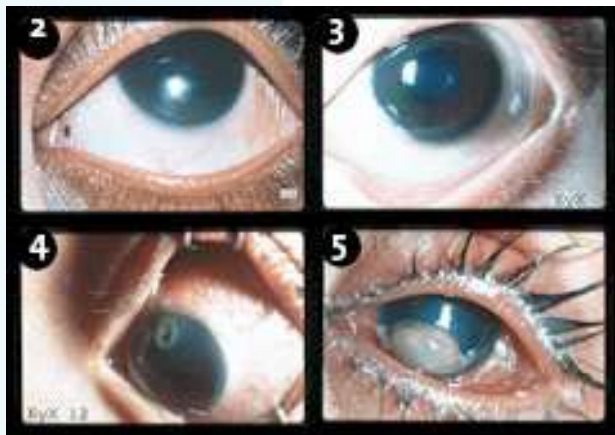


MACHAON : Surgeon

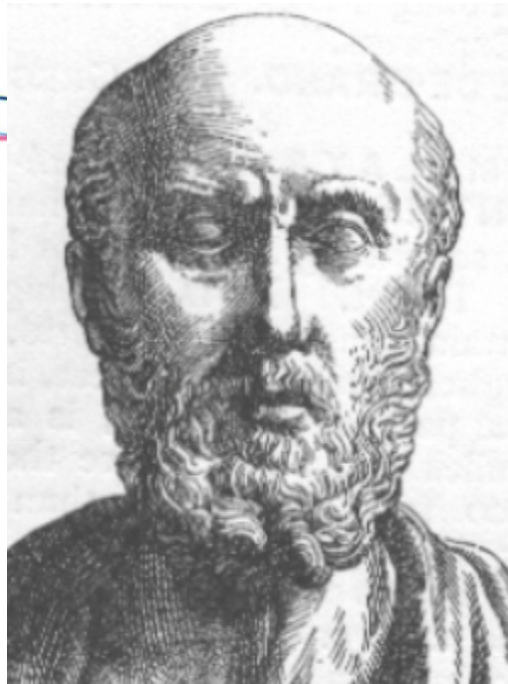
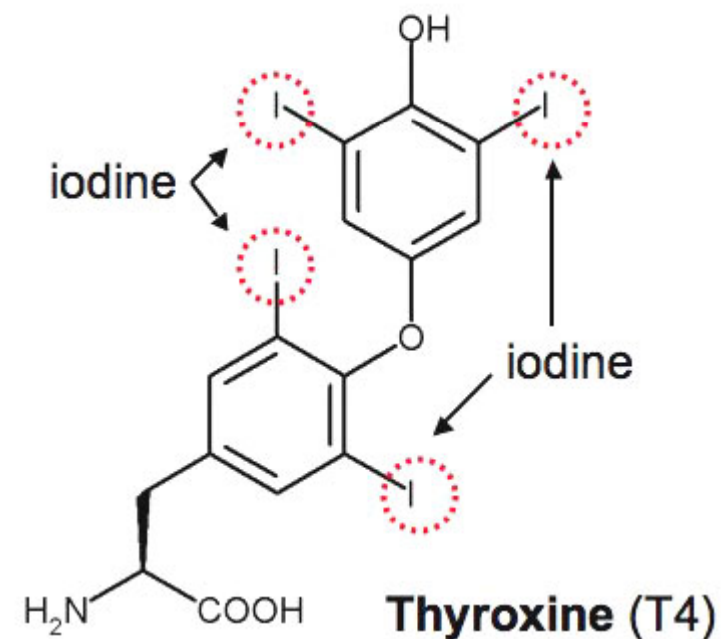


ASCLÉPIOS

Let food be your medicine and medicine be your food



Let food be your medicine and medicine be your food

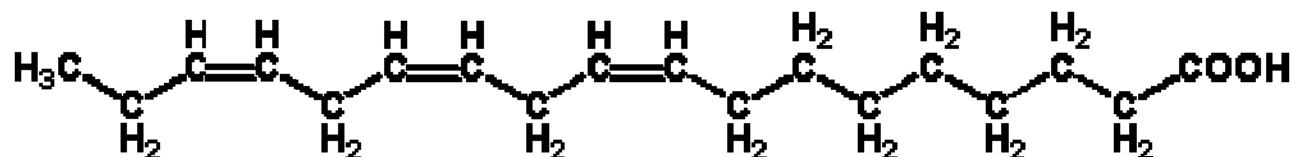
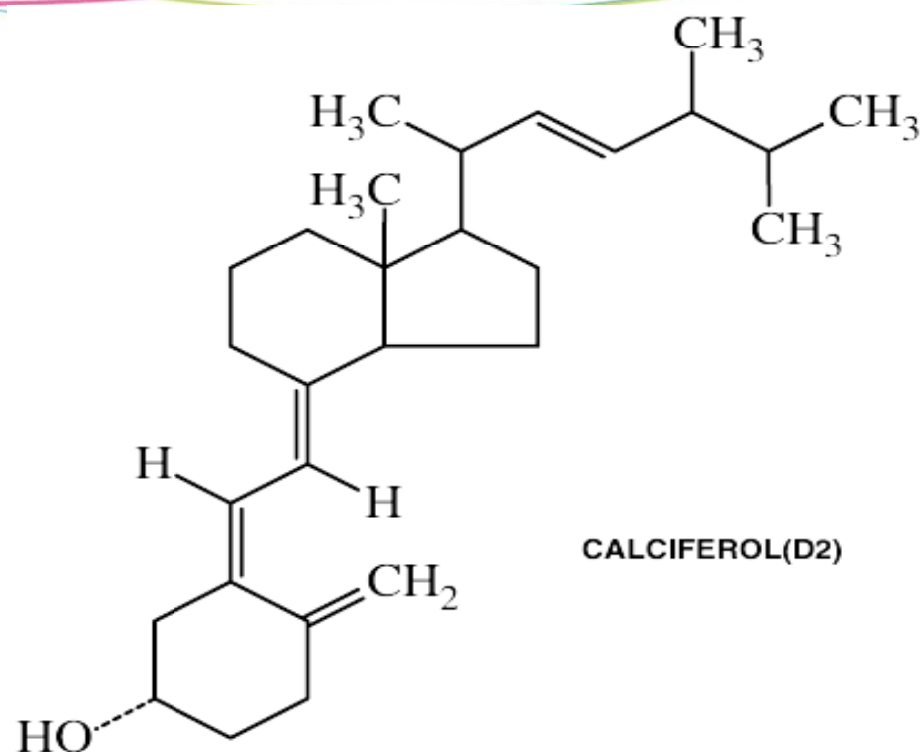


Let food be your medicine and medicine be your food



JB





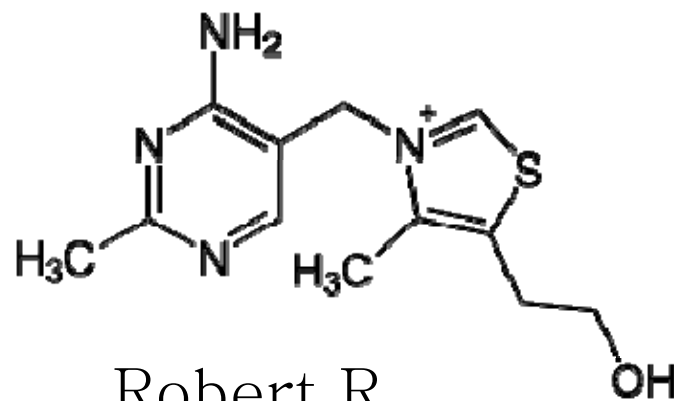
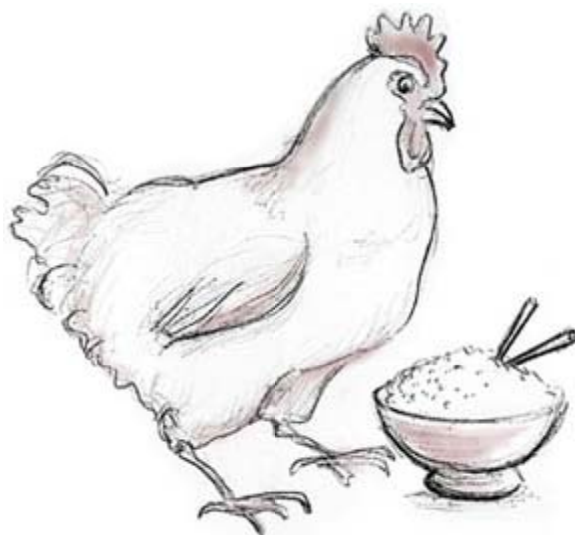
NUTRITION STARTED WITH OBSERVATION TRIALS, ERRORS, TRADITION

We are still in a learning process...

OBSERVATION: KEY FOR SUCCESS



Jacob de Bondt



Robert R.
Williams

1931

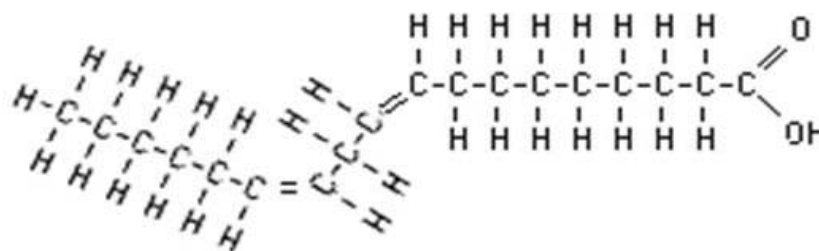
OBSERVATION: KEY FOR INNOVATION



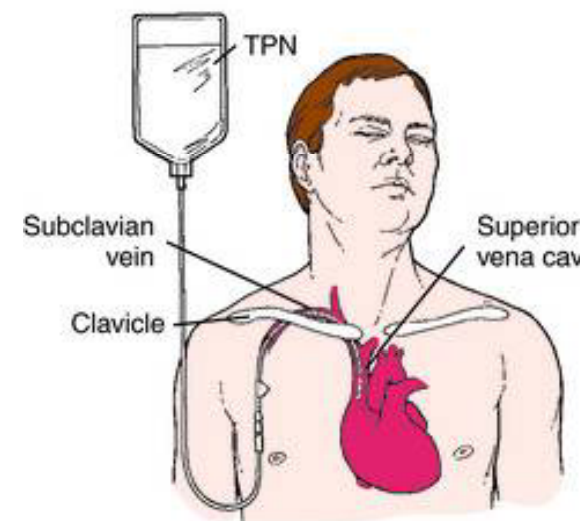
Burr &
Evans 1930



Epidemiology of Eskimos
1970



Linoleic acid, a polyunsaturated fatty acid.
Both double bonds are *cis*.



Parenteral
Nutrition
1980

1st DEMONSTRATION of EFFICACY: 1747



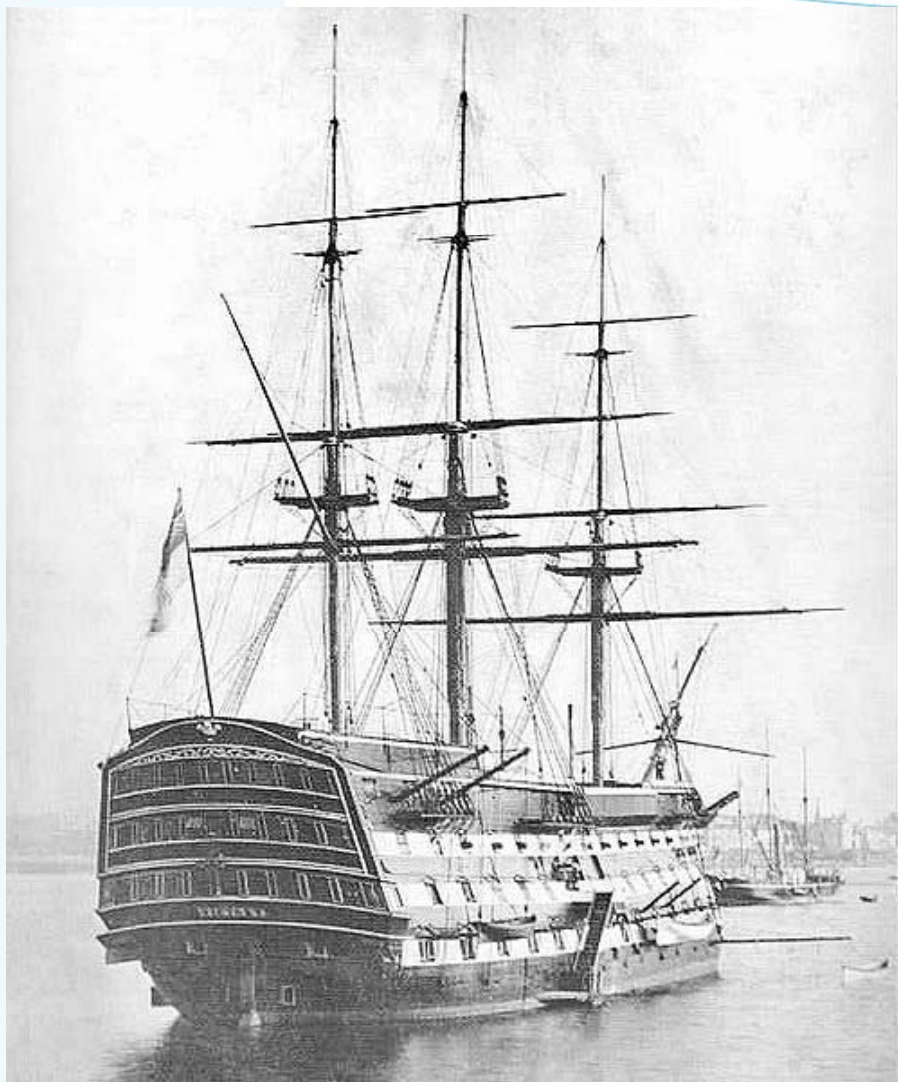
James LIND compared 6 drinks on 6 * 2 sick subjects:

- Cider,
- H₂ SO₄
- Vinegar
- Sea water
- Lime
- Garlic, mustard, horseradish

He concluded that Acid was the key factor,
because of its cleaning capacity.



1st CLINICAL TRIAL : 1794



HMS Suffolk sailing from London to India, Supported by Admiralty

Sir G. Blane (1794) demonstrated the efficacy of lime on half the crew.

1st Randomized, not blinded
Controlled (nothing vs lime)
Long term Trial.

47 years after the first report.

Validated by the Royal Academy of
Medicine 50 years later !

Cook used it since 1766 !

What is the active part of lemon ?

- Szent-Györgyi: *vitamin C* : 1933
- Lemon is more than Vit. C. :
Marti N. & al: Nat Prod Commun. 2009;4:677-700.
Hamdan D & al. Pharmazie. 2010; 65:141-7. : 94 compounds
- Lemon is still not well characterized !

To day Observation is not enough

- Observation:
 - Long history of useful practices
 - Tradition is still inspiring modern science
 - Reports correlation
- Intervention:
 - Cause and effect relationship
 - Identify the causal food / ingredient

Scientific opinions in our centuries.

- ILSI Europe: FuFoSe: Br J Nutr. 1999;81:S1-27: Scientific concepts of functional foods in Europe. Consensus document.
- Growth, development and differentiation.
- Functional food science and substrate metabolism.
- Functional food science and defense against R.O.S.
- Functional food science and the cardiovascular system.
- Functional food science and gastrointestinal physiology and function.
- Functional food science and behavior and psychological functions.

Functional Food Science

FUFOSE



Outcome

A working definition:

A food can be regarded as “functional” if it is satisfactorily **demonstrated** to affect beneficially one or more target **functions** in the body, **beyond** adequate **nutritional effects** in a way which is relevant to either an improved state of health and well-being and/or the reduction of risk of disease.

Conclusions from Fufose

- ILSI Europe: FuFoSe: Br J Nutr. 1999;81:S1-27: Scientific concepts of functional foods in Europe. Consensus document.
- Functional foods are foods, therefore safe products.
- They are providing benefits beyond usual nutrition.
- There are examples of foods/nutrients with functional benefits
- Markers
 - Exposure
 - Indication
- Evidence

Functional examples:

Table 1. Examples of opportunities for modulation of target functions related to growth, development and differentiation by candidate food components with possible markers*

Target functions	Possible markers	Candidate food components
Maternal adaptation during pregnancy and lactation	maternal weight body fat infant birth weight milk volume and quality	micronutrients n-3 and n-6 PUFA energy
Skeletal development	ultrasound measures anthropometric measures bone mineral density (e.g. DEXA)	calcium vitamin D vitamin C
Neural tube development	ultrasound measurements	folic acid
Growth and body composition	anthropometry body fat mass total body water procollagen propeptide excretion urinary creatinine excretion	growth factors essential amino acids unsaturated fatty acids
Immune function	cellular and non-cellular immune markers	vitamin A vitamin D antioxidant vitamins n-3 and n-6 PUFA trace elements arginine nucleotides and nucleosides probiotics
Psychomotor and cognitive development	tests of development, behaviour, cognitive function and visual acuity (electro-) physiological measurements	n- and n-6 PUFA iron zinc iodine

Conclusions from Fufuse

- ILSI Europe: FuFoSe: Br J Nutr. 1999;81:S1-27: Scientific concepts of functional foods in Europe. Consensus document.
- Functional foods are foods and safe products.
- They are providing benefits beyond usual nutrition.
- There are examples of foods/nutrients with functional benefits
- Markers are KEY elements to demonstrate a benefit
 - Exposure, Function, Intermediate end-point
 - Indicators or Factors.
- Evidenc

Markers for different objectives

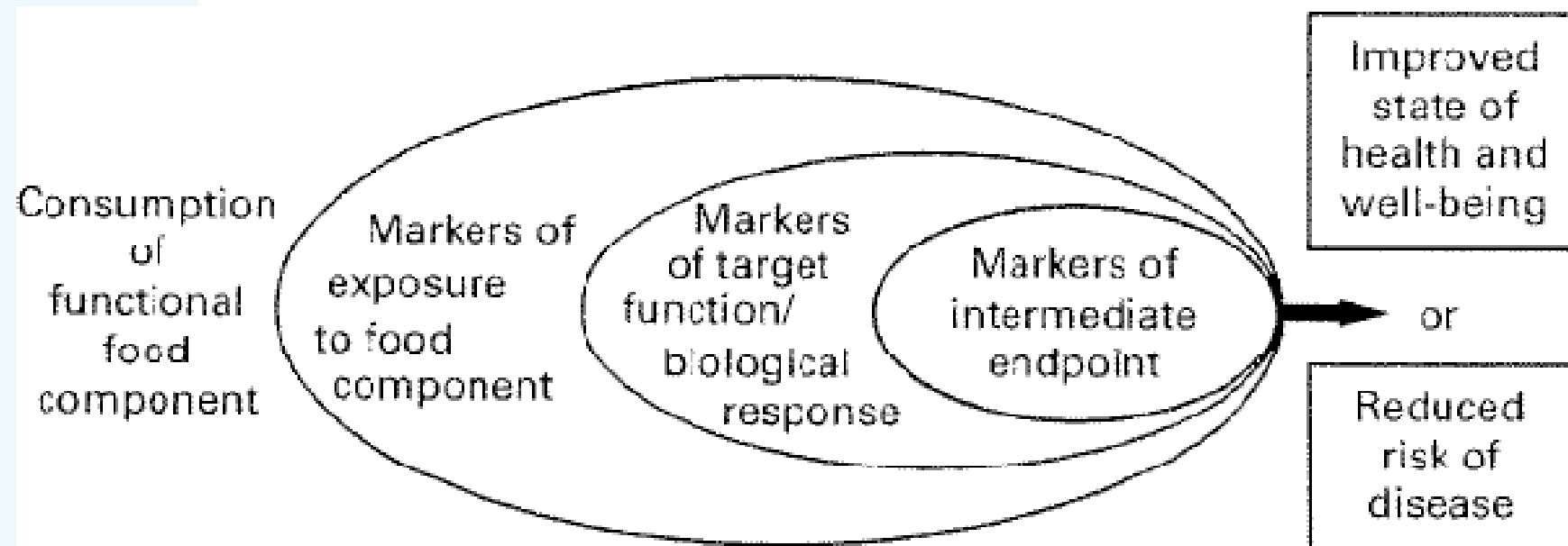


Fig. 1. *Classification of markers relevant to the effects of functional foods.* This is a diagrammatic representation to show how different types of markers would be expected to lie within a logical progression from the food component to the health outcome. The types of markers are completely independent of each other. Markers can be either indicators or, if they can be proven to be causal, factors (see Section 2).

Biomarkers for well-being and disease risk reduction discussed at the meeting

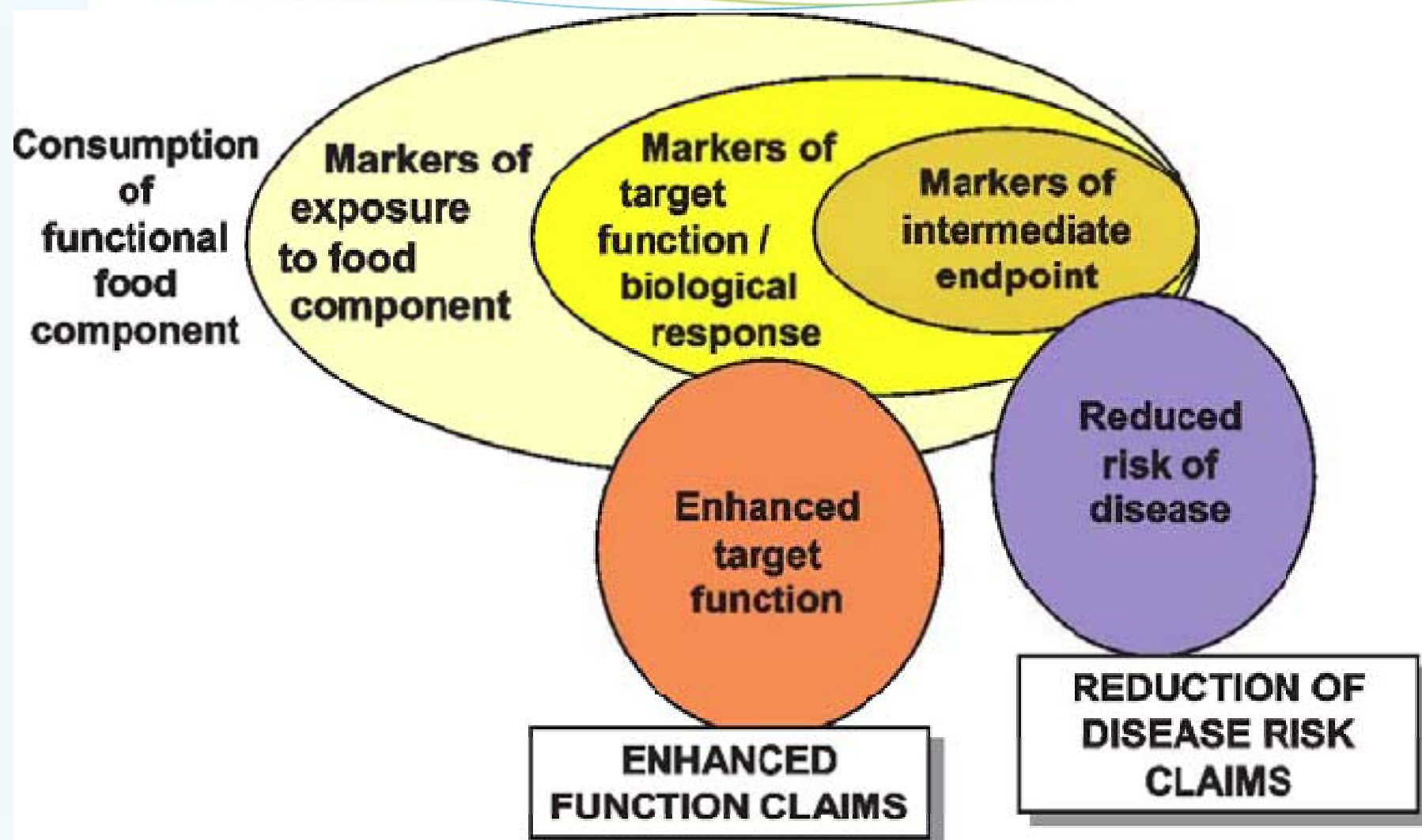
Physical performance	Muscle glycogen, endurance time trial
Gut function	GI hormones, e.g. CCK; physical/chemical parameters, e.g. viscosity; biological responses, physiological responses, e.g. transit time
Immune function	Whole-body measures, e.g. delayed hyperactivity, vaccine response
Appetite control	Reduction in food intake, reduction in energy intake, hunger rating profiles
Cognitive function	No conceptual framework – need for markers that represent complexity of real-world decision making
Atherosclerosis	Blood pressure, LDL cholesterol, HDL cholesterol, intima-media thickness
Obesity	BMI, measures of fatness
Diabetes	Glucose tolerance, fasting blood glucose, insulin levels
Cancer	Recurrence of colon polyps, aberrant crypt foci
Bone health	Bone density, calcium kinetics

Abbreviations: GI, gastrointestinal; CCK, cholecystokinin; LDL, low-density lipoprotein; HDL, high-density lipoprotein; BMI, body mass index.

Conclusions from Fufuse

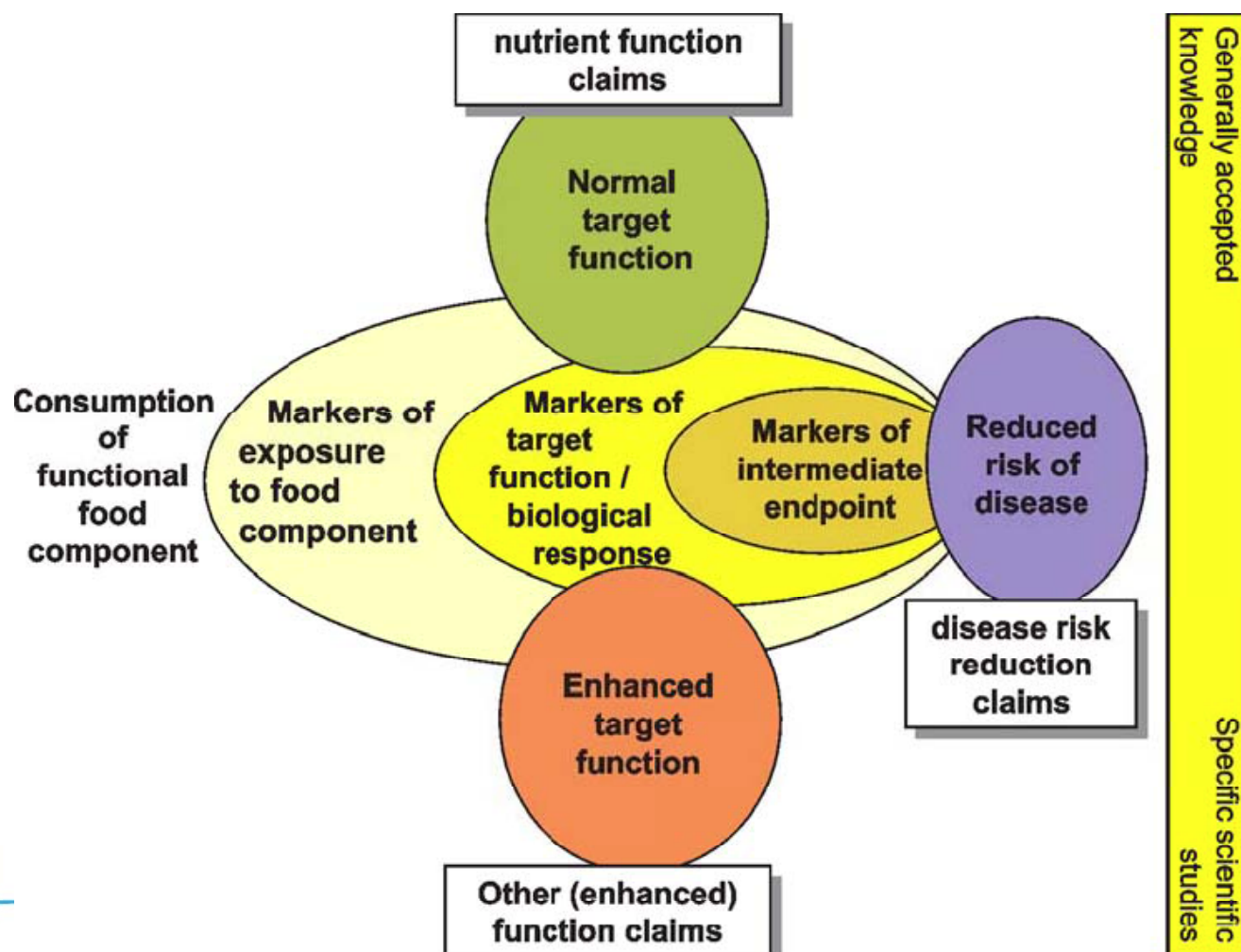
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- They are providing benefits beyond usual nutrition.
- There are examples of foods/nutrients with functional benefits
- Markers are KEY elements to demonstrate a benefit
 - Exposure, Function, Intermediate end-point
 - Indicators or Factors.
- Evidence from human studies are THE scientific basis.

Functional claims are possible !





- Eur J Nutr (2005) [Suppl 1] 44 : I/1–I/2: Consensus on Criteria





European Journal of Nutrition

Eur. J. Nutr. 2003; 42 (sup.1):3 - 119

Phase one: preparing the way. N.g. Asp et al.

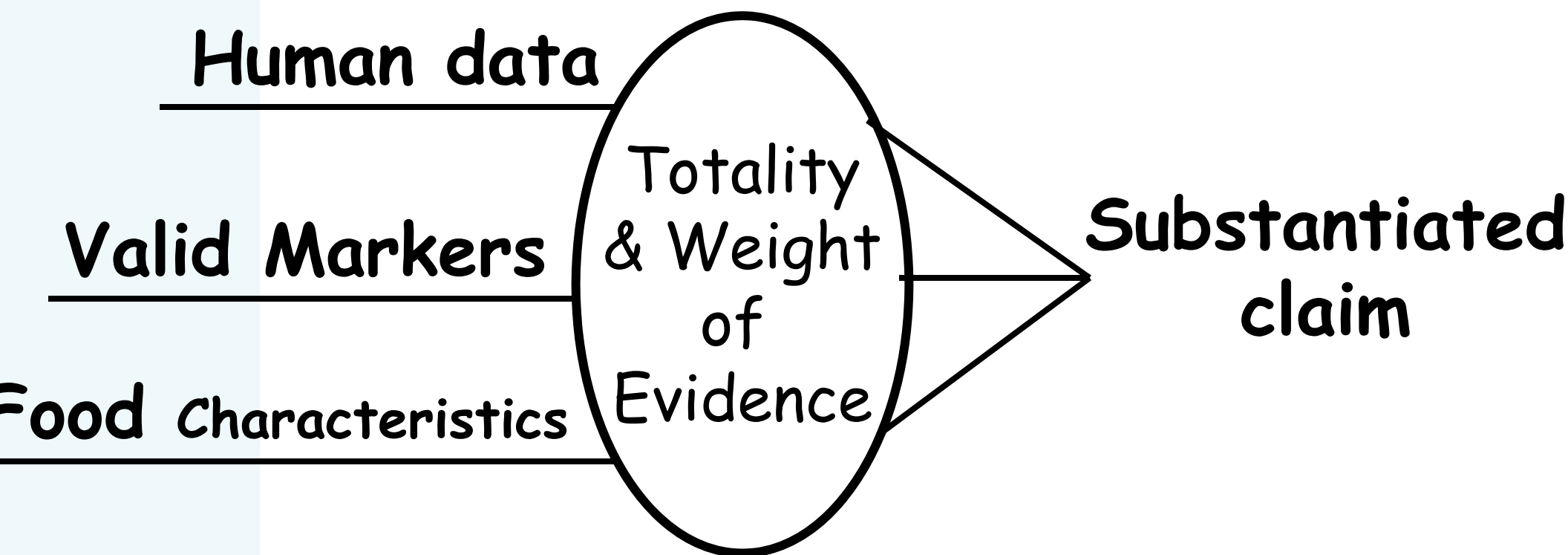
Eur. J. Nutr. 2004; 43 (sup.2):3 - 183

Phase two: moving forward. N.g. Asp et al.

Eur. J. Nutr. 2005; 44 (sup.1):3 - 30

Consensus on Criteria: P.j. Aggett et al.

PASSCLAIM Summary Scheme



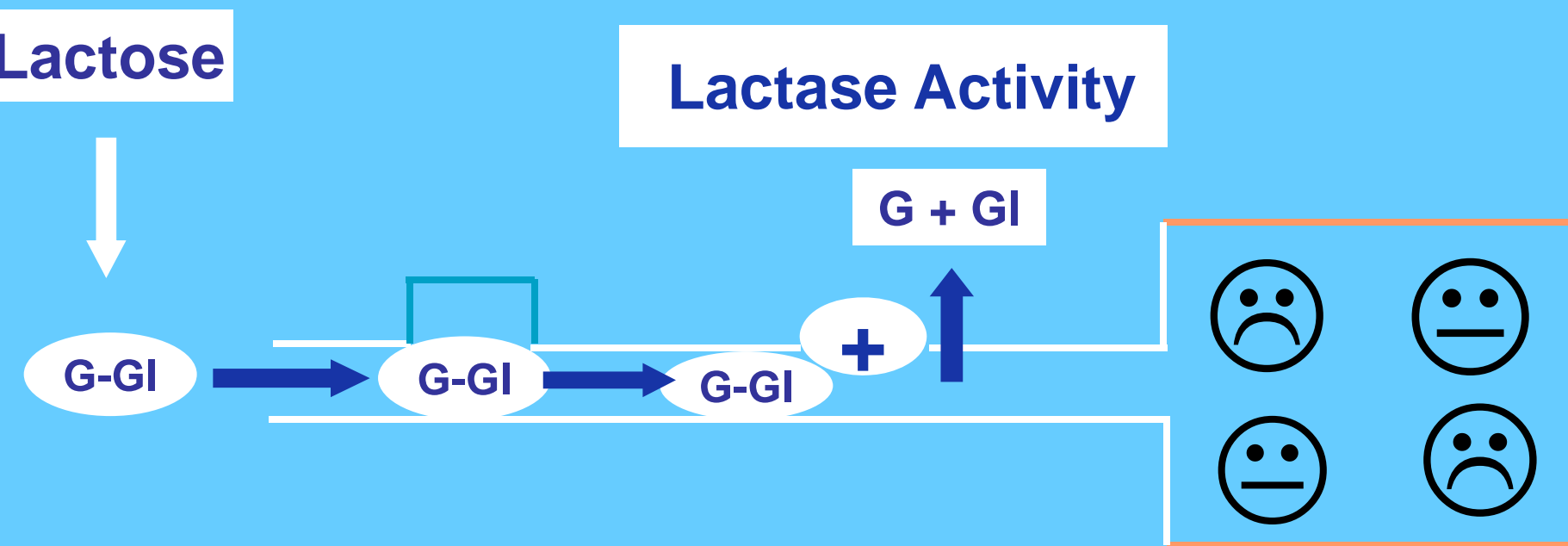
Common Sense Criteria Valid everywhere

- Characterised Food
- Specified claim or benefit
- Validated marker(s)
- Human intervention data
Relevant studies: Product, Subjects
- **Convincing evidence:**
Significant changes
Repetition (Literature, or trials)

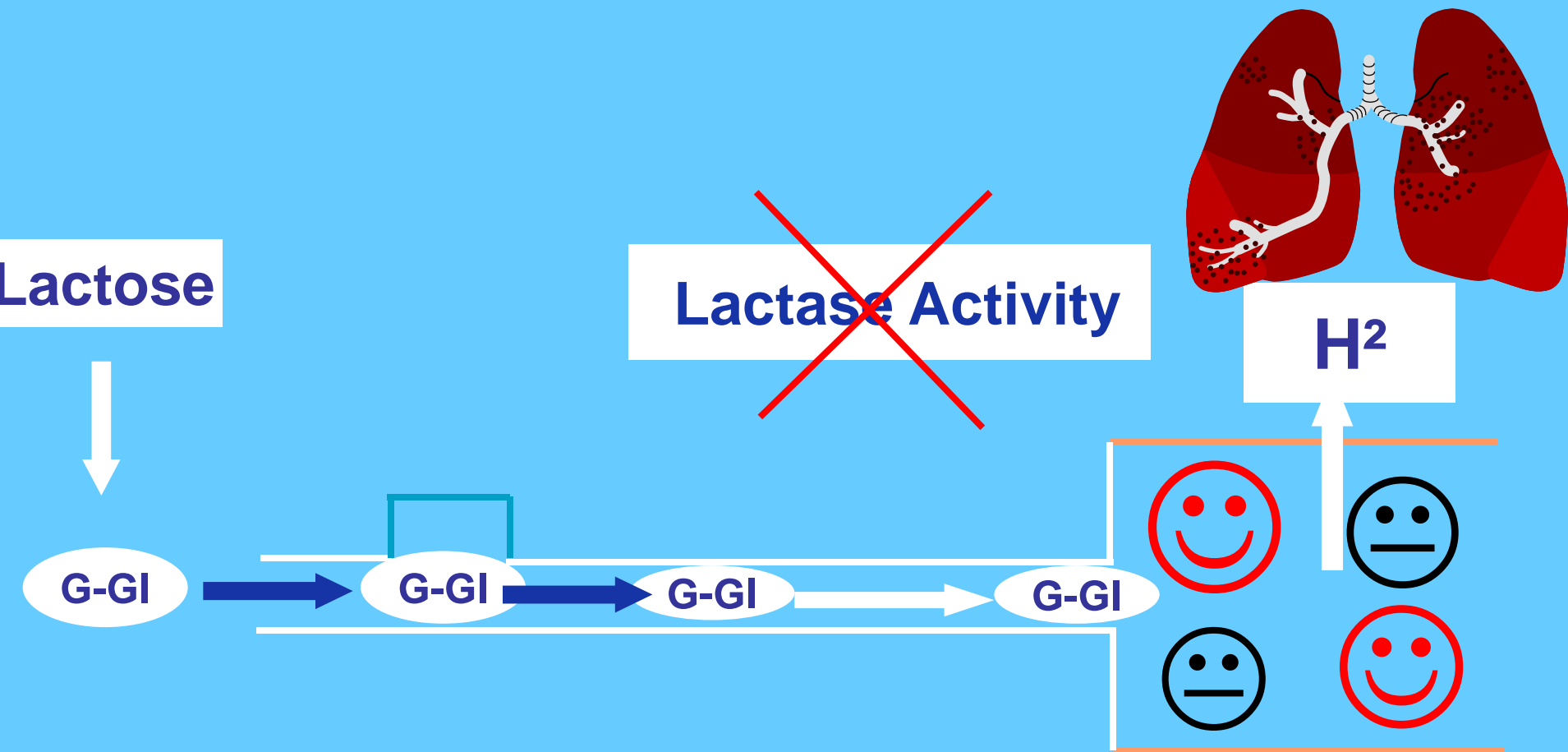
Some probiotics provide enzymatic activities that help digestion of food

- Tradition told us: Yogurt is a dairy food every one can enjoy.
- Science tells us : Yogurt helps lactose malabsorbers to digest lactose.

Lactose digestion assessment



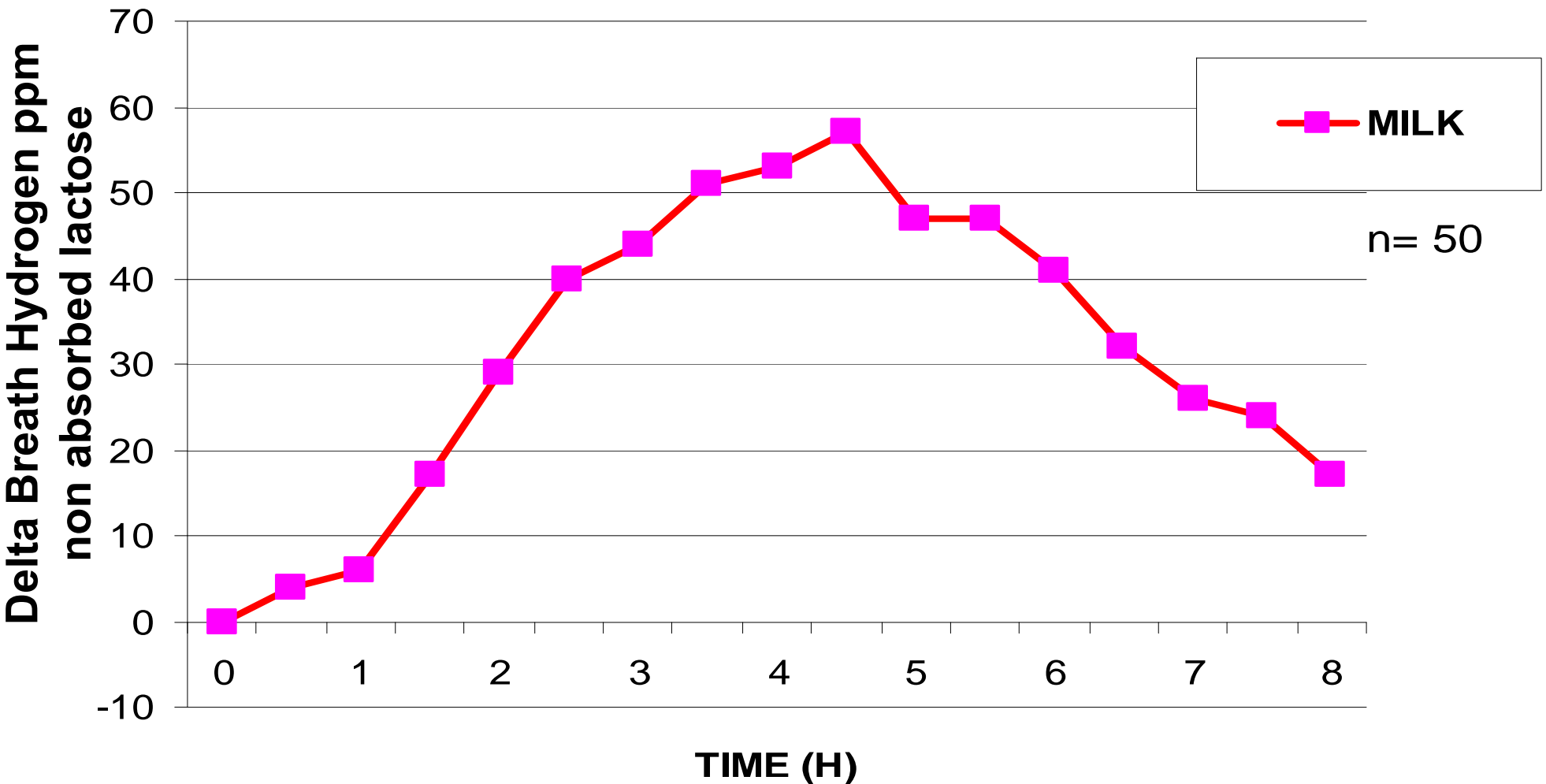
Breath-test methodology



80 % of adults cannot digest lactose
in milk but the northern European

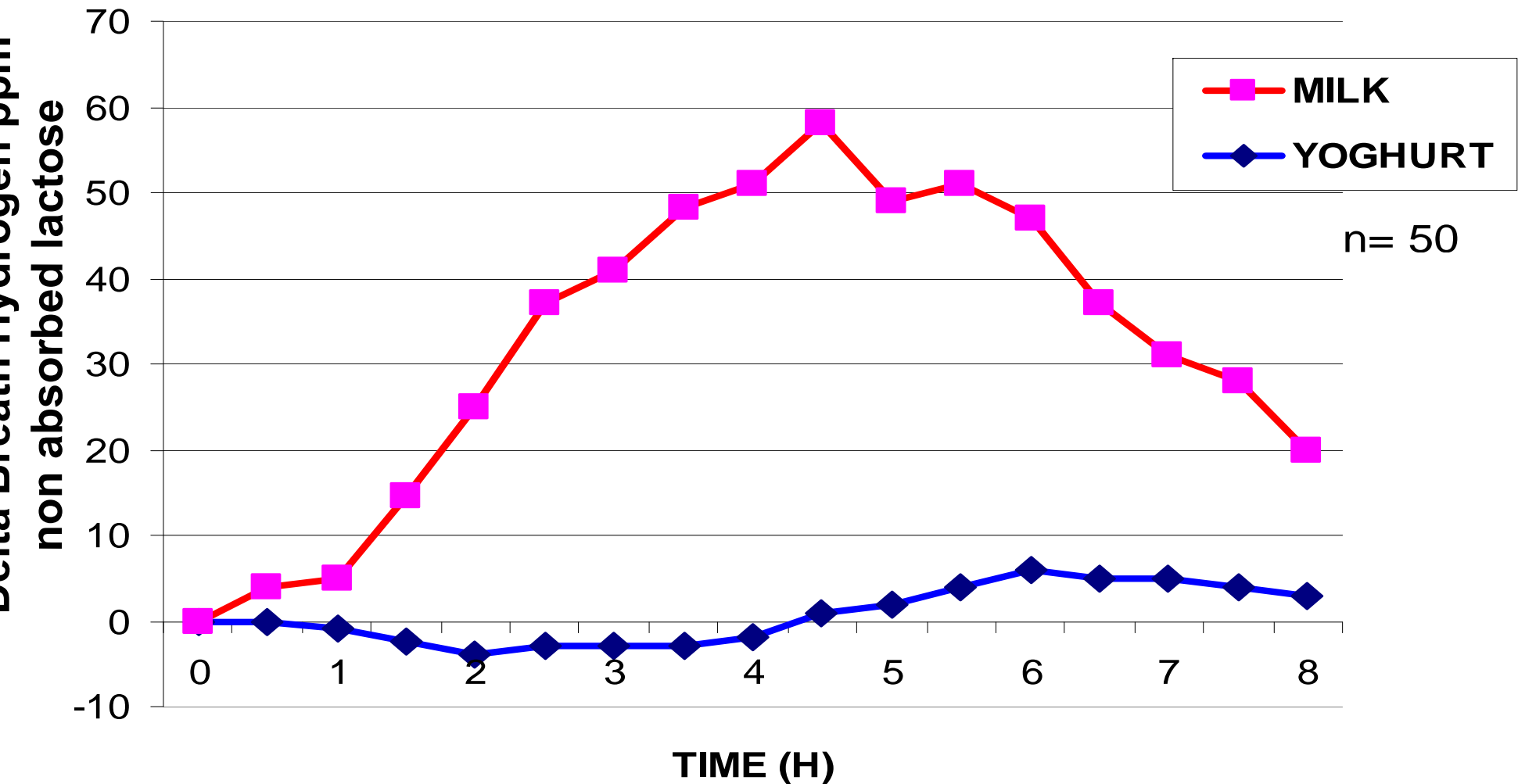
Breath test to assess Lactose digestion

Lactose in milk is not absorbed



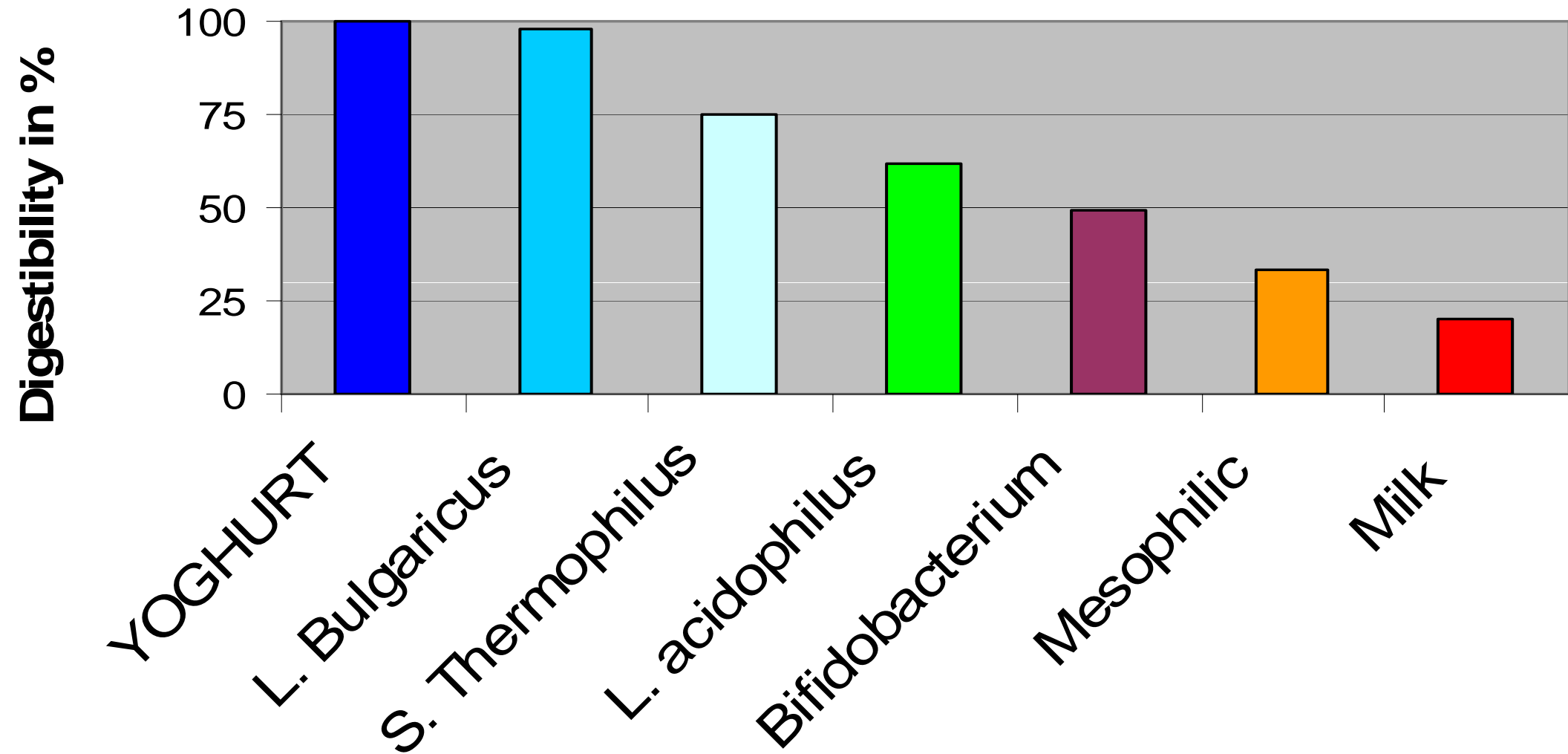
Yoghurt improves lactose absorption

YOGHURT IMPROVED LACTOSE ABSORPTION



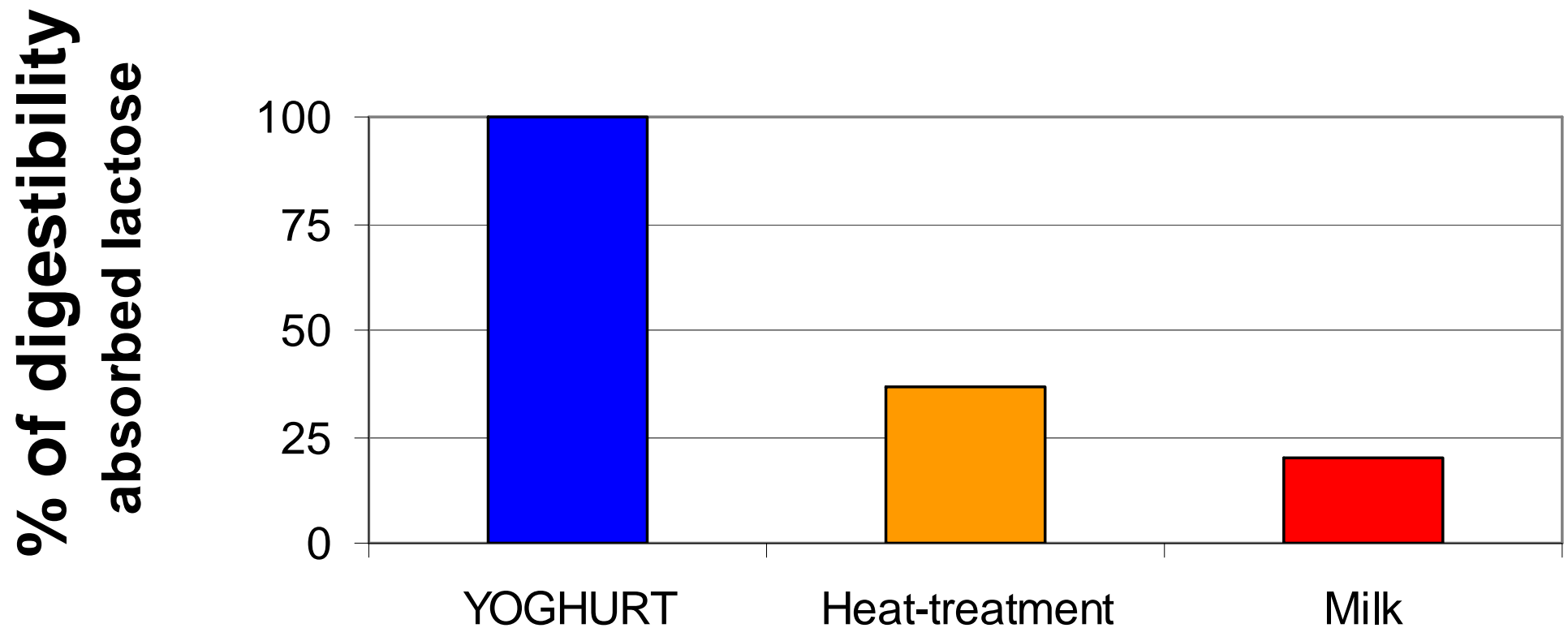
Not all species are equal

Lactose Digestibility



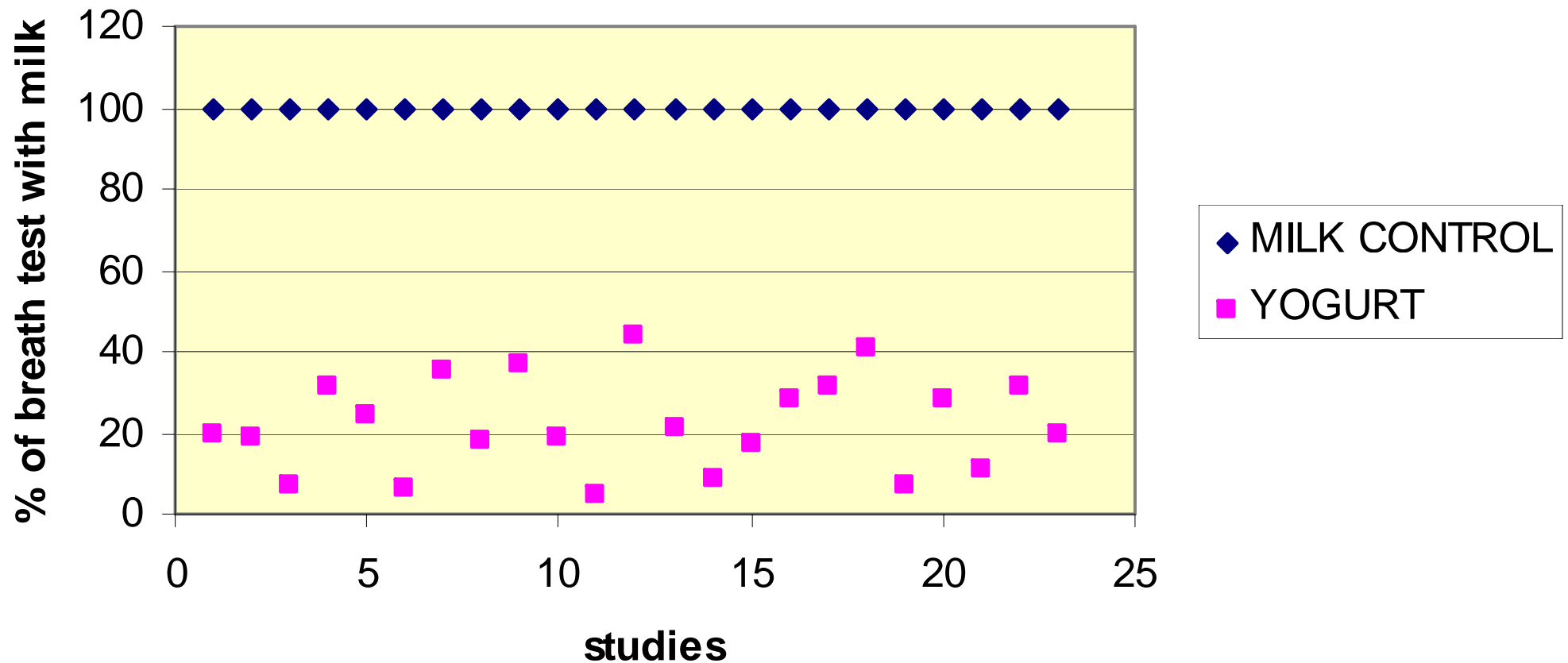
Yoghurt cultures must be **ALIVE**

Killing yogurt cultures (heat)
suppressed lactose digestion benefit



23 published human trial confirmed improvement of lactose digestibility by different yogurts

YOGURTS & LACTOSE DIGESTION



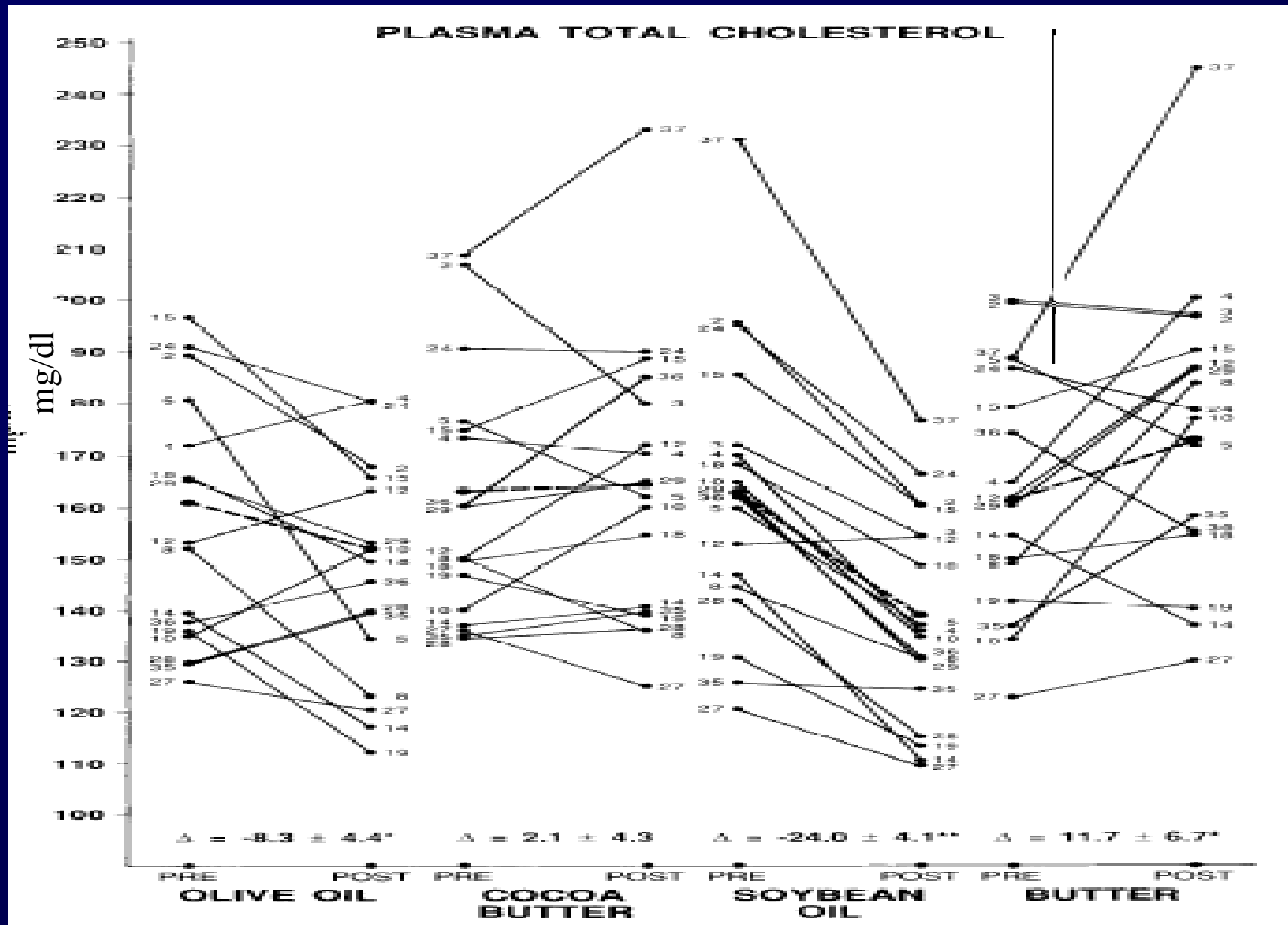
Guidance for Substantiating the Evidence for Beneficial Effects of Probiotics: Impact of Probiotics on Digestive System Metabolism¹⁻³

Sylvie Rabot,⁴ Joseph Rafter,⁵ Ger T. Rijkers,⁶ Bernhard Watzl,⁷ and Jean-Michel Antoine⁸

J Nutr. 2010 Mar;140(3):677S-89S.

We Know the Response to Foods/Components Vary

Variation in the RESPONSE to foods and components is common-place



Kris-Etherton, et al. (1993) Metabolism 42:121-9



Improve slow gastrointestinal transit

Transit time: Time during which a marker pass through the digestive tract .

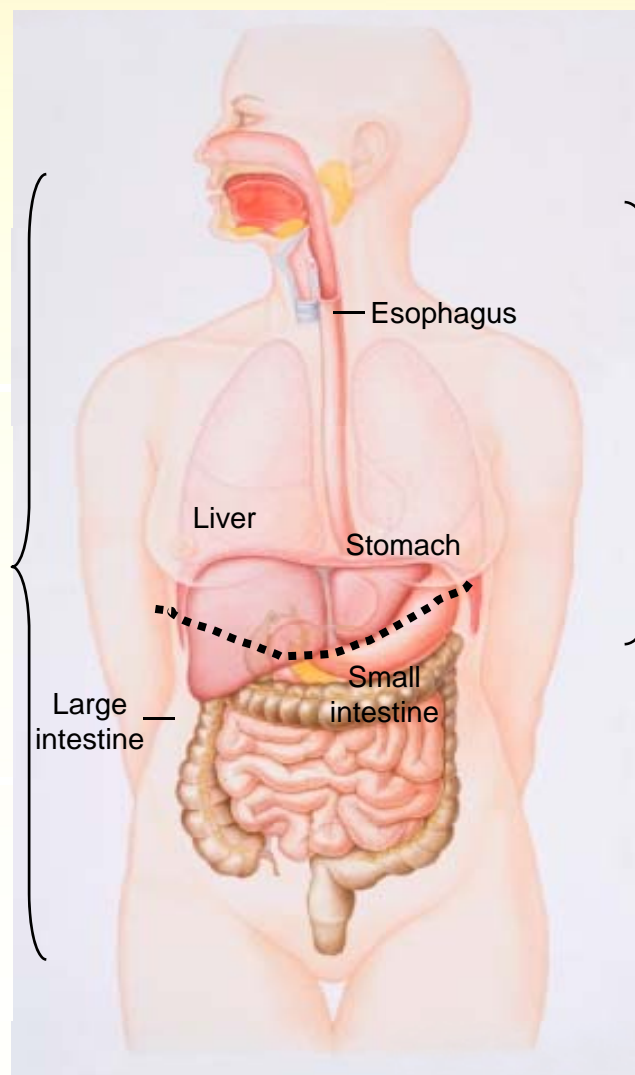
rofeacal TT=whole gut TT

colored marker in stools

éance et al, 2001

éance et al, 2003

shida et al, 2008



Segmental transit

Small bowel TT

Breath test

Agrawal et al., 2009

Colonic TT

Radio-opaque marker (abdominal x-ray)

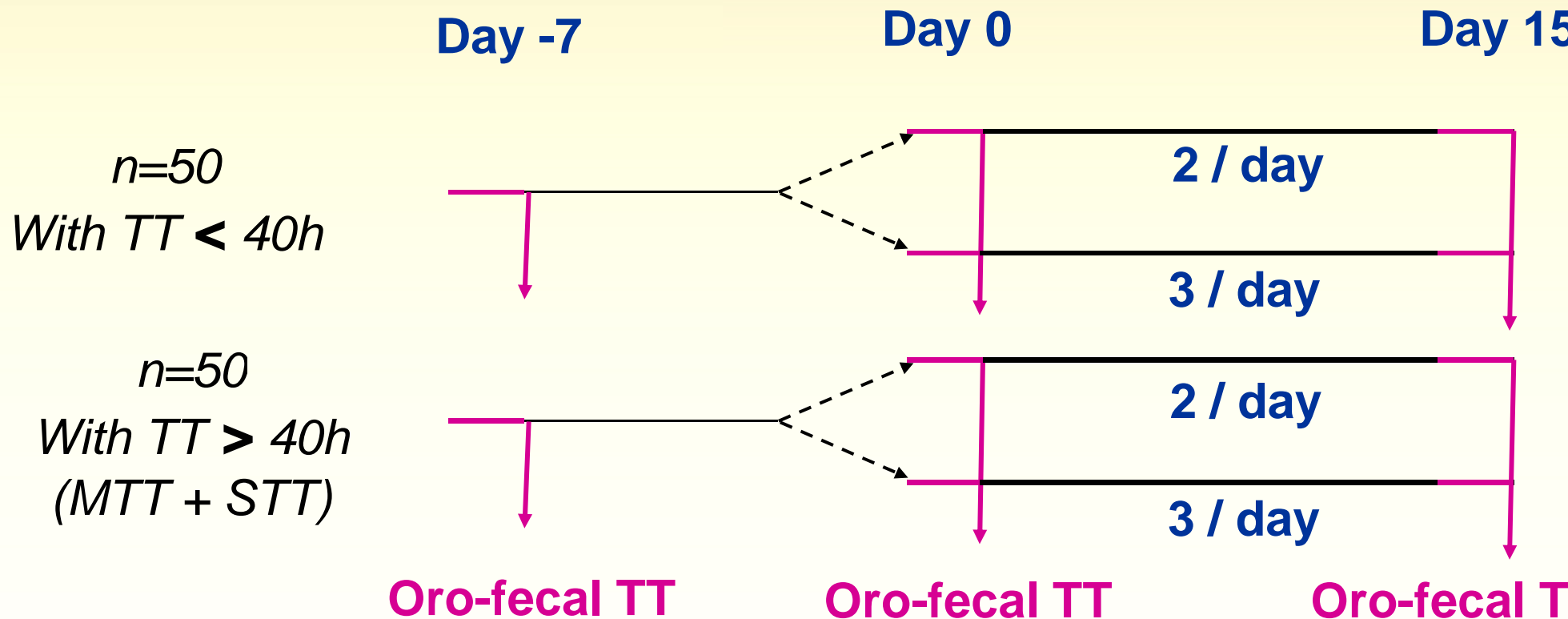
Agrawal et al., 2009

Bouvier et al, 2001

Marteau et al, 2002



Design of gut transit study



n = 100 free living elderly (over 65 years old) eating 2 or 3 serving per day of Activia for 15 days.
Transit time (O-f TT) was measured by coloured markers.



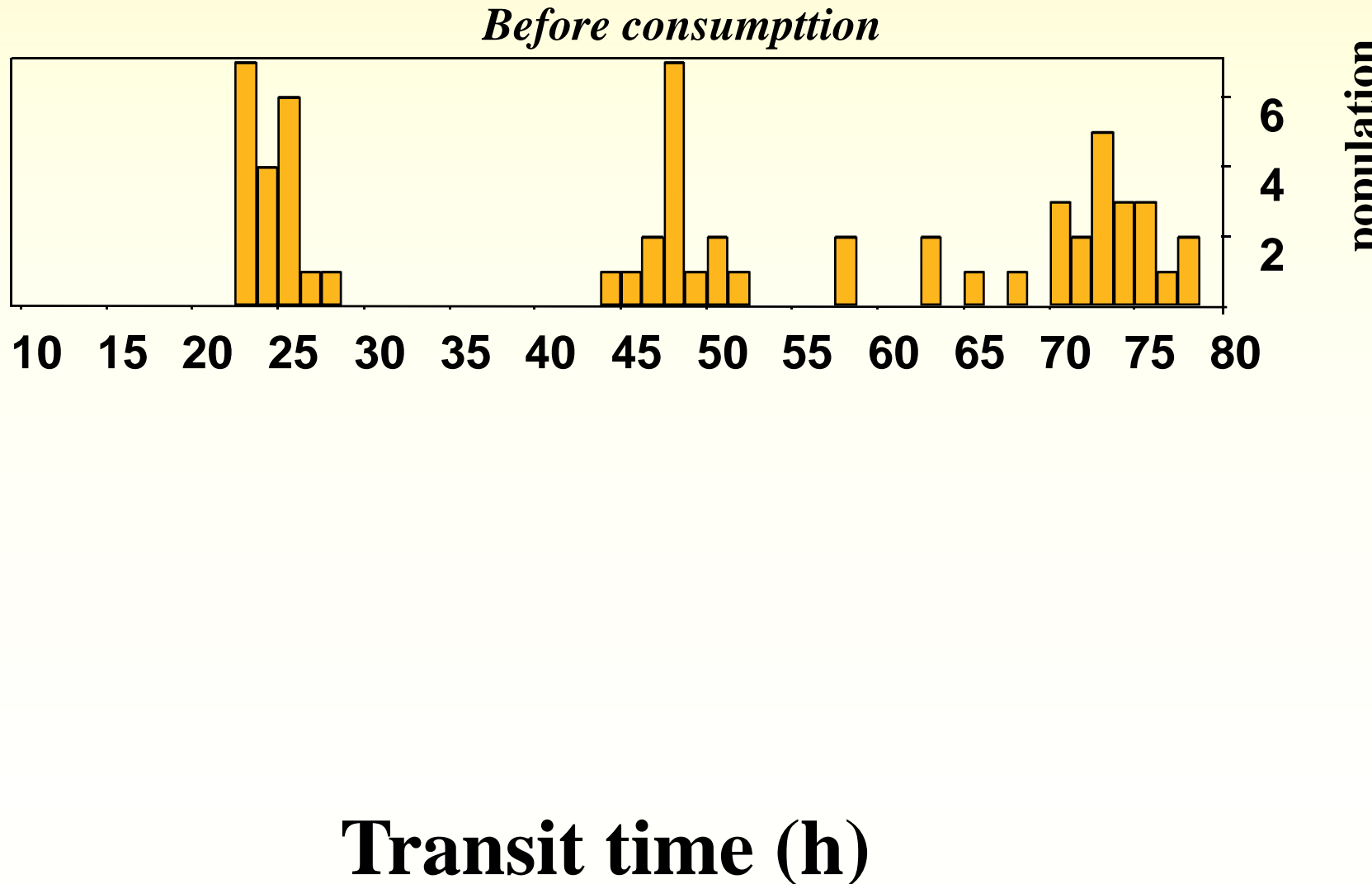
Improves slow transit time

Méance S. et al., Micr. Ecol. Health dis. 2001; 13: 217-222

Volunteers :
Free living
elderly

Products :
Activia (125ml)
per day

Transit Time:
Coloured
markers





Improves slow transit time

Méance S. et al., Micr. Ecol. Health dis. 2001; 13: 217-222

Volunteers :

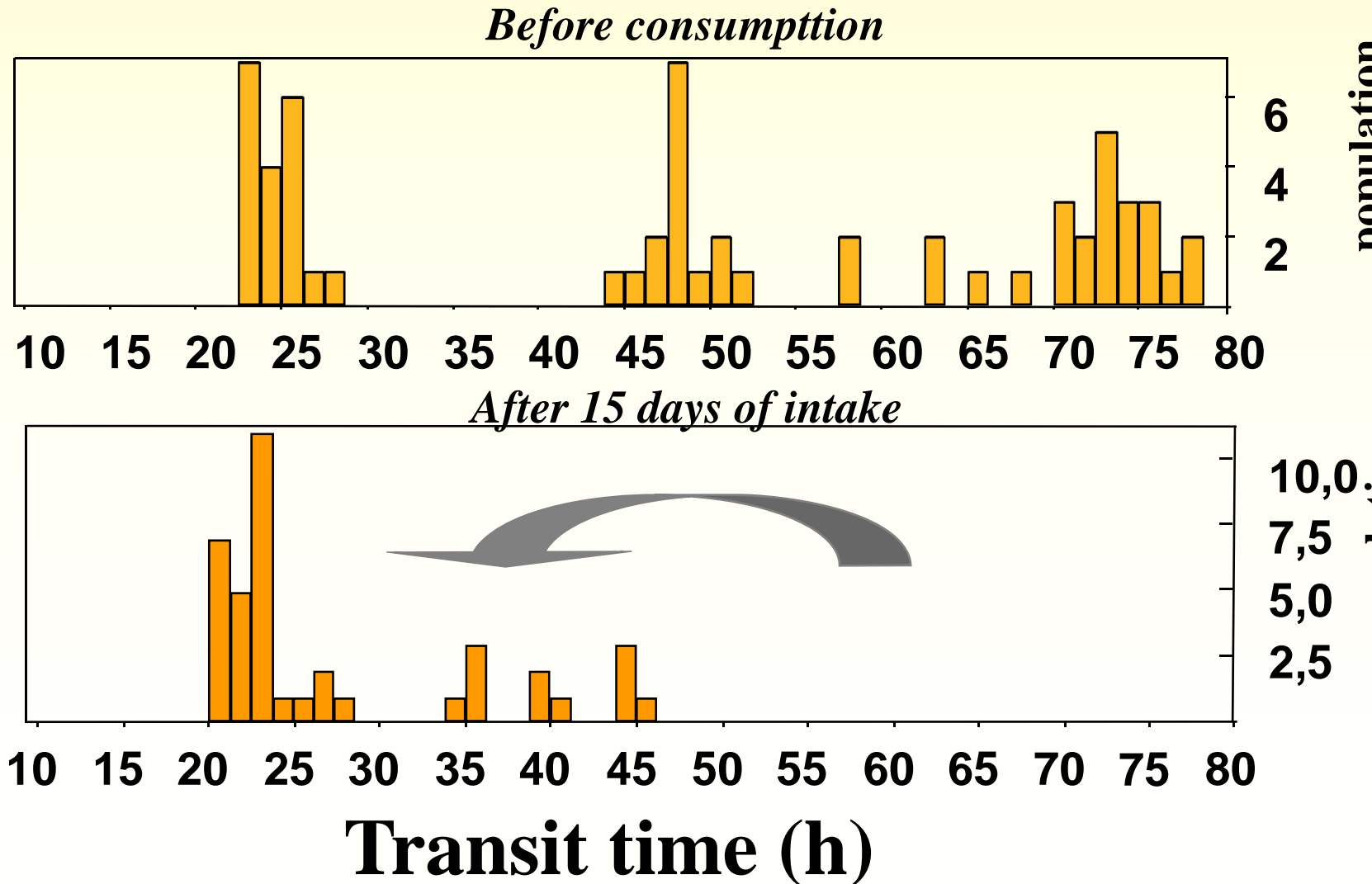
Free living elderly

Products :

Activia (125ml) per day

Transit Time:

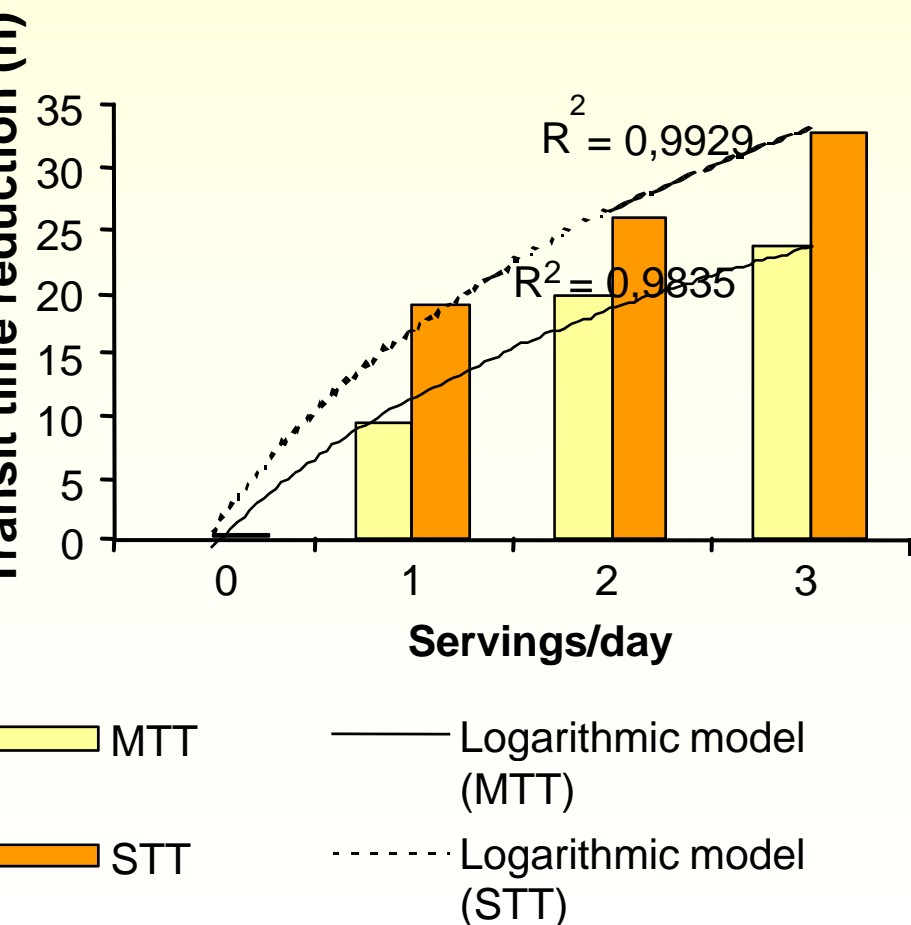
Coloured markers



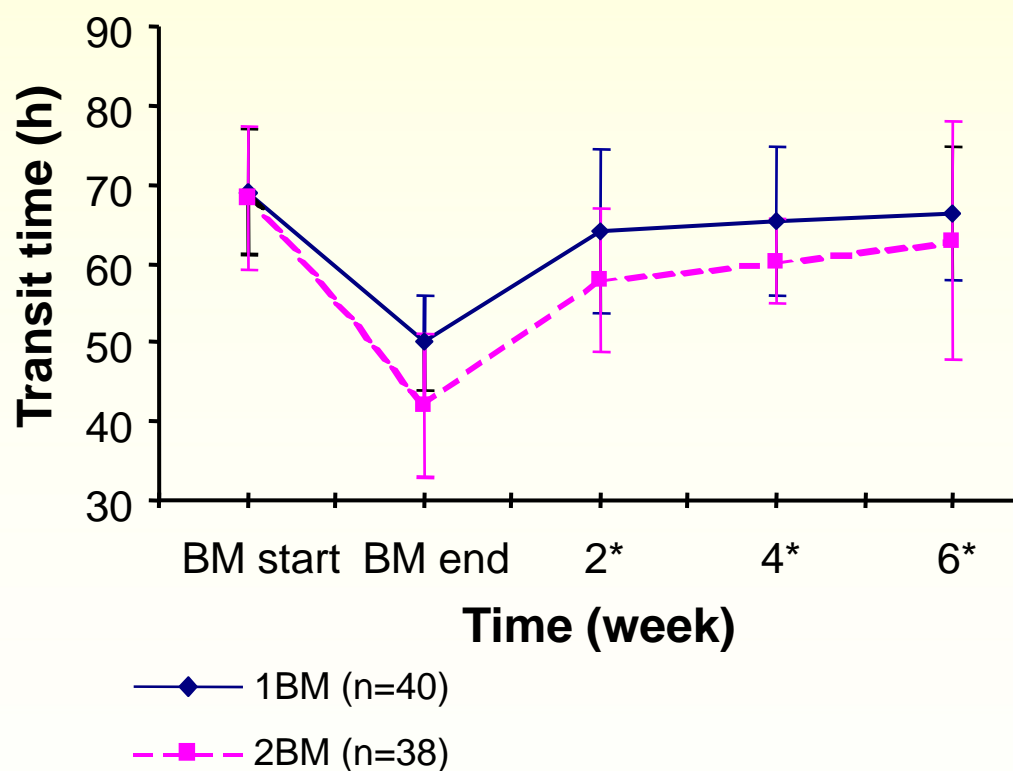


Scientific demonstration

Dose-effect of Activia on transit (summary of 2 studies)



The effect is long lasting

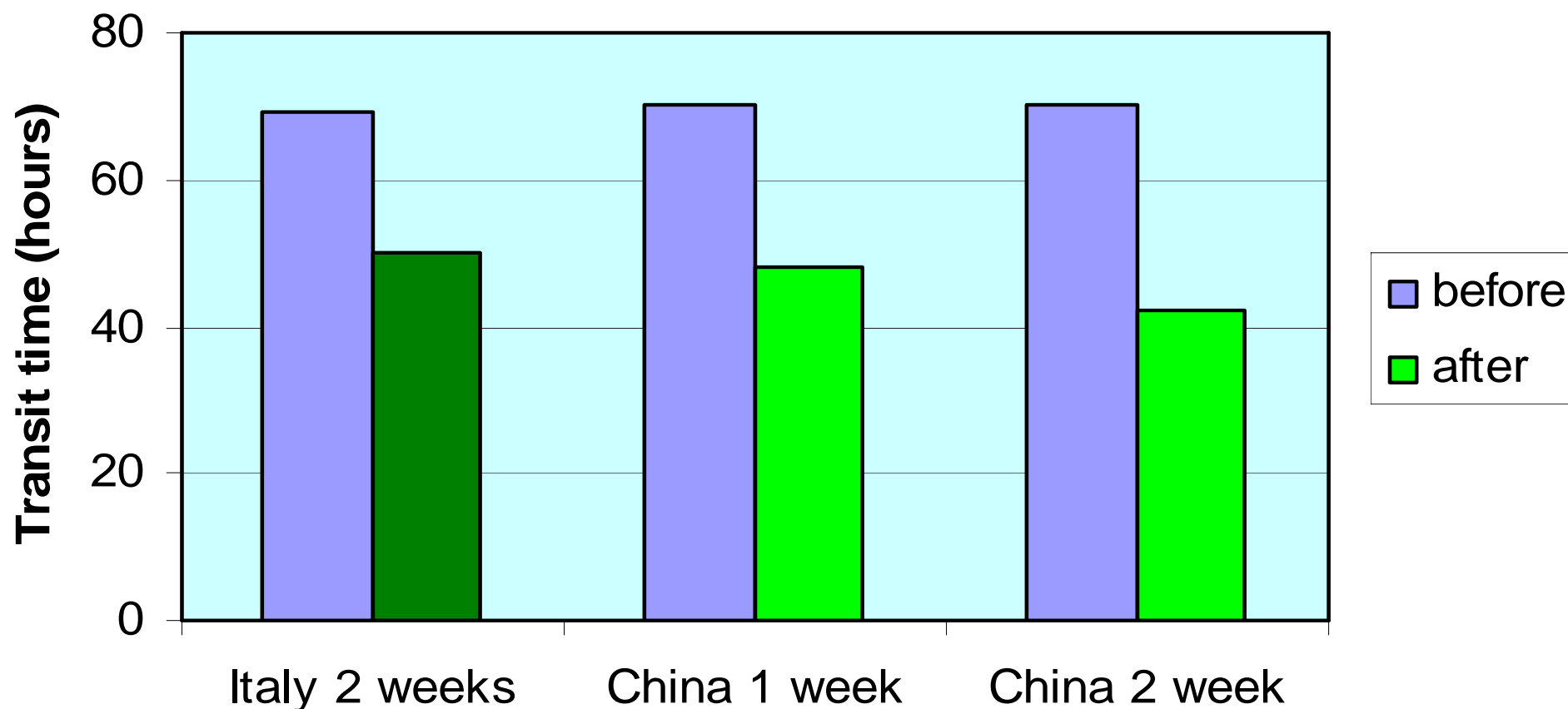


* $p < 0.05$ paired t test for baseline versus follow-up at 2, 4 and 6 weeks



Similar Benefits of Activia on slow transit time in women in Italy and China

Effect of Activia on Gut Transit Time



NORMALISATION OF SLOW TRANSIT TIME:
IS IT A DEMONSTRATED **BENEFIT** ?

Consumers' answer: **YES !**

EXPERTS' ANSWER: no evidence !

Karl Popper principle:



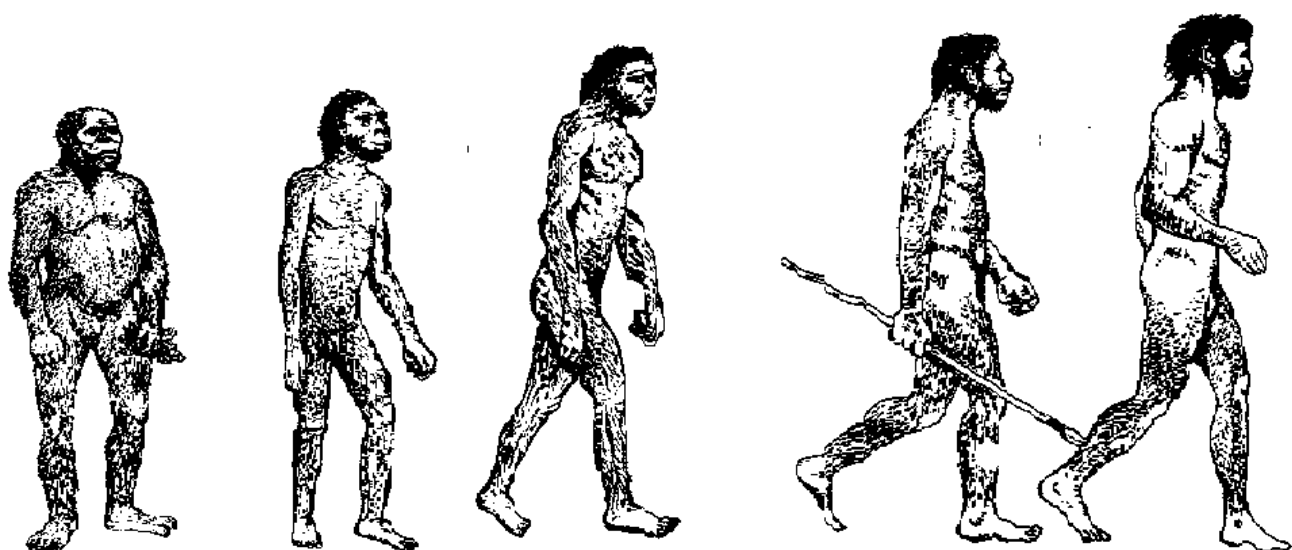
A theory is
"scientific"
only if it is refutable
Scientists are looking for
questions.

They are good at identifying
gaps.
They are not often good gap
assessors,
nor gap managers

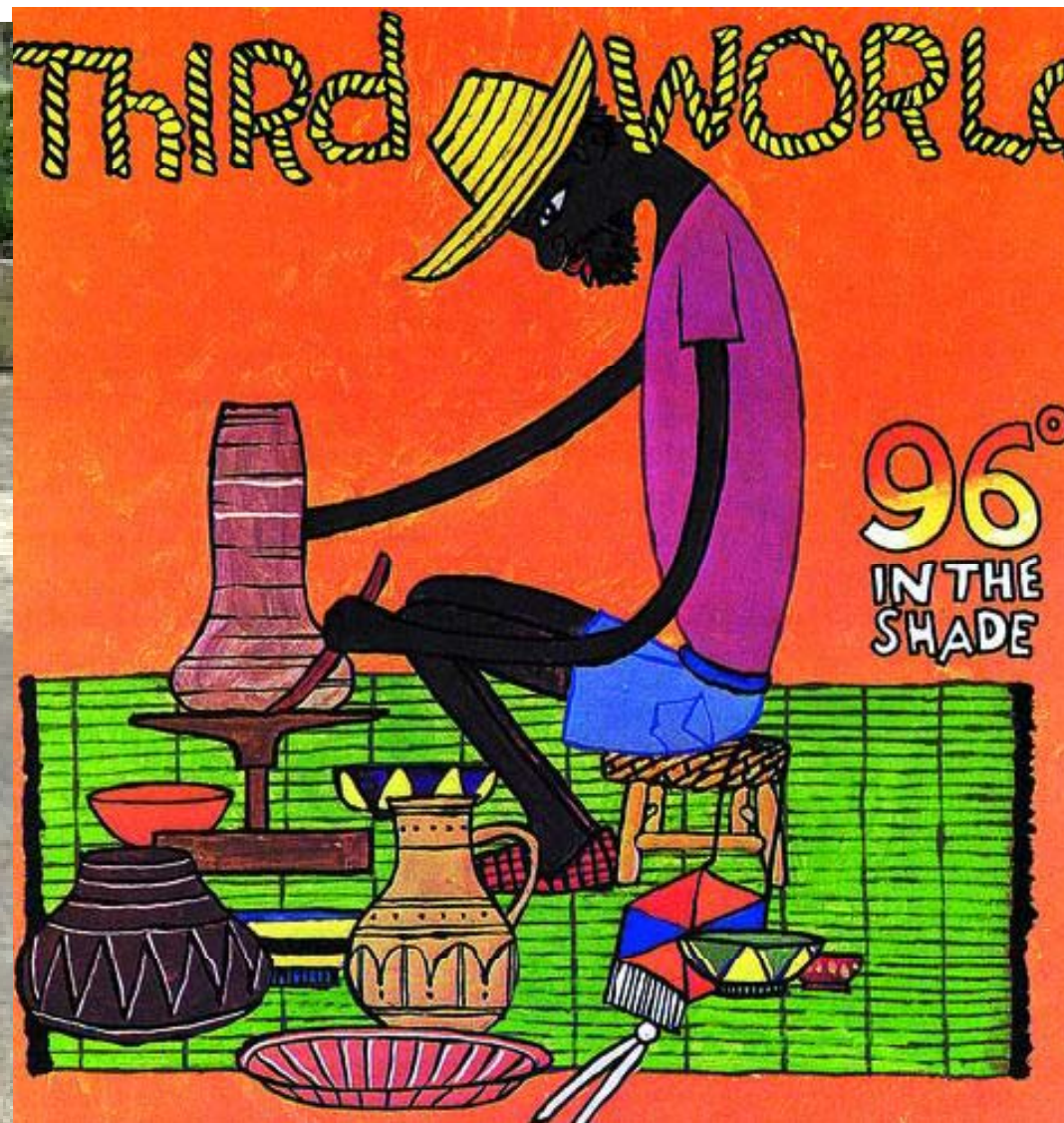
Old challenge were:



Bonhomme 2009



Up-coming challenges are:



DIETARY BENEFITS MUST BE AFFORDABLE

Food is a key partner to improve health.
Improvements are needed

We can benchmark risk management
With risk identification,
risk quantification and
risk management

DIETARY BENEFITS MUST BE AFFORDABLE

- There is a need for a fair assessment
 - of benefit identification,
 - benefit quantification
 - and benefit management

Specially when scientific evidence are accessible to all on the web to everyone.

Convincing & affordable evidence

One clinical
study costs
around TEN
millions
meals of the
average
population



m2

Key-message: Clinical studies in nutrition are specific, and especially the accentuated steps (boxes 1, 2, 5, 7, 9).

Even if clinical studies have the same pattern in pharma and food, the effects to demonstrate are smaller in food and thus more difficult to detect.

maricye, 5/19/2010