Facts and Fads of Lipids

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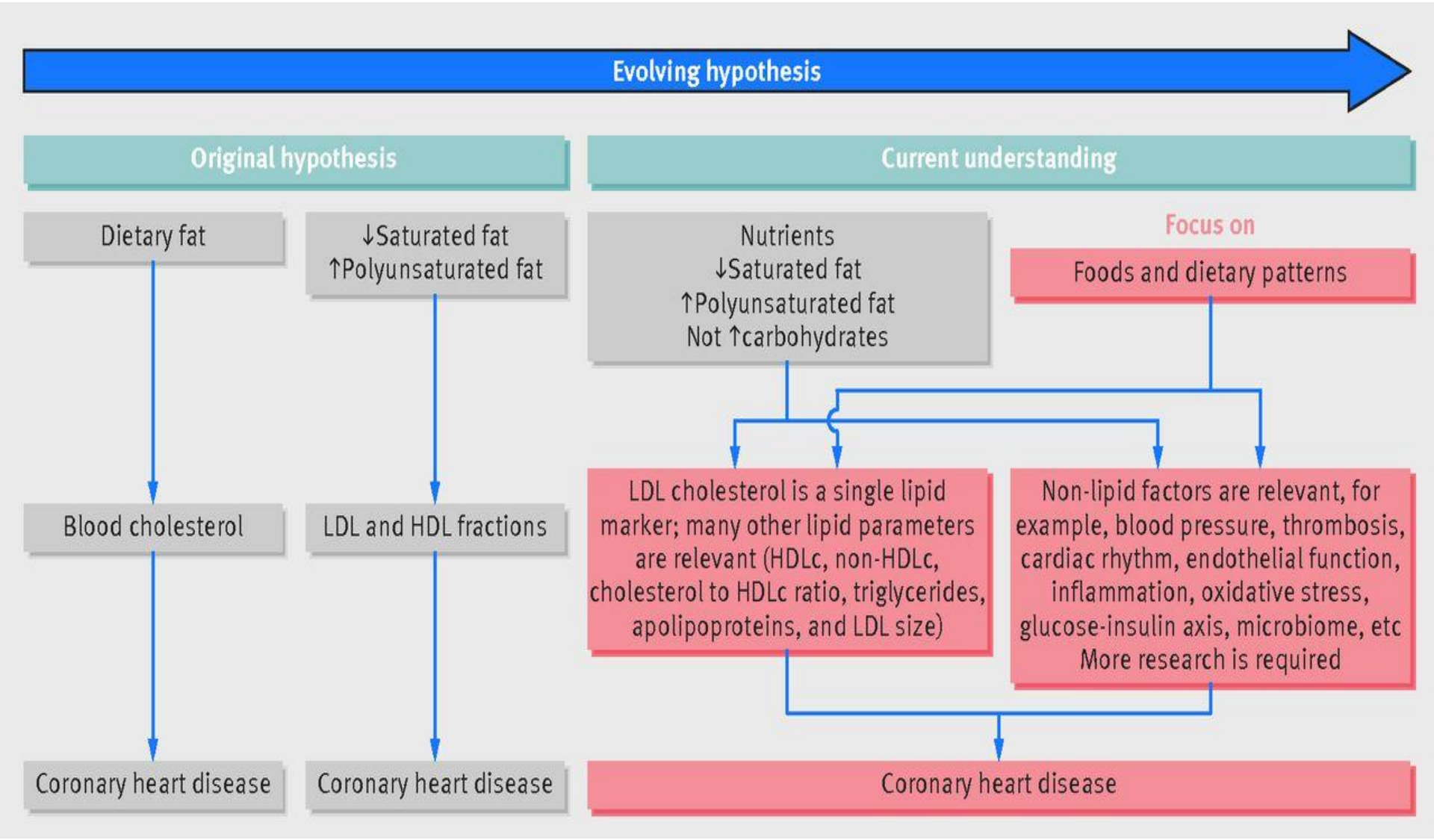
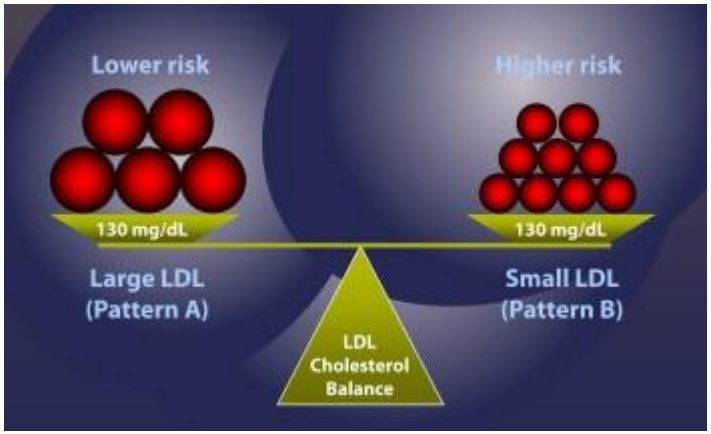
Diet-heart hypothesis and current understanding



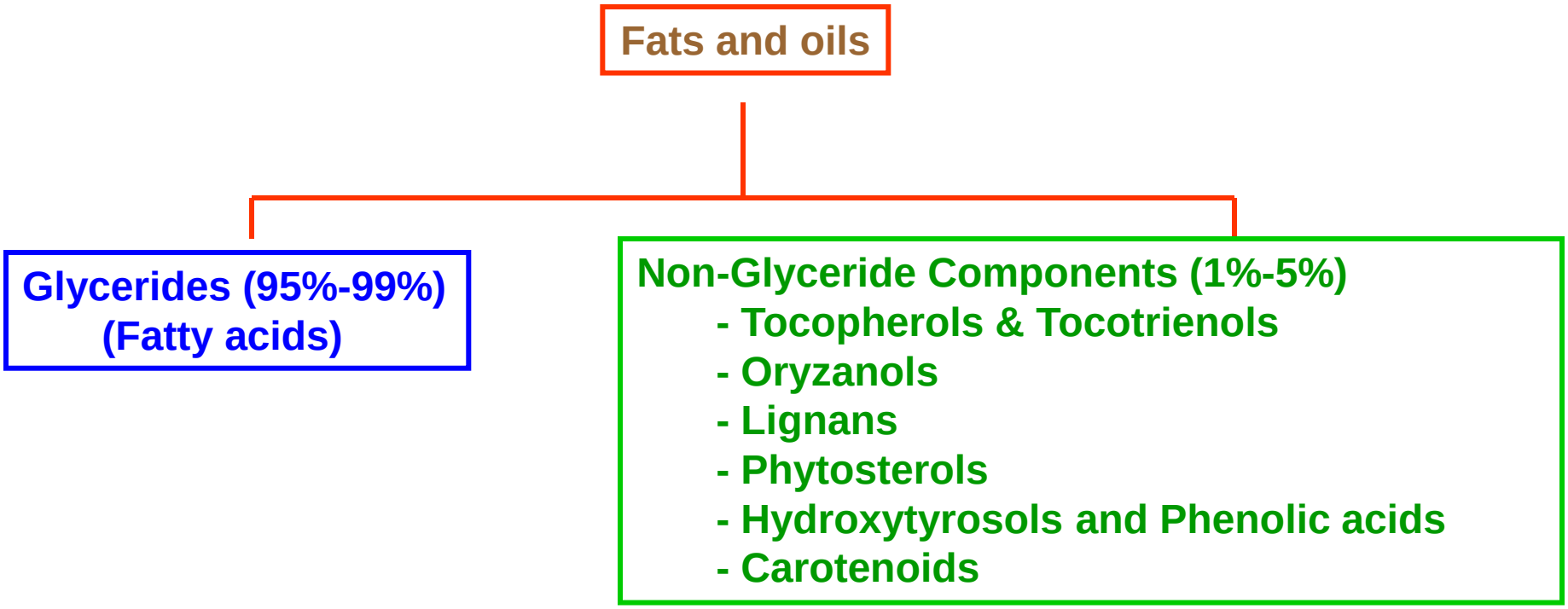
BMJ, 2018

Atherogenic lipoprotein phenotype

- Elevated levels of plasma triglycerides in both fasting and postprandial state
- ↓ HDL & ↑ LDL-B (small, dense LDL)
- Commonly observed in diabetics and those with metabolic syndrome
- Associated with Three fold increase in CHD risk



FATS AND OILS AND THEIR COMPONENTS



Biological effects of Non-glyceride components in vegetable oils

Non-glyceride components	Vegetable oils	Biological effects
Tocopherols	All vegetable oils	Antioxidant
Tocotrienols	Palm & Rice bran	Antioxidant
Phytosterols	All vegetable oils*	Hypocholesterolemic
Carotenes	Red palm	Provitamin A and antioxidant
Oryzanols	Rice bran	Hypocholesterolemic and antioxidant
Sesamin	Sesame	Hypocholesterolemic & Anti-inflammatory
Sesamolin and sesamol	Sesame	Antioxidant
Hydroxytyrosol and Phenolic acids	Olive	Antioxidant

* Rice bran and corn oil are the richest sources

Fatty acids present in fats/oils

- Saturated fatty acids (SFA)
- Monounsaturated fatty acids (MUFA)
  - *cis* MUFA
  - *trans* MUFA[a]
- Polyunsaturated fatty acids (PUFA)
  - n-6 PUFA (linoleic acid)
  - n-3 PUFA (α-linolenic acid[b] , Long chain n-3 PUFA[c])

[a] Present in hydrogenated fat (Vanaspati)

[b] Present in vegetable oils such as soyabean, mustard, canola, linseed oils

[c] Active form of n-3 PUFA present in fish and fish oil

Fatty acid composition of cooking oils

SFA rich oils

- Coconut oil (~ 90%)
- Palm oil (~ 48 %)
- Ghee (~ 65 %)

MUFA rich oils

- Olive oil (~ 70%)
- Groundnut oil (~ 50%)
- Rice bran oil (43%)
- Palm oil (~ 40 %)
- Sesame oil (~ 41%)

PUFA rich oils

n-6 PUFA :

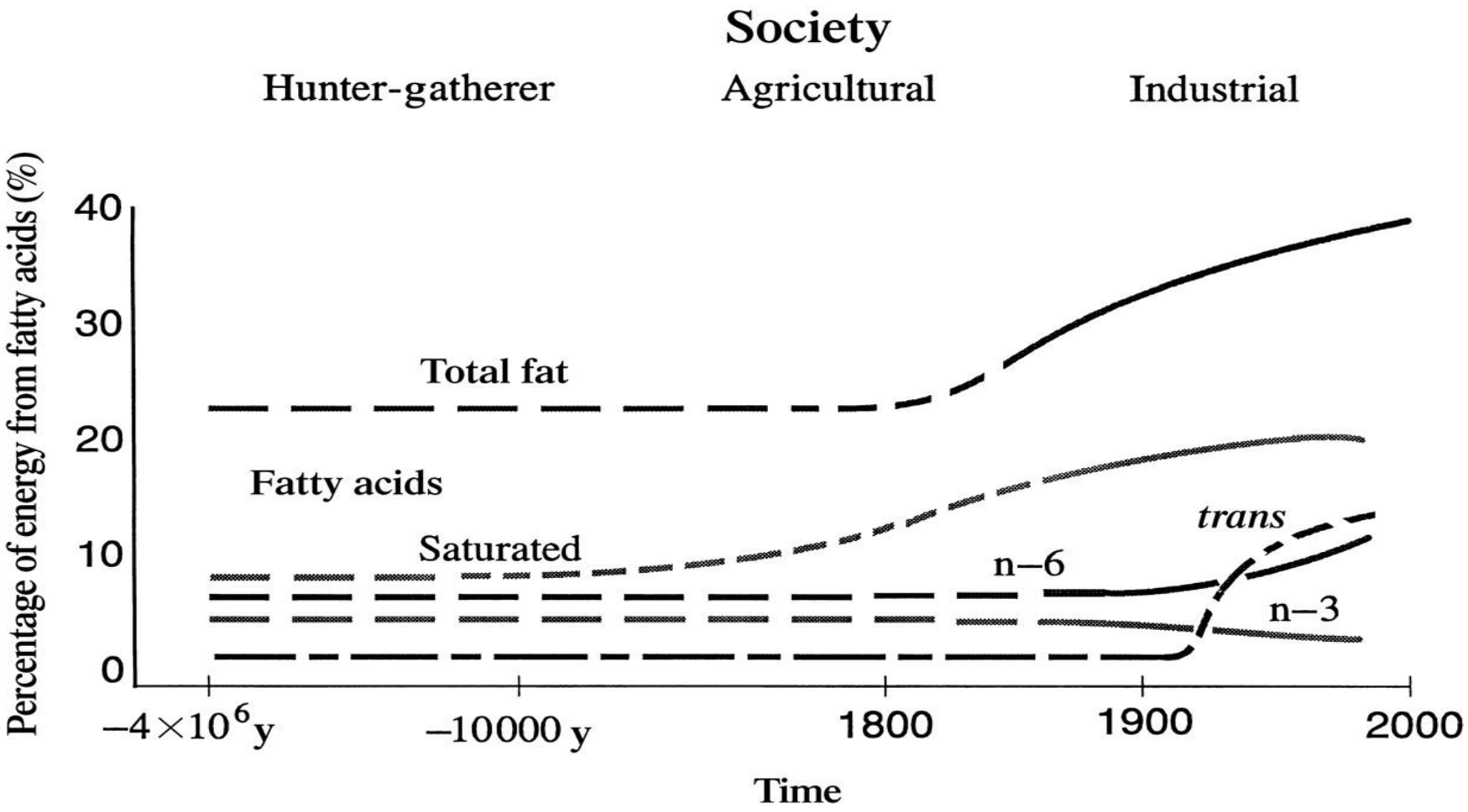
- Safflower oil (~ 75%)
- Sunflower oil (~ 60%)
- Corn oil (~ 55%)

n-3 PUFA:

- Mustard oil[a] (~14%)
- Soy bean oil[a] (~7%)
- Canola oil[a] (~10%)
- Linseed oil[a] (~ 55%)

[a] Present in the form of α-linolenic acid (ALA)

Changes in dietary fat intake



World Rev Nutr Diet, 2001

Dietary intervention trials on coronary events

Trial	Subject	Dietary Intervention	Duration years	Change in CHD [a]
DART	1015 MI patients, males	↓ Total fat	2	- 9%
Finnish mental Hospital	676 males	saturated → unsaturated	6	- 43%
Los Angels Veteran	426 males	,,	8	- 31%
Oslo Diet Heart Study	206 MI patients, males	,,	5	- 25%
MRC Soy oil	199 MI patients, males	,,	4	- 12%
Lyon Diet Heart Study	302 MI patients, males	Mediterranean diet	2	- 73%

[a] change in CHD refers to the percentage difference in coronary event rates in the treatment compared to control group

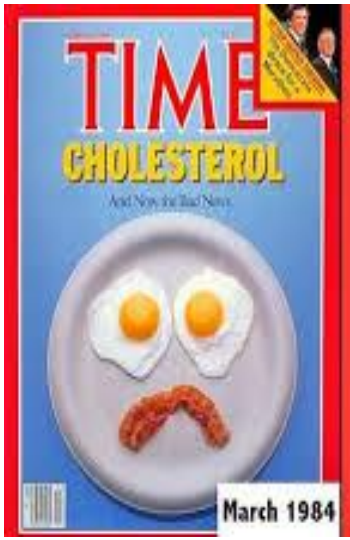
J Am Coll Nutr, 2001

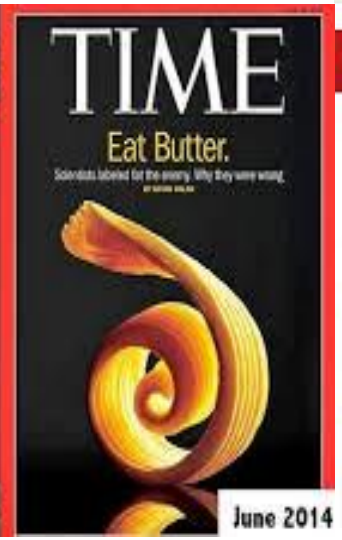
Saturated fatty acids and CHD risk

- High intake of SFA increase CHD risk
- Replacement of 5% of energy from saturated fat by unsaturated fat reduce CHD risk by 42%
- SFA increase plasma cholesterol by impairing LDL cholesterol uptake by liver
- Type of saturated fatty acids has different effect on lipoprotein metabolism
  - Lauric (C12:0), Myristic (C14:0) and Palmitic acids (C16:0) increase plasma cholesterol
  - Stearic acid (C18:0) - no effect (stearic acid can be metabolized to oleic acid (C18:1) by SCD-1)
- Hypercholesterolemic effects of SFA depends on PUFA content of the diet

Ann Rev Nutr, 2017

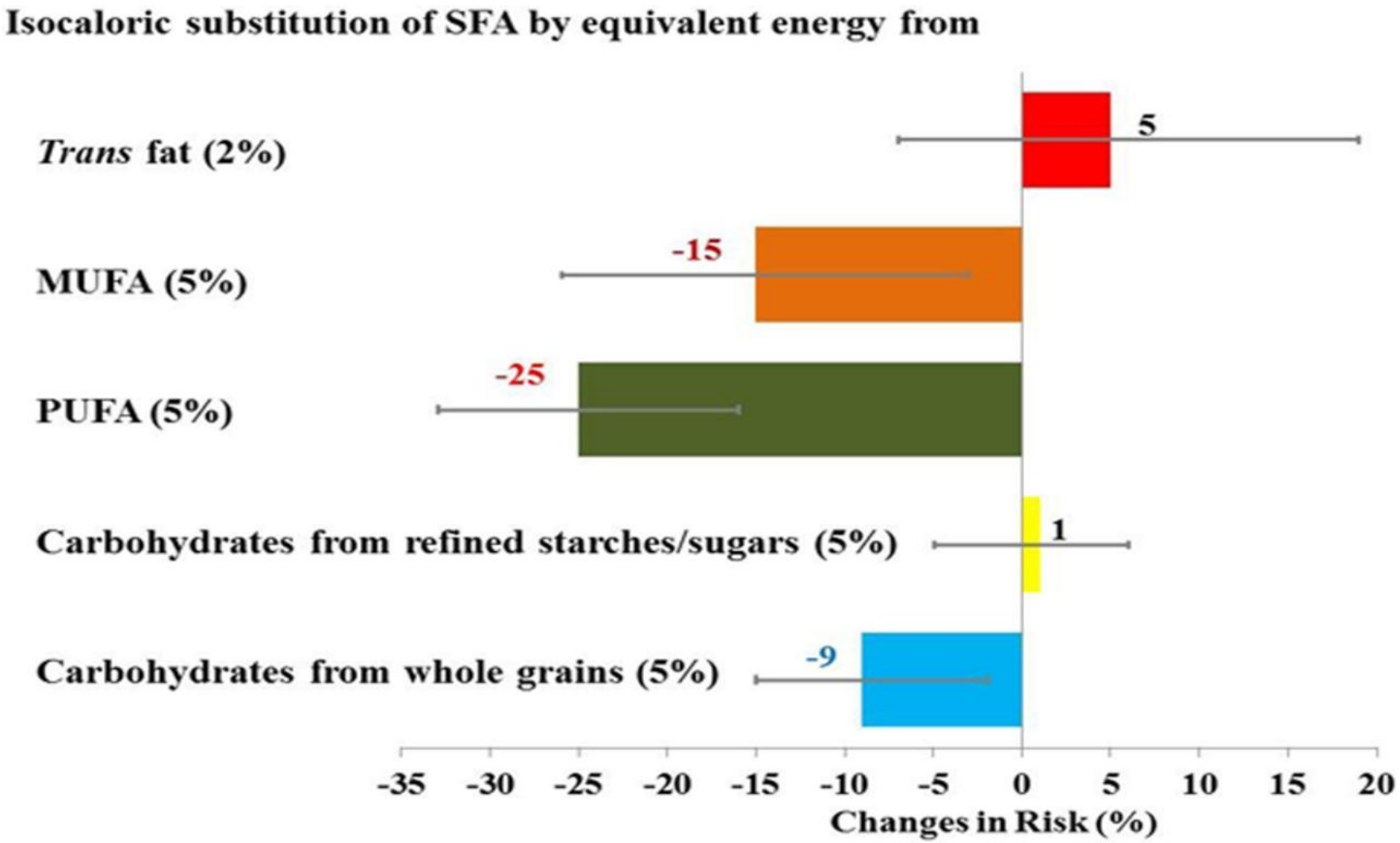
Is saturated fat good or bad?





- **Several, but not all prospective epidemiological studies have not shown a relation between saturated fat intake and CHD risk**

Health effects of saturated fat depends on which macronutrient it is replaced



J Am Coll Cardiol, 2015

Dairy products, saturated fats and CHD risk

- **Dairy products are the major sources of saturated fats (50-60% of fatty acids are saturated fats).**
- **Prospective cohort studies showed inconsistent results regarding the association between dairy products consumption and CHD risk irrespective of fat contents.**
- **Recent cohort study showed that replacement of animal fats including dairy fat with PUFA reduce CHD risk.**
- **Consumption of fermented dairy products, specifically cheese is associated with reduced CHD risk**
- **Current dietary recommendations suggest to consume low fat dairy products.**

Curr Nutr Rep, 2018

Nutrient dense foods that also contain substantial amounts of saturated fats

Food	Nutrients	Evidence linking food to CVD and diabetes
Eggs	High quality protein, Vitamin D, Riboflavin, Lutein, zeaxanthin and choline.	➢ RCT showed two eggs/d has beneficial effects on CVD and improved glycemic control in type 2 diabetes
Dark Chocolate	Stearic acid major SFA. Rich in iron, magnesium, potassium, phosphorus, zinc, selenium and fibre. Contains polyphenols, flavinols and catachins.	➢ RCT showed beneficial effects on CVD biomarkers (HDL, LDL, BP). ➢ Meta-analysis of observational studies showed reduction in CVD risk
Cheese	Full fat cheese is high in medium and long chain SFA. Also contain bioactive fatty acids (conjugated linolenic acid, phytanic acid, *trans* palmitoleic acid), protein, calcium, magnesium and lactic acid bacteria (produce short chain fatty acids)	➢ Meta-analysis of observational studies showed cheese intake is associated with reduced risk of CVD. ➢ Mechanistic studies and RCTs showed cheese intake has favorable effects on CVD biomarkers (blood lipids and BP) and these effects cannot be predicted based on SFA and sodium contents.
Meat	High quality protein, bioavailable iron, minerals and vitamins	➢ Meta-analysis of observational studies showed intake of red meat but not processed meat associated with reduced risk of CVD. ➢ Recent meta-analysis of RCTs showed red meat intake of ≥ 0.5 servings/d does not increase CVD risk.

BMJ, 2019

Monounsaturated Fatty Acids & CHD Risk

- Low CHD mortality in Mediterranean population who use olive oil as the primary source of dietary fat (16-29 % of energy from MUFA)
- Reduced postprandial lipaemia (faster clearance of postprandial lipids)
- Greater reduction in fasting triglycerides.
- Reduction in coagulation factors (factor VIIc and factor VIIa).
- Increased fat oxidation rate (greater fat burning and less fat storage)
- Shift from small, dense LDL to large buoyant LDL.

Curr Atheroscler Rep, 2016

Nut consumption and CHD risk

- Beneficial role of nuts consumption in reducing the incidence and mortality of CHD.
- High fat content (~ 80% of the calories comes from fat).
- MUFA is the predominant fatty acids present in most of the nuts.
- High content of vitamin E, fiber, potassium, magnesium and copper.

Fat content of selected nuts (g/100g)

Nuts	Total fat	SFA	MUFA	n-6 PUFA	n-3 PUFA
Almonds	51	4	32	12	-
Walnuts	66	6	9	38	9
Brazil nuts	66	15	24	20	0.1
Pecans	73	6	41	21	1.0
Pistachios	44	5	23	13	0.2
Macadamias	76	12	59	1.3	0.2
Peanuts	49	7	24	16	-

Risk of CHD death by frequency of nut consumption from prospective epidemiological studies

Study	Subjects	Endpoint	Nut consumption	Relative risk (95%CI)
California seventh day Adventist Healthy Study	27,321	CHD	< 1 times/week	1.00
			≥ 5times/week	0.45
Iowa Women's Health Study	41,837	Fatal CHD	never	1.00
			1 time/week	0.70
			4 times/week	0.43
Nurses' Health Study	86,016	Total CHD	never	1.00
			≤ 1 time/week	0.91
			2-4 times/week	0.77
			≥ 5 times/week	0.65
CARE study	3,575	Total CHD	< 1 time/week	1.00
			≥ 2 times/week	0.75

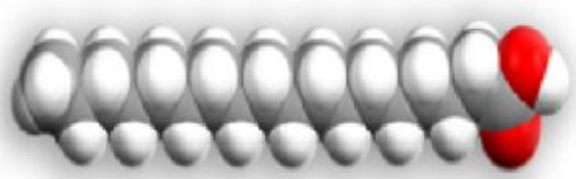
Prog cardiovas Dis, 2018

Trans fatty acids

- **Geometrical isomers of MUFA & PUFA having at least one double bond in *trans* configuration**

Stearic Acid

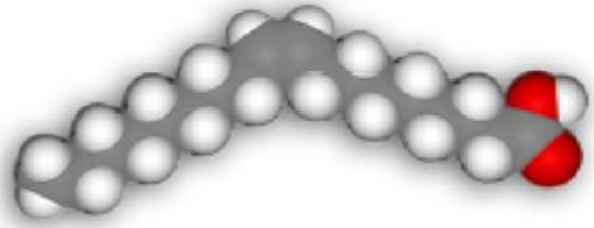
C18:0



Solid: Melting Point = +70°C

Oleic Acid

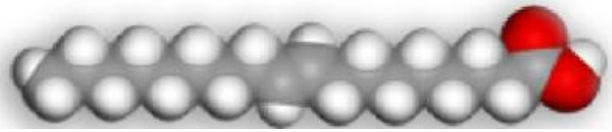
C18:1 *cis*



Liquid: Melting Point = -5°C

Elaidic Acid

C18:1 *trans*



Solid: Melting Point = 42°C

Sources of *trans* fatty acids

Partially hydrogenated vegetable oils

- Industrially produced *trans* fatty acids (*i-TFA*)
- Elaidic acid major isomer
- 10-40%

Ruminant fats

- Naturally occurring *trans* fatty acids (*r-TFA*)
- Vaccinic acid major isomer
- Conjugated linolenic acid
- 2-5%

Trans fat (iTFA) intake and cardiovascular disease risk

- **2en% increase in intake of *trans* fatty acids associated with 23% increase in relative risk of CHD. (*NEJM, 2006*)**

- **Meta analysis showed that the intake of iTFA but not rTFA positively associated with all cause mortality, total CHD and CHD mortality. (*BMJ, 2015*)**

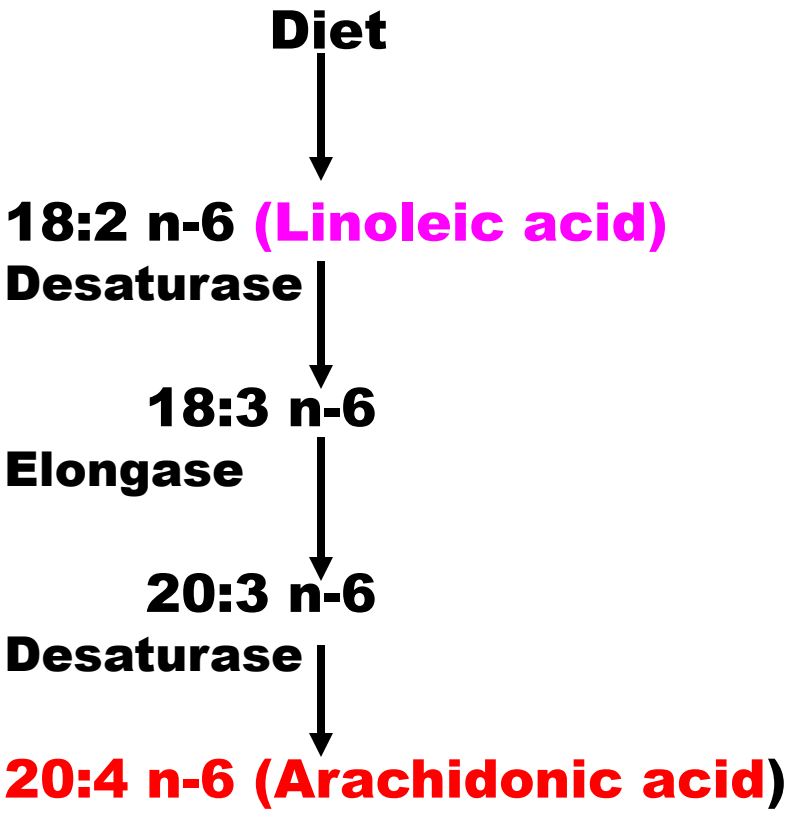
- ***Trans* fat ban in New York city resulted in 6.2% decline in hospital admission for heart attack and stroke (*JAMA cardiology, 2017*)**

Ruminant *trans* fatty acids (rTFA) and cardiovascular disease risk

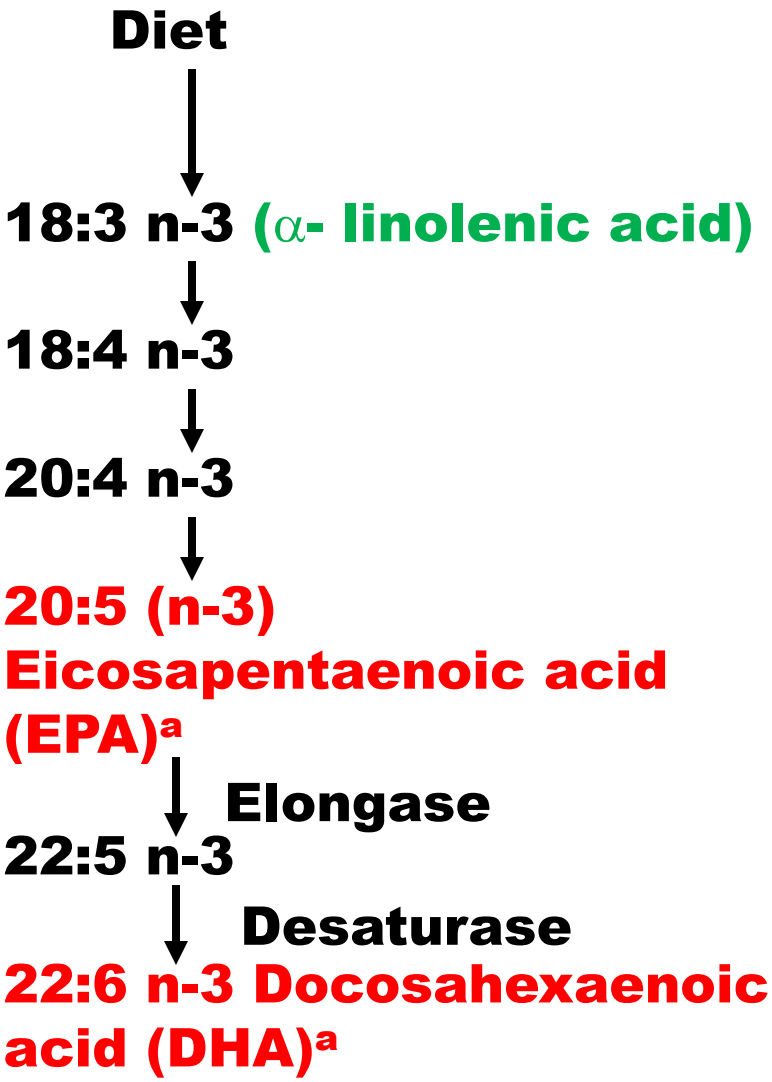
- **Type of *trans* isomer present in ruminant fat is different and may exert different metabolic effects.**
- **Epidemiological studies showed that rTFA may be less detrimental to heart health than iTFA.**
- **Recent meta analysis of randomized clinical trials showed no association between rTFA intake and CHD risk at the current intake level and up to 4en%**

Brit J Nutr, 2014

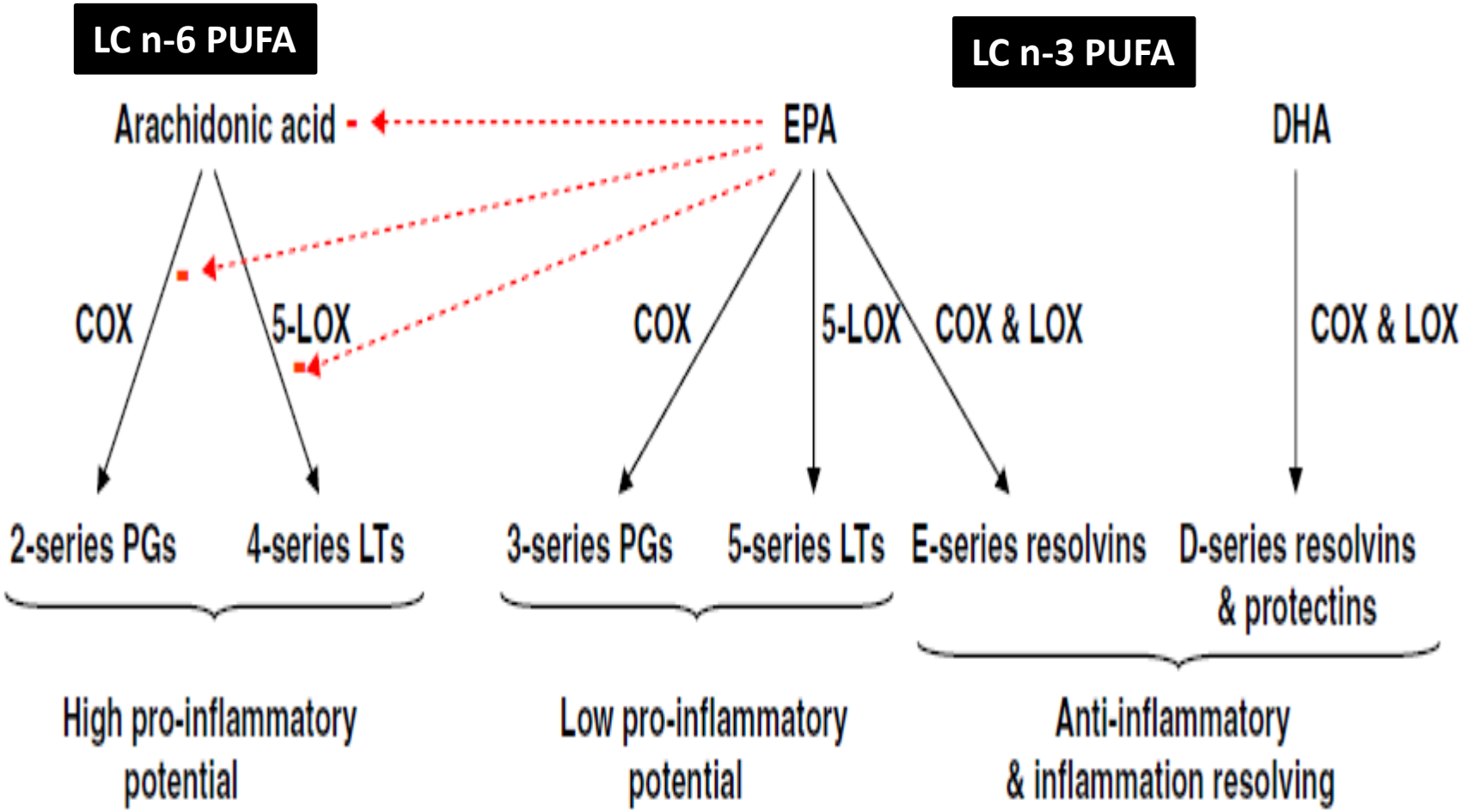
Metabolic Transformation of PUFA



[a]DHA & EPA active n-3PUFA present in fish oil



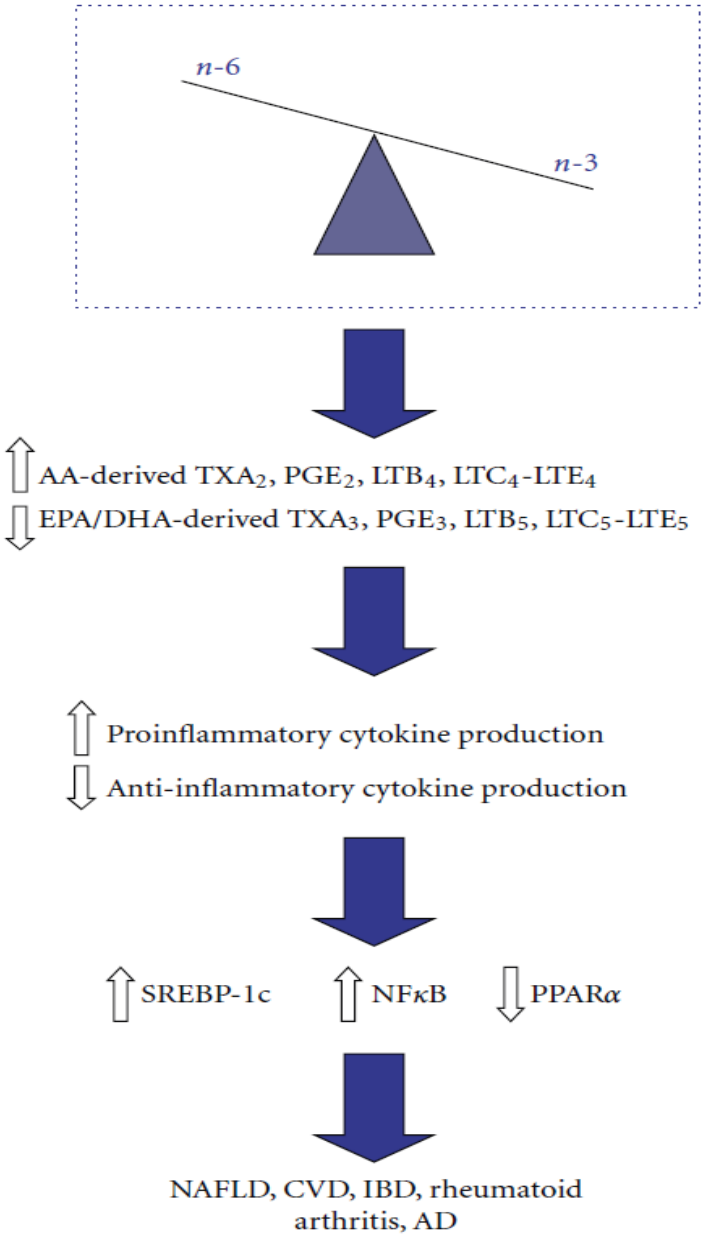
Synthesis and actions of lipid mediators produced from AA, EPA & DHA



Relative significance of n-6 and n-3 PUFA

- Metabolic effects of n-6 and n-3 PUFA are different
- n-3 PUFA more effective in ↓ plasma lipids
- Eicosanoids derived from n-3 PUFA are anti-inflammatory and anti-therombogenic compared to that of n-6 PUFA
- n-6 and n-3 PUFA competes each other for desaturation and chain elongation pathway
- Optimal balance between n-6 and n-3 PUFA in the diet is important

Health implications of high n-6 PUFA intake



J Nutr Met, 2016

Beneficial effects of n-3 PUFA (EPA & DHA) in CVD

Improve lipoprotein profile
↓ TG, ↓ Sd LDL & ↑ HDL

Improve endothelial function

↓ Blood Pressure

↓ Blood clotting

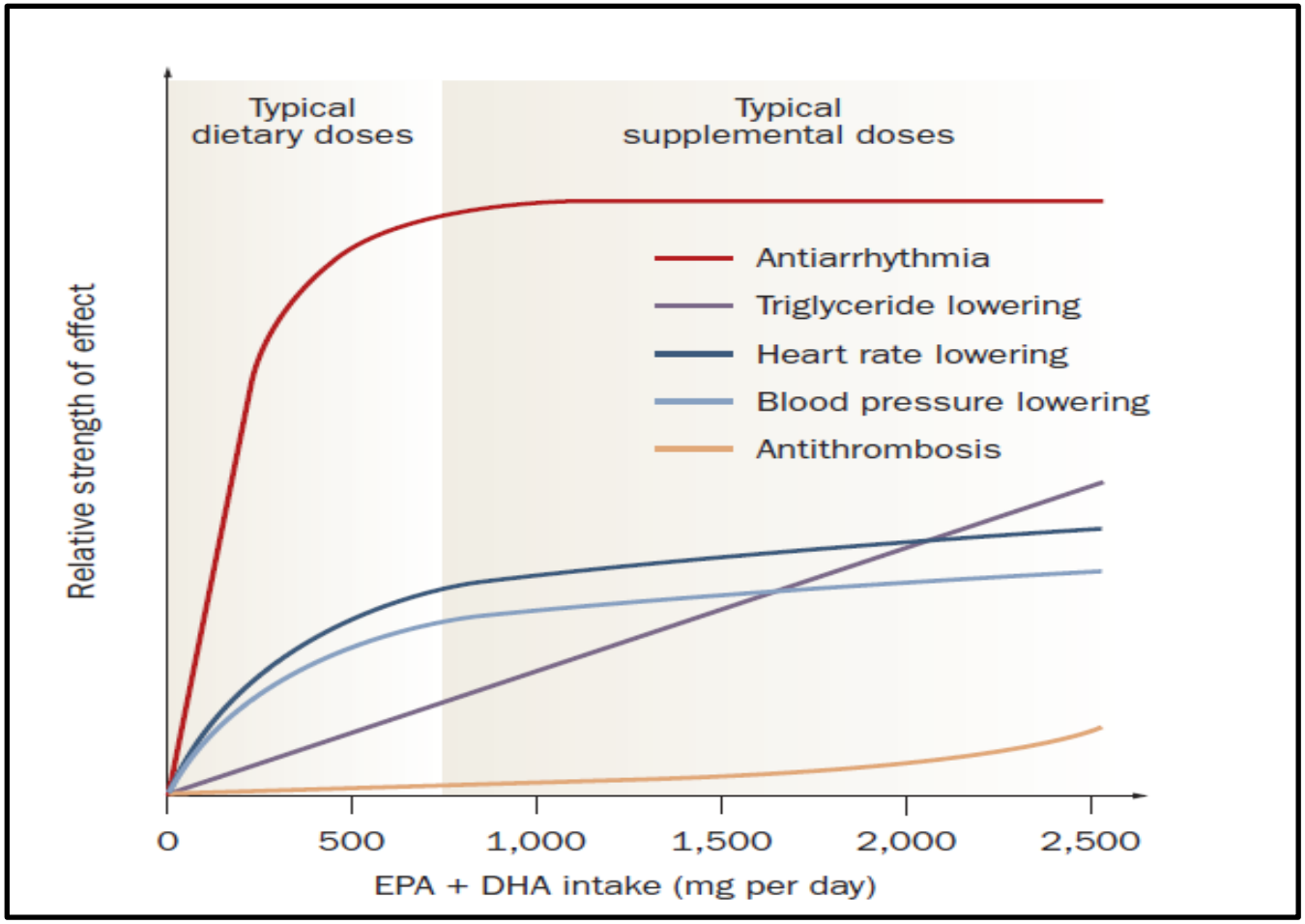
Anti-inflammatory

Plague stabilization

Antiarrhythmic

J Am Coll Cardiol, 2011

Dose response effects of EPA & DHA on CHD risk factors



- **Antiarrhythmic and antithrombotic effects can be clinically beneficial within weeks**
- **Heart rate lowering can be achieved over a period of months**
- **Triglyceride lowering and BP lowering over a period of months to years**

Nat Rev Cardiol, 2009

Strength of evidence on dietary fat and risk of chronic diseases

Evidence	Decreased risk	No relationship	Increased risk
CVD			
Convincing	LC n-3 PUFA		SFA (C12:0 - C16:0) and *trans* fat
Probable	ALA, Oleic acid	Stearic acid (C18:1)	
Type 2 Diabetes			
Possible	LC n-3 PUFA		SFA
Cancer			
Possible	LC n-3 PUFA		Animal fat

FAO-WHO report, 2010

Current recommendations of dietary fat intake

Total fat

- 20 to 35 en% (40-70 gm)
- Diet should provide more PUFA & MUFA

SFA

- < 10en% (20 gm)
- < 7en% (14 gm) in high risk individuals
- Restrict intake of red meat, butter, cream and high fat dairy products

MUFA

- 15-20 en% (30-40gm)

***Trans* fat**

- Do not have any nutritional value
- < 1en% (2gm)
- Limit intake of commercial bakery products like cakes, biscuits, sweets, deep fried foods & ready to eat foods

PUFA

- < 10en% (20gm)
- Minimum of 3en% (6gm)of n-6 PUFA necessary to prevent EFA deficiency
- 0.6-1.2 en% (1.2 – 2.4gm) of n-3 PUFA (ALA)
- Green leafy vegetables, nuts and seeds (ALA rich)
- n-6/n-3 ratio should be 5-10
- Two servings (~ 200gm) of fish/week (preferably oily fish) to provide sufficient EPA & DHA (~ 500mg)

Cholesterol

- < 300 mg/d
- < 200mg/d in high risk individuals
- Avoid egg yolk, red meat & high fat dairy products

Recommendations for dietary fat intake in Indians

Age/Gender/ physiological groups	Physical activity	Minimum level of Total fat (%E)[a]	Fat from foods other than visible fats[d] %E	Visible fat[g]	
				%E	g/p/d
Adult man	Sedentary	20	10	10	25
	Moderate				30
	Heavy				40
Adult Woman	Sedentary	20	10	10	20
	Moderate				25
	Heavy				30
	Pregnant women	20	10	10	30
	Lactating women				30
Infants	0 - 6 months	40-60	Human milk		
	7 - 24 months	35[b]	10[c]	25	25
Children	3-6 years	25	10	15	25
	7-9 years				30
Boys	10 – 12 years				35
	13 – 15 years				45
	16 – 18 years				50
Girls	10 – 12 years				35
	13 – 15 years				40
	16 – 18 years				35

[a] FAO/WHO report, 2008
[b] gradually reduce depending on physical activity
[c] Human milk/infant formula + complementary foods
[d] if higher than 10%E, visible fat requirement proportionately reduces
[g] cooking oils, butter, ghee and margarine

RDA for Indians, 2010

Food based guidelines to ensure optimal fat quality in Indian diets

- Use of two or more vegetable oil is recommended (complete dependence of single vegetable oil does not ensure optimal intake of various fatty acids)
- Recommended oil combinations
  - Preferred vegetable oils along with ALA containing oils
  - Vegetable oils containing high LA along with oil containing moderate or low LA levels (recommended when other dietary components provide high ALA levels or fish is consumed)
- Butter and ghee consumption should be kept to a minimum
- Avoid using vanaspati as the cooking medium

- **Tropical oils (coconut oil, palm oil, palm kernel oil) should be substituted for the foods that require sold fats (bakery fats, shortening etc)**

- **Regular consumption of ALA containing foods (pearl millet, pulses, green leafy vegetables, fenugreek, flaxseed, chia seed, mustard seed and walnut) and whole nuts (almonds and pistachios)**

- **Non vegetarians should prefer fish (200gm/week)**

- **Minimizing consumption of premixed, ready to eat, fast foods, bakery foods prepared in vanaspati**

- **Choose low fat dairy foods (double toned milk with fat content <1.5%) or curd prepared from such milk.**

Recommended oil combinations (1:1 proportion)

Oil containing LA + oil containing both LA & ALA	Oil containing high LA + oil containing moderate or low LA
Groundnut/ sesame/ rice bran/ cottonseed + mustard Groundnut/sesame/rice bran /cottonseed + canola Groundnut/sesame/rice bran /cottonseed + soybean Palmolein + soybean Saffower/sunflower/palmolein + mustard	Sunflower/safflower + palmolein/olive Safflower/sunflower + groundnut / sesame/rice bran

Quantities of selected foods which provide 0.1 gm ALA (n-3 PUFA)

Sources	gm
Cereal/millet	
Wheat & pearl millet (Bajara)	70
Pulses	
Blackgram, Rajmah & Cowpea	20
Vegetables	
Green leafy	60
Purslane (lunia)	25
Other vegetables	400
Spices	
Fenugreek seed	5
Mustard seed	1
Nuts	
Walnut	1.2
Unconventional oil seeds	
Chia seed	0.6
Flax seed	0.5
Perilla seed	0.3

Diabetes technol ther, 2011

Fish or fish oil supplements?

- **AHA recommendations**
  - **0.5 gm/d for primary prevention of CHD**
  - **Patients with CHD consume 1gm/d EPA and DHA fish oil supplements in consultation with a physician**
  - **4gm/d for the treatment of patients with very high triglycerides**

- **Dietary sources of fatty fish as the main source of n-3 PUFA is preferred (Vitamin D, selenium, naturally occurring antioxidants and fish proteins)**

- **Selenium has several cardiovascular benefits (antioxidant, antithrombotic, reduces myocardial infarct size and ischemia-induced ventricular arrhythmias and improves recovery from ischemia/reperfusion injury)**

- **Environmental toxins (mercury, PCB, chlordane, dioxins and DTT)**

Nat Rev Cardiol, 2009

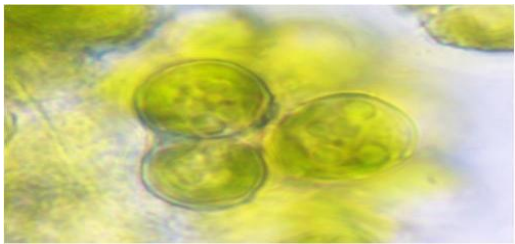
Novel n-3 PUFA supplements

Krill oil

- Krill are tiny shrimp-like crustaceans that flourish in the extremely cold water of Antarctic ocean
- Unlike in fish oil, EPA & DHA in krill oil is in phospholipid form
- Bioavailability of EPA & DHA is better in phospholipid form
- Krill oil contain potent antioxidant astaxanthin

Algal oil

- **Algae are the primary producers of the oceans' ecosystems, providing the foundation of the oceanic food chain**
- **Synthesise LC n-3 PUFA that are subsequently consumed by other marine life**
- **Vegetarian friendly and easily to grow on large scale**
- ***Schizochytrium* sp and *Thraustochytrium* sp produces high DHA and minimal EPA**
- **Currently used in commercial products (infant formulas, food additives and pharmaceutical products)**



Key messages

- **Minimum intake of visible fats (vegetable oils/butter/ghee/margarine) for Indian adults range between 20-40gm/d/p .**
- **Single vegetable oil does not ensure optimal intake of fatty acids and balance of n-6 and n-3 PUFA. Hence ICMR-NIN recommends to use two or more vegetable oils.**
- **Non-vegetarians should prefer non-fried oily fish (200gms of salmon, sardines, mackerel, tuna *etc* per week).**
- **Include nuts (unsalted) such as almonds, walnuts, peanuts, hazelnuts, pistachios and n-3 PUFA rich oil seeds such as chia seed and flax seed.**
- **Avoid using Vanaspati as the cooking medium and limit the intake of processed foods containing *trans* fats**