# Fastfoodová strava a NAFLD

Piják M.R.

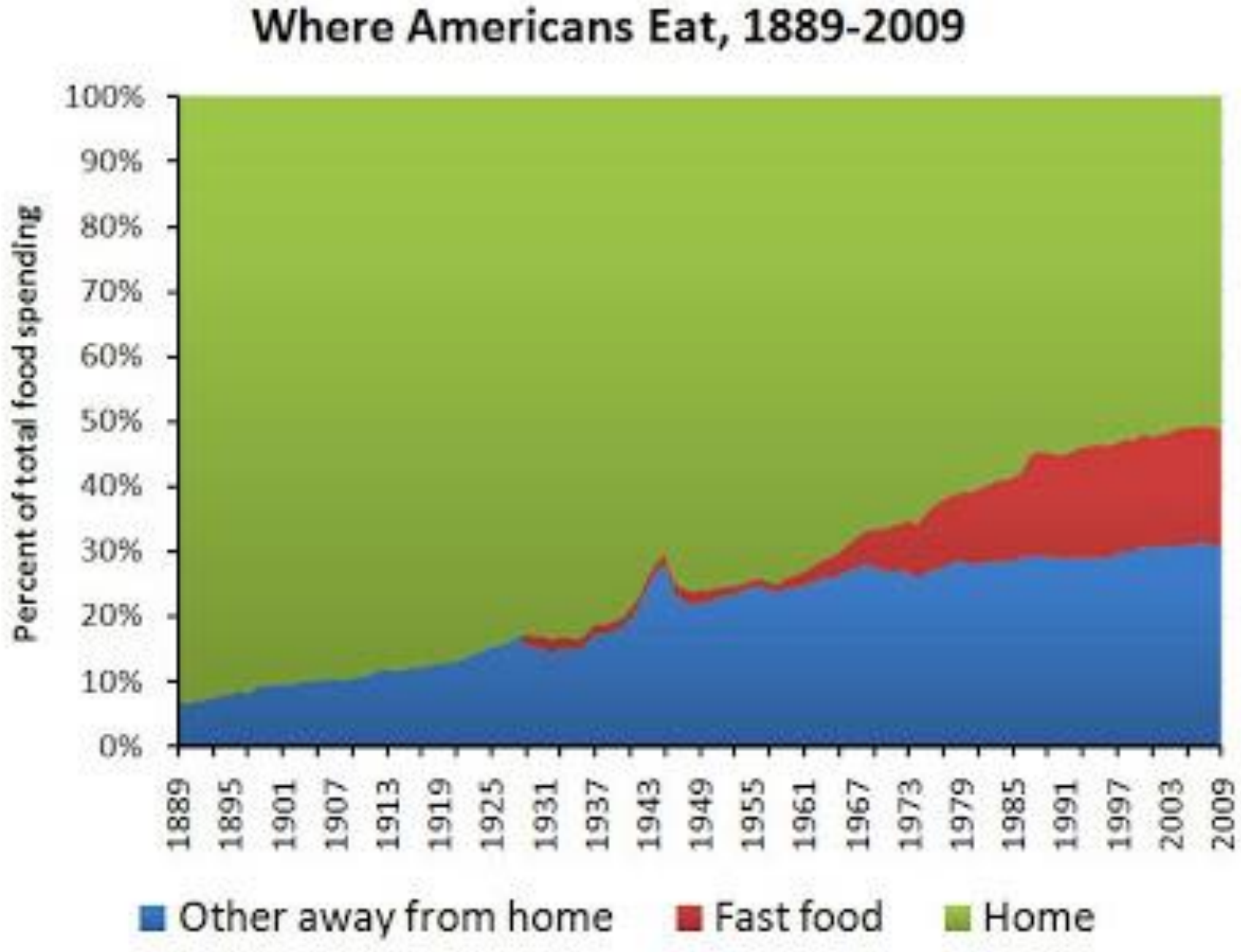
I. Interná klinika  LF SZU a UNB Dionýza Diešku,
Univerzitná nemocnica Bratislava,
Nemocnica akad. L. Dérera,

45. Májové hepatologické dni
Hepatológia 2017: Životný štýl a pečeň
18.-20.5.2017

Syllabus

1. **Úvod**
2. Epidemiológia
3. Endokrinné disruptory
4. Pomer makroživín
5. Sacharidy
6. Tuky
7. Bielkoviny
8. Záver


BK STACKER
WHOPPER
AMERICA'S FAVORITE BURGER
MADE FRESH TO ORDER
MAKE IT A VALUE MEAL
KIDS MEAL


Where Americans Eat, 1889-2009
Percent of total food spending
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
1889
1895
1901
1907
1913
1919
1925
1931
1937
1943
1949
1955
1961
1967
1973
1979
1985
1991
1997
2003
2009
Other away from home
Fast food
Home

# Fastfoodová strava má silnú pozitívnu asociáciu s nárastom hmotnosti a IR, z čoho možno usudzovať, že zvyšuje riziko obezity a DM II

## Fast-food habits, weight gain, and insulin resistance (the CARDIA study): 15-year prospective analysis

Lancet 2005; 365: 36–42 Mark A Pereira, Alex I Kartashov, Cara B Ebbeling, Linda Van Horn, Martha L Slattery, David R Jacobs Jr, David S Ludwig

**Background** Fast-food consumption has increased greatly in the USA during the past three decades. However, the effect of fast food on risk of obesity and type 2 diabetes has received little attention. We aimed to investigate the association between reported fast-food habits and changes in bodyweight and insulin resistance over a 15-year period in the USA.

**Methods** Participants for the CARDIA study included 3031 young (age 18–30 years in 1985–86) black and white adults who were followed up with repeated dietary assessment. We used multiple linear regression models to investigate the association of frequency of fast-food restaurant visits (fast-food frequency) at baseline and follow-up with 15-year changes in bodyweight and the homoeostasis model (HOMA) for insulin resistance.

**Findings** Fast-food frequency was lowest for white women (about 1·3 times per week) compared with the other ethnic-sex groups (about twice a week). After adjustment for lifestyle factors, baseline fast-food frequency was directly associated with changes in bodyweight in both black ($p=0·0050$) and white people ($p=0·0013$). Change in fast-food frequency over 15 years was directly associated with changes in bodyweight in white individuals ($p<0·0001$), with a weaker association recorded in black people ($p=0·1004$). Changes were also directly associated with insulin resistance in both ethnic groups ($p=0·0015$ in black people, $p<0·0001$ in white people). By comparison with the average 15-year weight gain in participants with infrequent (less than once a week) fast-food restaurant use at baseline and follow-up (n=203), those with frequent (more than twice a week) visits to fast-food restaurants at baseline and follow-up (n=87) gained an extra 4·5 kg of bodyweight ($p=0·0054$) and had a two-fold greater increase in insulin resistance ($p=0·0083$).

**Interpretation** Fast-food consumption has strong positive associations with weight gain and insulin resistance, suggesting that fast food increases the risk of obesity and type 2 diabetes.

# FF strava už po 7 dňoch indukuje výrazný vzostup ALT a IR u zdravých ľudí

**Fast-food-based hyper-alimentation can induce rapid and profound elevation of serum alanine aminotransferase in healthy subjects**

S Kechagias et al. for the **Fast Food Study Group** Gut. 2008; 57: 649–654.

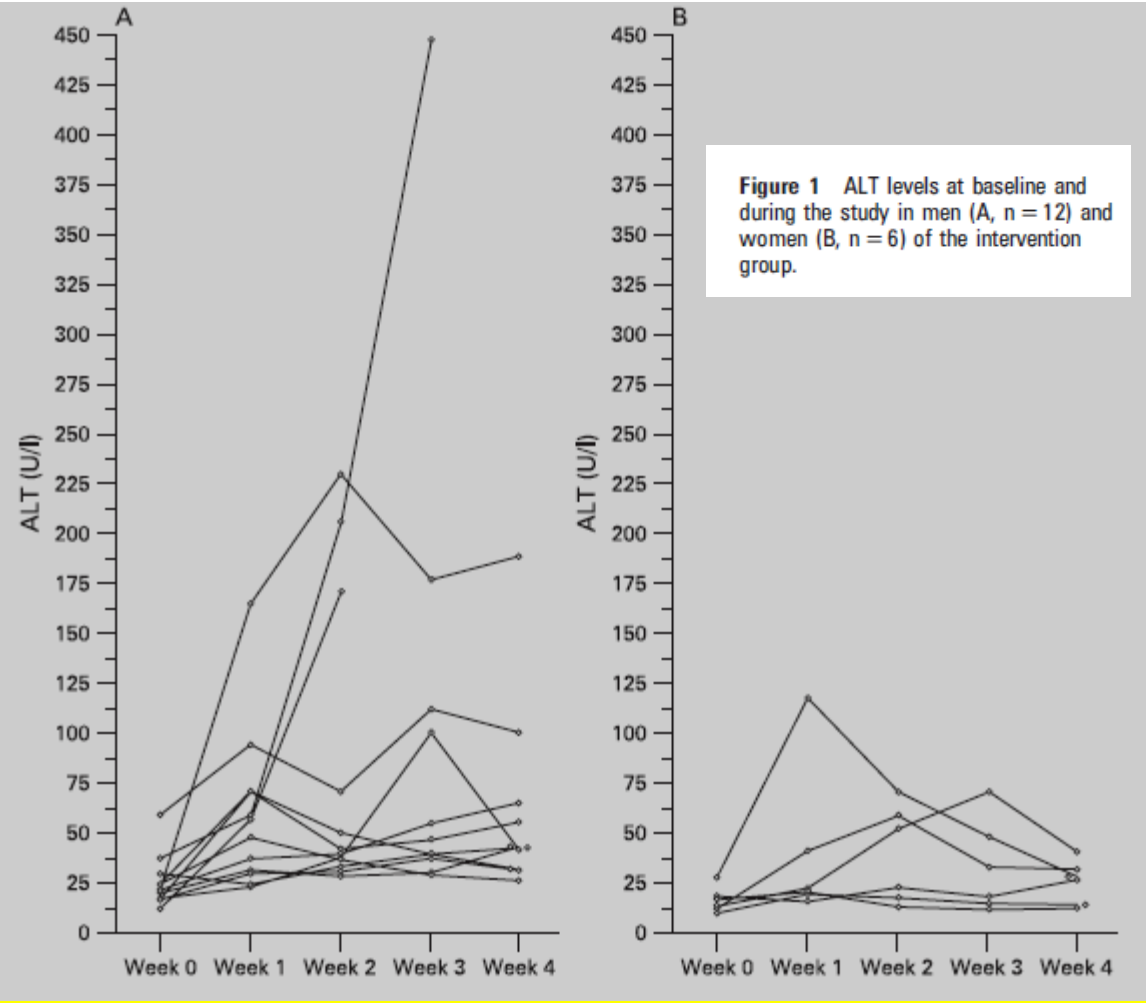



**Figure 1** ALT levels at baseline and during the study in men (A, n = 12) and women (B, n = 6) of the intervention group.

We conclude that chronically or intermittently elevated ALT can be of **purely nutritional origin**, particularly when found in the absence of liver steatosis. The fact that **14 out of 18 participants had pathological ALT levels after just 1 week** clearly displays that elevated ALT levels after a short over-indulgent holiday can be caused not only by alcohol ingestion, but also by a higher caloric intake than usual combined with a sedentary behaviour.

**Interestingly, insulin resistance according to homeostasis model assessment (HOMA)24 increased significantly in the intervention group during the study period.**

# IR je hlavným determinantom metabolického zdravia a hrá kľúčovú úlohu v patogenéze NAFLD. IR je včasnou abnormalitou v priebehu obezity, met.sy a DM II a jej prevalencia v USA je 35%*

Dve hlavné kaskády protínov-protínových interakcii zodpovedné za intracelulárne účinky inz:

1. Cesta regulujúca intemediárny metabolizmus
2. Cesta kontrolujúca rastové procesy a mitózy

Za patologických okolností môže existovať disociácia týchto dvoch ciest v tom zmysle, že cesta regulujúca intermed. Metabolizmus je porušená, kým cesta regulujúca rastové procesy a mitózy ostáva nezmenená.

IR = inhibícia účinku inzulínu na viaceré metabolické dráhy:

- Inhibícia transportu glukózy do buniek
- Inhibícia glykogenosyntézy s následným pretrvávaním produkcie glukózy pečeňou
- Inhibícia anti-lipolýzy s následným zvýšením koncentrácie MK v krvi
- Inhibícia de novo lipogenézy (ukladanie tuku z netukových zdrojov)

*Li C., et al. Trends in hyperinsulinemia among nondiabetic adults in the U.S. Diabetes Care. 2006;29:2396–2402.

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# Prevalencia NAFLD koreluje s prevalenciou obezity

## The global NAFLD epidemic

Loomba R & Sanyal, AJNature Reviews Gastroenterology and Hepatology 2013;10:686-690

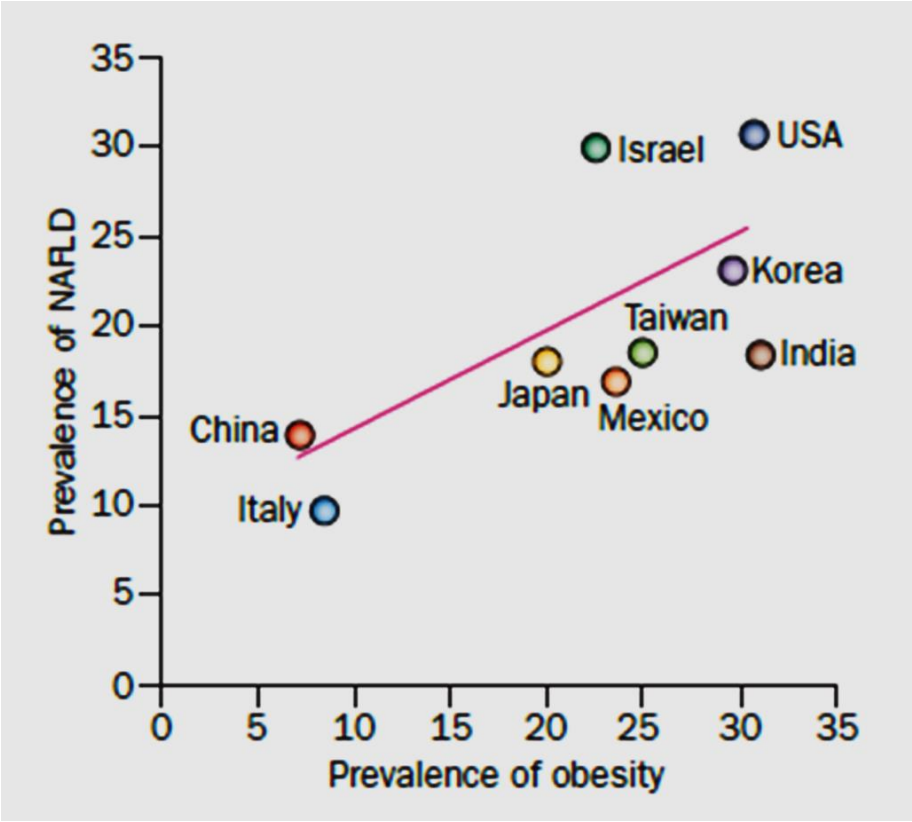



**Table 1** | East/West differences in NAFLD

| Characteristic | East | West |
|---|---|---|
| Prevalence | 10–20% | 20–30% |
| Rural versus urban differences in prevalence | Yes | No |
| Prevalence of obesity | Low but rising | High |
| Prevalence in type 2 diabetes | Higher | Lower |
| NAFLD in those with normal weight | Higher | Lower |
| Natural history data | Limited data | Cohort studies |

# Global Epidemiology of Nonalcoholic Fatty Liver Disease—Meta-Analytic Assessment of Prevalence, Incidence, and Outcomes

Younossi Z.M. et al HEPATOLOGY, VOL. 64, NO. 1, 2016

- Meta-analýza zahrňovala 8,515,431 ľudí a jej cieľom bolo stanovenie prevalencie, incidencie, rizikových faktorov a následkov v dlhodobom horizonte vo svete.

- NAFLD sa vyskytovala **na všetkých kontinentoch a priemerný výskyt bol 25%** dospelej populácie **s nárastom o 10%** v roku 2010, v porovnaní s rokom 2005.

- Najvyššia výskyt bol v Južnej Amerike (31%) a na Strednom Východe (32%) a najnižší v Afrike (14%).

- Pozoruhodným zistením bol relatívne **vysoký výskyt NAFLD v ázijskej populácie (27%)**, kde bola tiež vysoká prevalencia obezity (64%), čo môže byť ale dôsledkom, že sa použila nižšia hranica cut-point.

- **Výskyt NASH u bioptovaných osôb s NAFLD bol 59%, čo je takmer 2x viac, ako uvádzali predošlé štúdie (cca 30% pacientov.)**

# Vznik cirhózy pri NASH 2x rýchlejší ako pri CHC


*PNPLA3* polymorphisms)

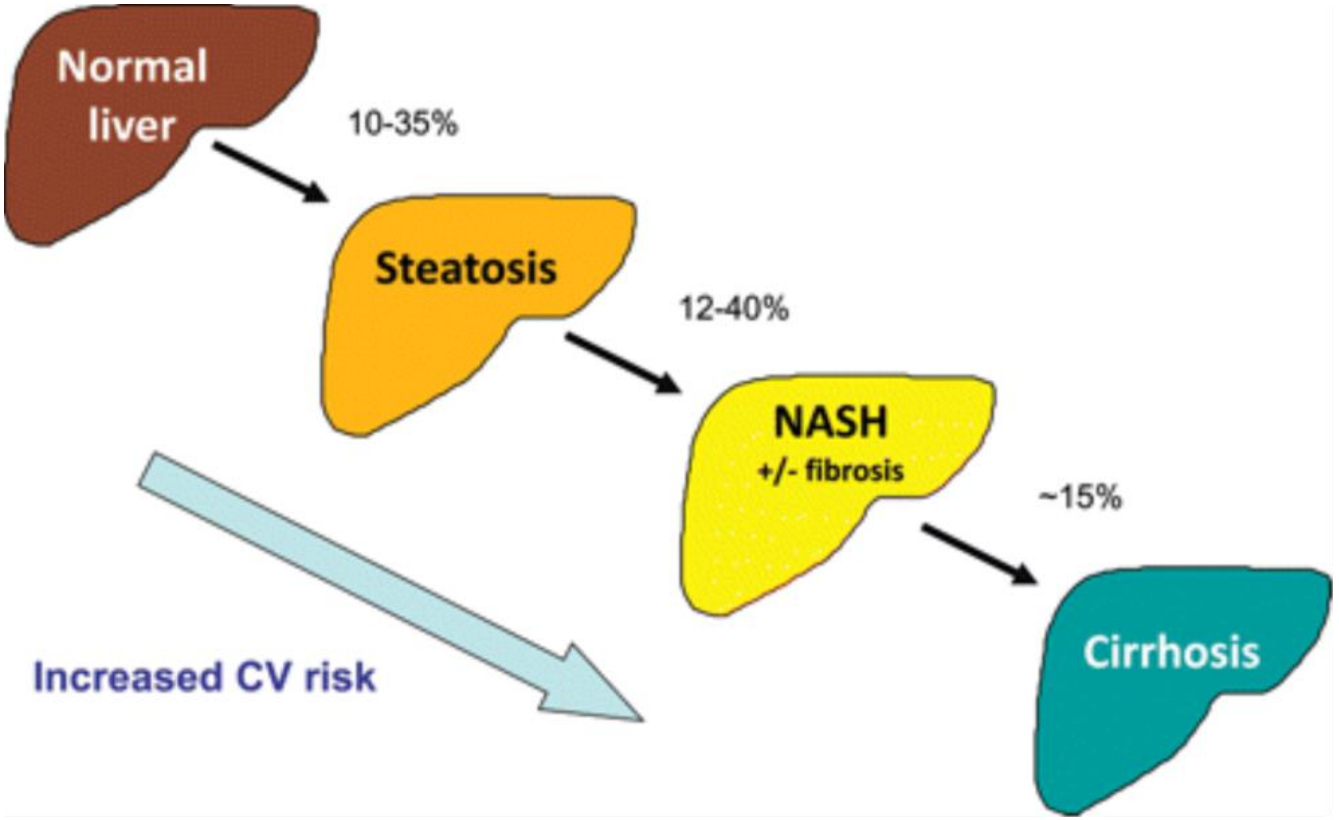
**Vývoj cirhózy v závislosti na čase:**
**CHB: 20%/5r.**
**NASH: 20% (10-29%)/10r.**
**CHC: 20%/20r.**

*Liou I, Kowdley KV. Natural history of nonalcoholic steatohepatitis. J Clin Gastroenterol 2006;40(Suppl. 1):S11-S16.*

# NAFLD: nový dôležitý rizikový faktor KVCH?

## Non-alcoholic fatty liver disease: a new and important cardiovascular risk factor?

Eur Heart J. 2012;33(10):1190-1200. doi:10.1093/eurheartj/ehr453




Variable progression of non-alcoholic fatty liver disease (usually over several years), with different grades of severity in each stage of simple steatosis and non-alcoholic steatohepatitis. These stages are generally reversible, apart from more severe forms of non-alcoholic steatohepatitis + fibrosis. Cardiovascular risk is increased as non-alcoholic fatty liver disease becomes more severe.[3,9,10]

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# Prevalencia IR a DM2 koreluje výrobou chemických syntetických látok

**Endocrine disruptors: New players in the pathophysiology of type 2 diabetes?**

Chevalier N., Fénichel P. Diabetes Metab. 2015;41:107–115.

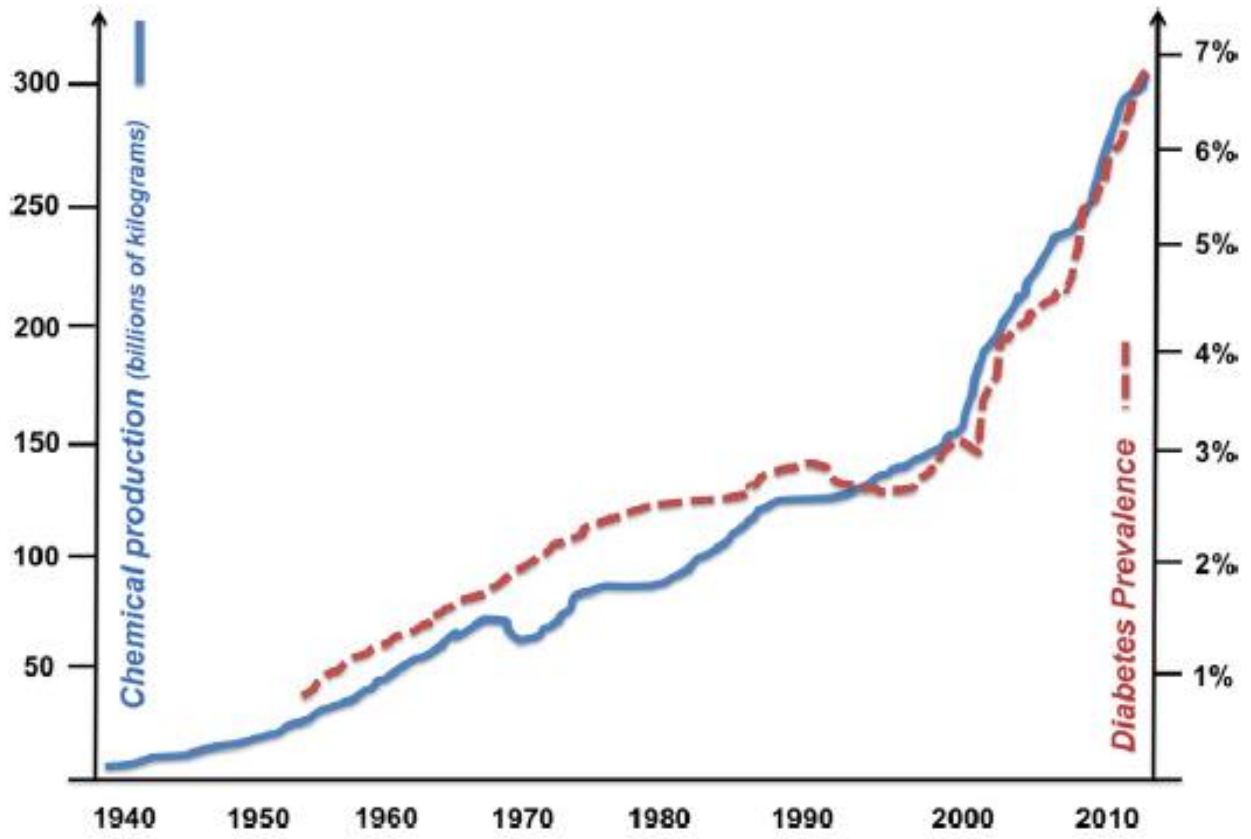



Fig. 3. Correlation between synthetic chemical production in the United States (from US Tariff Commission reports) and prevalence of type 2 diabetes (from the Centers for Disease Control and Prevention and IDF Diabetes Atlas) since 1939.

Adapted from Neel et al. [8].

# Fastfoodová strava ako významný zdroj EDC

## Recent Fast Food Consumption and Bisphenol A and Phthalates Exposures among the U.S. Population in NHANES, 2003–2010

Zota, AR, et al. Environ Health Perspect 124:1521–1528;

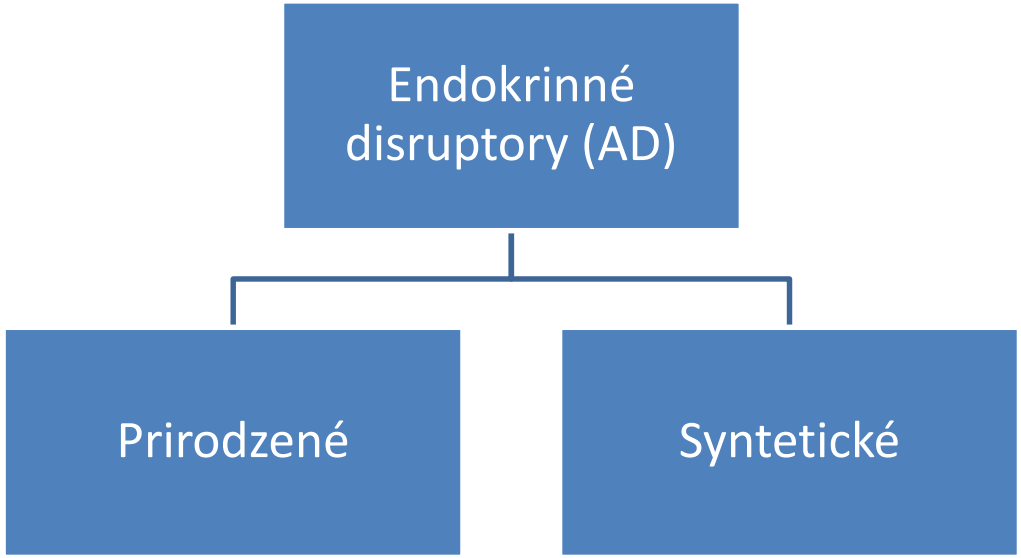
- Cieľom štúdie boli zistiť vzťah medzi nedávnym príjmom FF a BPA a močovými metabolitmi di(2-ethylhexyl) ftalátu (ΣDEHPm) and diisononyl falátu (DiNPm) v populácii USA. Išlo o kombináciu údajov 8,877 pacientov z National Health and Nutrition Examination Survey (NHANES 2003–2010).

- **Autori zistili pozitívnu závislosť na dávke medzi príjmom FF a expozíciou ftalátmi, ale nie BPA**. Účastníci s vysokým príjmom FF (≥ 34.9% TEI z FF) mali o 23.8% (95% CI: 11.9%, 36.9%) and o 39.0% (95% CI: 21.9%, 58.5%) vyššie konc. ΣDEHPm a DiNPm, v porovnaní s nekonzumentami.

- FF pochádzajúca z tuku bola tiež pozitívne spojená s ΣDEHPm and DiNPm (*p*-trend < 0.0001). Po prispôsobení na iné potravinové skupiny bola ΣDEHPm spojená s konzumáciou cereálii a iných potravín a and DiNPm bol spojený s konzmáciou mäsa a cereálii.

percent of total energy intake (TEI)

# Najväčšie zdroje BPA




- Endogenné rastlinné fytochemikálie (fytoestrogény)
- Exogénne zvieracie hormóny

**Bisphenol - A**

Present in:
- *Clear food containers*
- *Plastics*

Effects:
→ *Breast cancer*
→ *Cervical cancer*
→ *Reproductive damage*

**DDTs**

Present in:
- *Pesticides*

Effects:
Immediate
→ *Nerve damage*
→ *Paralysis*
Long term:
→ *Cancer*
→ *Reproductive damage*

**Phthalates**

Present in:
- *Cosmetics*
- *Vinyl*
- *Glues*
- *PVC*

Effects:
→ *Reproductive damage*
→ *Male feminisation*

# Najdôležitejšie prirodzené potravinové zdroje EDC v potravinovom reťazci

| Substance category | Examples | Sources/information | Occurrence in foods |
|---|---|---|---|
| **Natural hormones** | **Estrogens**<br>17β-Estradiol<br>Estrone<br>Estriol<br>**Progestagens**<br>Progesterone<br>**Androgens**<br>Testosterone | Produced naturally in the body. Present in foods produced by animals or through release in human and animal slurry practices. | |
| **Phytoestrogens** | **Lignans**<br>Enterodiol<br>Enterolactone<br>**Isoflavones**<br>Genistein<br>Daidzein/equol<br>**Coumestrol** | Produced naturally in some plants. Equol, a gut bacterial fermentation product of daidzein, may be the most estrogenic isoflavone. | |
| **Mycotoxins** | Zearalonone | A natural fungal toxin produced by *Fusarium* spp. with estrogenic properties. | |


L. Connolly, 2009

**Prirodzené estrogény sú 100 000x potentnejšie ako xenoestrogény**

# Nutričné dávky genisteinu u hlodavcov mužského pohlavia majú adipogénné účinky a sú spojené so zhoršením inzulínovej senzitivity

## Genistein affects adipose tissue deposition in a dose-dependent and gender-specific manner.

Penza M., et al. Endocrinology. 2006;147:5740–5751.

- We hypothesized that the adipose effects of genistein are dose and gender dependent. Four-week-old C57BL/6 male and female mice received daily oral doses of genistein (50–200,000 μg/kg·d) or 17β-estradiol (E2) (5 μg/kg·d) **for 15 d** or a diet containing 800 ppm genistein.

- **Genistein increased epididymal and renal fat pad and adipocyte size** at doses up to 50,000 μg/kg·d or at 800 ppm in the diet **in males but not in females. The alteration in adipocity correlated with changes in peripheral insulin resistance.**

- The antiadipogenic action of genistein and down-regulation of adipogenic genes required the expression of ERβ. In conclusion, **nutritional doses of genistein are adipogenic in a gender-specific manner,** whereas pharmacological doses inhibited adipose deposition.

# MSG: nový rizikový faktor obezity, NASH A HCC?

ER

Journal of Autoimmunity 30 (2008) 42–50

journal of autoimmunity

www.elsevier.com/locate/jautimm

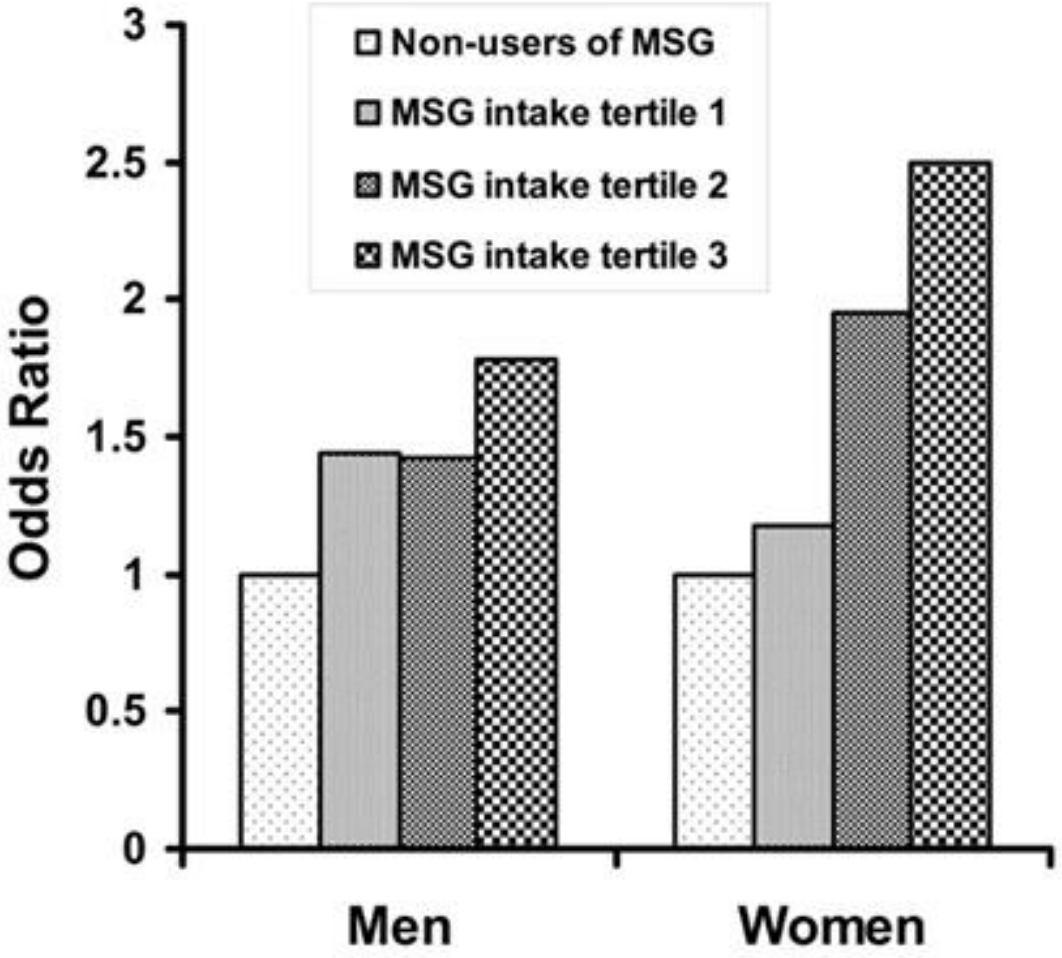
## Monosodium glutamate (MSG): A villain and promoter of liver inflammation and dysplasia

Yuko Nakanishi [a], Koichi Tsuneyama [a,b,*], Makoto Fujimoto [c], Thucydides L. Salunga [a,b,d], Kazuhiro Nomoto [a], Jun-Ling An [a], Yasuo Takano [a], Seiichi Iizuka [e], Mitsunobu Nagata [e], Wataru Suzuki [e], Tsutomu Shimada [e], Masaki Aburada [e], Masayuki Nakano [f], Carlo Selmi [g,h,**], M. Eric Gershwin [h]

Chronic inflammation is a common theme in a variety of disease pathways, including autoimmune diseases. The pathways of chronic inflammation are well illustrated by nonalcoholic steatohepatitis (NASH), which is of a serious concern due to its increasing prevalence in the westernized world and its direct correlation with lifestyle factors, particularly diet. Importantly, NASH may ultimately lead to the development of hepatocellular carcinoma. We previously reported that injection of monosodium glutamate (MSG) in ICR mice leads to the development of significant inflammation, central obesity, and type 2 diabetes. To directly address the long-term consequences of MSG on inflammation, we have performed serial analysis of MSG-injected mice and focused in particular on liver pathology. By 6 and 12 months of age, all MSG-treated mice developed NAFLD and NASH-like histology, respectively. In particular, the murine steatohepatitis at 12 months was virtually undistinguishable from human NASH. Further, dysplastic nodular lesions were detected in some cases within the fibrotic liver parenchyma. We submit that MSG treatment of mice induces obesity and diabetes with steatosis and steatohepatitis resembling human NAFLD and NASH with pre-neoplastic lesions. These results take on considerable significance in light of the widespread usage of dietary MSG and we suggest that MSG should have its safety profile re-examined and be potentially withdrawn from the food chain.

# Association of monosodium glutamate intake with overweight in Chinese adults: the INTERMAP Study.

He K et al. Obesity (Silver Spring). 2008 ;16:1875-80.




Odds ratio of overweight (BMI ≥ 23.0 kg/m2) by gender according to MSG intake.

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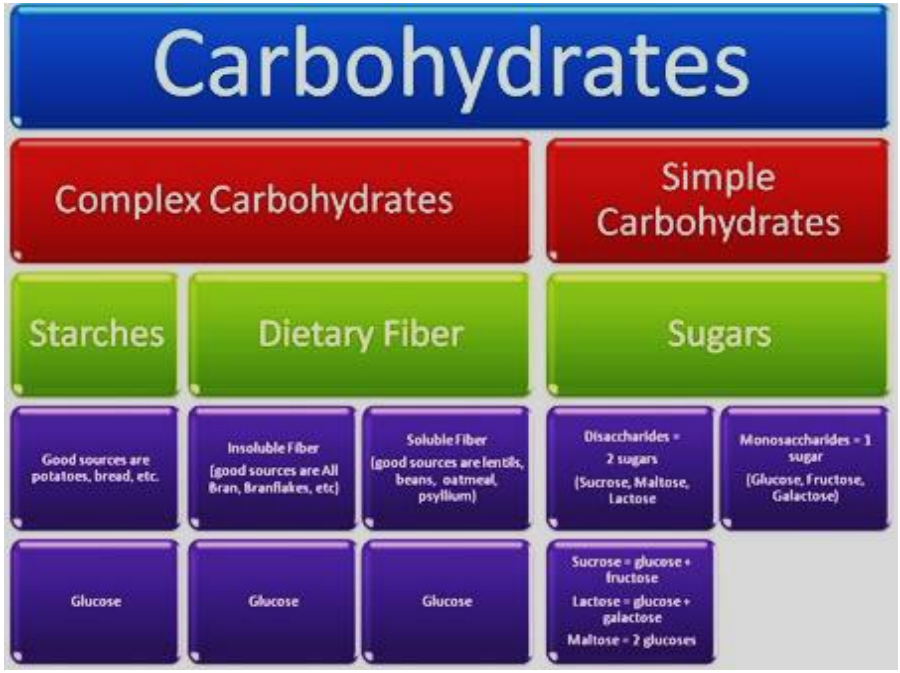
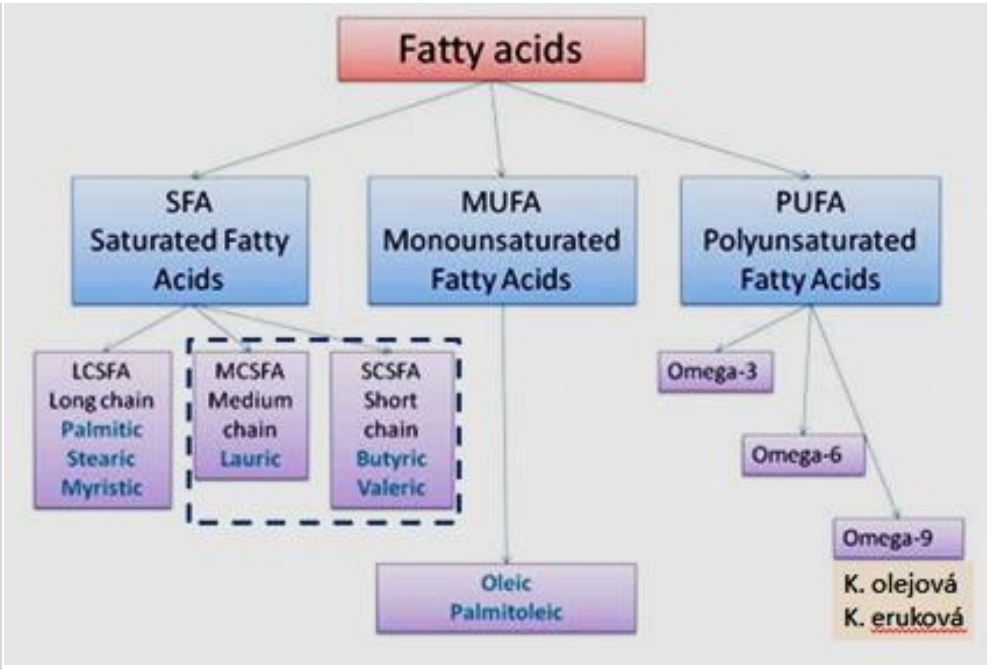
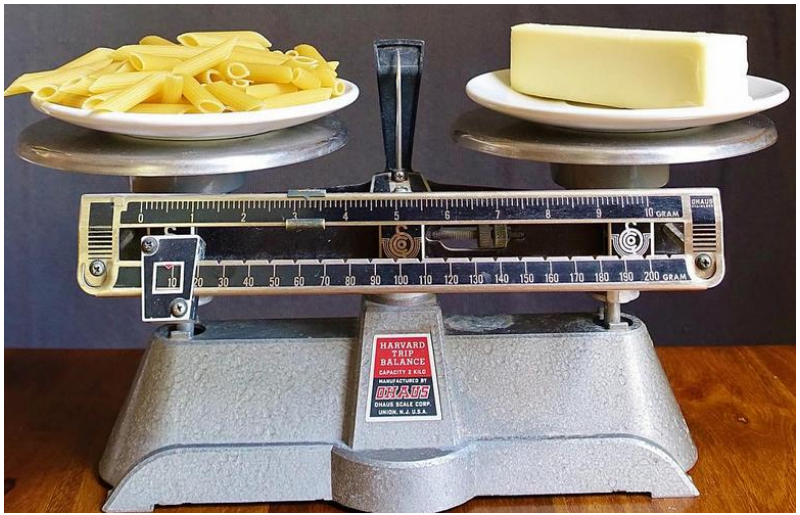
# Základ dietetickej terapie obezity a NAFLD

1. Kalorická reštrikcia (energetický deficit)
2. Optimálny pomer  energet. makroživín (?? tuky vs. acharidy) a ??bielkovín



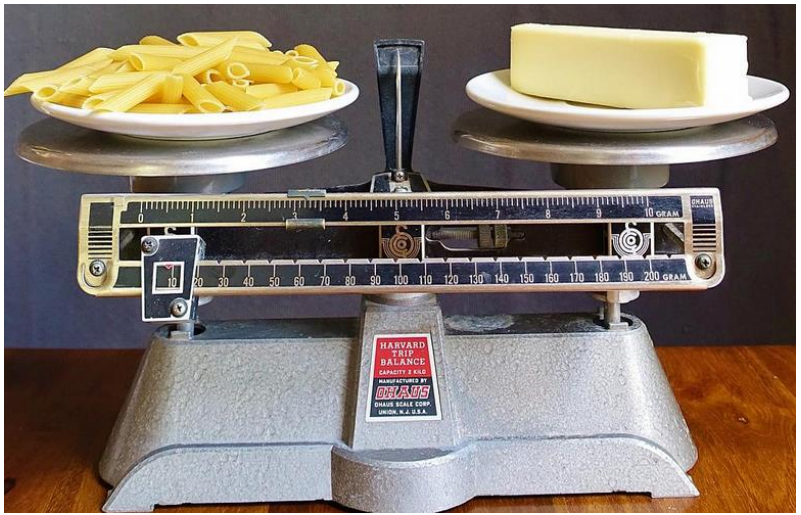



# Základ dietetickej terapie obezity a NAFLD

1. **Kalorická reštrikcia (energetický deficit)**
2. **Optimálny pomer makroživín (?? tuky vs. acharidy) a ??bielkovín**
3. **Optimálne zloženie a pomer mikroživín (energetická a nutričná denzita)**

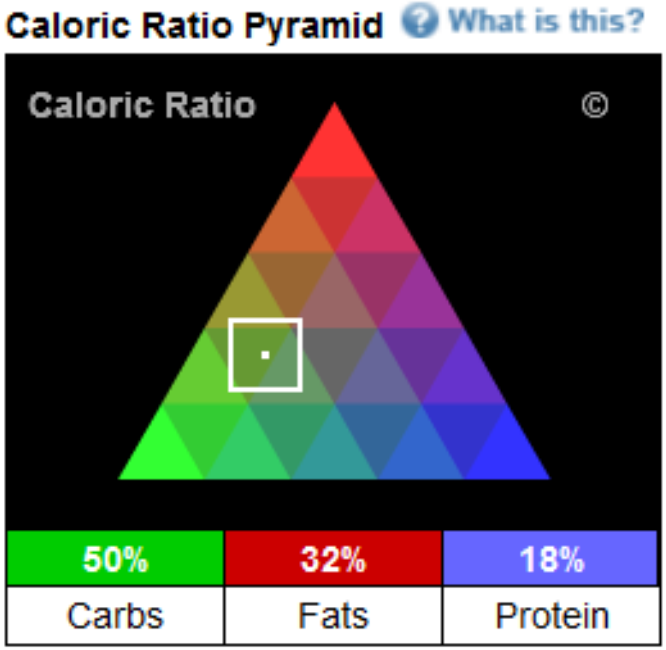
Micronutrients are the nutrients required in small amounts.

Phytochemicals and antioxidants, Vitamins and certain minerals are examples of micronutrients.


**Rastlinná strava je zdravšia, pretože okrem nízkeho množstva SFA s dlhším reťazcom, ktoré podporujú IR obsahuje menej methionínu a inzulinotropných AK (napr. BCAA)**

# RIZIKO KOMBINÁCIE SACHARIDOV S TUKMI: PIZZA EFEKT




1. Zníženie GI a protrahovaná mierna hyperglykémia → vyrovnanejší glykemický profil
2. Prolongovaná mierna hyperinzulinémia → IGF vyššie riziko kardiometab. komplikácii a kancerogenézy

Clinical Practice Guidelines

CrossMark

EASL JOURNAL OF HEPATOLOGY

June 2016,Volume 64, Issue 6, Pages 1388–1402

# EASL–EASD–EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease☆

**Table 5. Elements of a comprehensive lifestyle approach to NAFLD treatment.**

| Area | Suggested intervention |
|---|---|
| Energy restriction | • 500-1000 kcal energy defect, to induce a weight loss of 500-1000 g/week |
| | • 7-10% total weight loss target |
| | • Long-term maintenance approach, combining physical activity according to the principles of cognitive-behavioural treatment |
| Macronutrient composition | • Low-to-moderate fat and moderate-to-high carbohydrate intake<br>• Low-carbohydrate ketogenic diets or high-protein |
| Fructose intake | • Avoid fructose-containing beverages and foods |
| Alcohol intake | • Strictly keep alcohol below the risk threshold (30 g, men; 20 g, women) |

pISSN 2287-2728
eISSN 2287-285X

CMH

http://dx.doi.org/10.3350/cmh.2013.19.4.325
Clinical and Molecular Hepatology 2013;19:325-348

**Review**

# KASL clinical practice guidelines:
# Management of nonalcoholic fatty liver disease

The Korean Association for the Study of the Liver (KASL)*

## [Recommendation]

7. A reduction in total energy consumption, as well as a low-carbohydrate and low-fructose diet, is recommended for NAFLD patients. (B1)

# Features of nutritional treatment for nonalcoholic steatohepatitis recommended by international guidelines

| International guide | Body weight reduction | Caloric reduction | Carbohydrates | Fat | Vitamin E | Ref. |
|---|---|---|---|---|---|---|
| WGO | 5%-10% | 25% | ↓ Fructose | ↓ SFAs↑ ω3:ω6 ratio | NI | LaBrecque et al[99] 2014 |
| AASLD, ACG, AGA | 3%-10% | NE | NE | NE | 800 IU/d | Chalasani et al[104] 2012 |
| AISF | 0.5 kg/wk | NE | ↓ Fructose | ↓ SFAs | NI | Loria et al[105] 2010 |
| ENDO CHINA | 3%-10% | 500-1000 | NE | NE | 800 IU/d | Gao et al[106] 2013 |

WGO: World Gastroenterology Organization; AASLD: American Association for the Study of Liver Diseases; ACG: American College of Gastroenterology; AGA: American Gastroenterological Association; AISF: Italian Association for the Study of the Liver; ENDO CHINA: Chinese Society of Endocrinology; SFAs: Saturated Fatty Acids; NE: Not specified; NI: Not indicated.

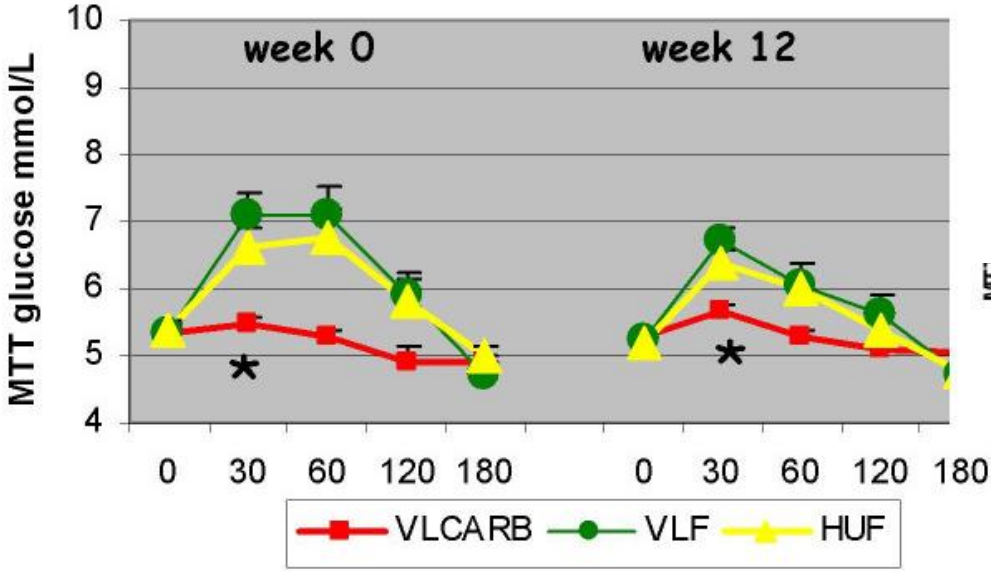
# Klinické štúdie dokumentujúce benefit LCD pri NAFLD

**Huang MA et al. One-year intense nutritional counseling results in histological improvement in patients with non-alcoholic steatohepatitis: a pilot study.**
**Am J Gastroenterol. 2005 May;100(5):1072-81**.
Pilotná štúdia s 23 pac. s NASH. 9/15 pac. ktorí dodržovali diétu malo po 12 mes histologické zlepšenie.

**Tendler D et al. The effect of a low-carbohydrate, ketogenic diet on nonalcoholic fatty liver disease: a pilot study. Dig Dis Sci. 2007 ;52:589-93.**
5 pac. S BMI 36.4 kg/m(2) a biopsiou potvrdenou NAFL užívalo LCKD **(sacharidy <20 g/d** počas 6 mes. Priemerný pokles hmotnosti bol -12.8 kg (range 0 to -25.9 kg) a 4/5 pac. vykazovalo zlepšenie steatózy a stupňa zápalu.

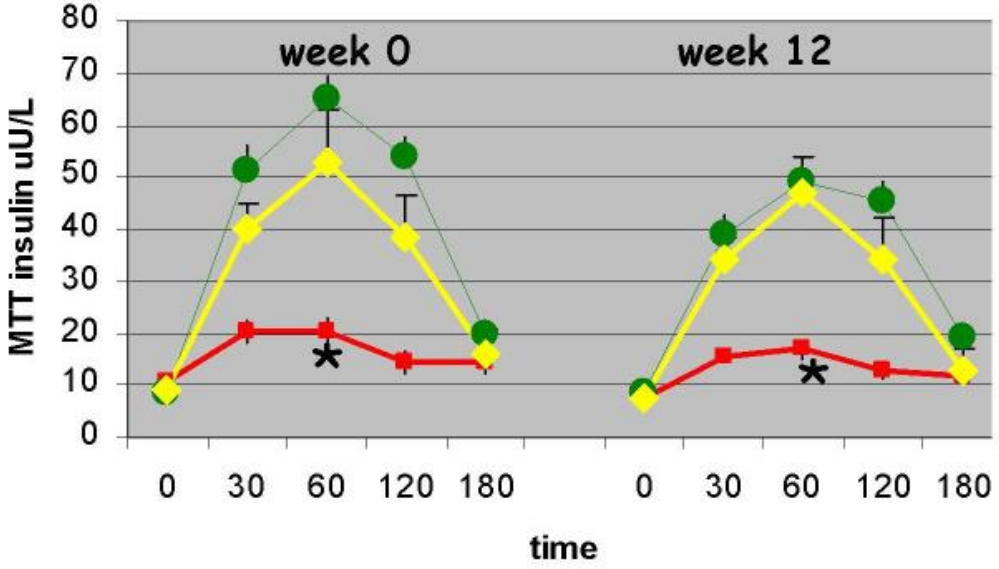
**Browning JD, et al. Short-term weight loss and hepatic triglyceride reduction: evidence of a metabolic advantage with dietary carbohydrate restriction. Am J Clin Nutr. 2011;93:1048–1052.**
18 pac. S NAFLD s BMI 35 ± 7 kg/m2 konzumovalo LCKD (sacharidy **<20 g/d**) resp. hypokalorickú diétu (CRD) (1200–1500 kcal/d) počas 2t. Pokles hmotnosti bol v oboch skupinách rovnaký (−4.0 ± 1.5 kg pri CRD ) a (−4.6 ± 1.5 kg pri LCKD ). Pokles TG v pečeni bol výraznejší v LCKD , ako v CRD skupine , (*P* = 0.008), (−55 ± 14% vs. −28 ± 23%).

# Plasma glucose and insulin response for 3 h meal tolerance test (MTT) by dietary treatment




| | PROT | FAT | CARB |
|---|---|---|---|
| VLCARB | 36% | 61% | 3% |
| VLF | 20% | 13% | 67% |
| HUF | 26% | 28% | 46% |

VLCARB = very low carbohydrate diet (n = 24)
VLF = very low fat diet (n = 22)
HUF = high unsaturated fat (n =21).



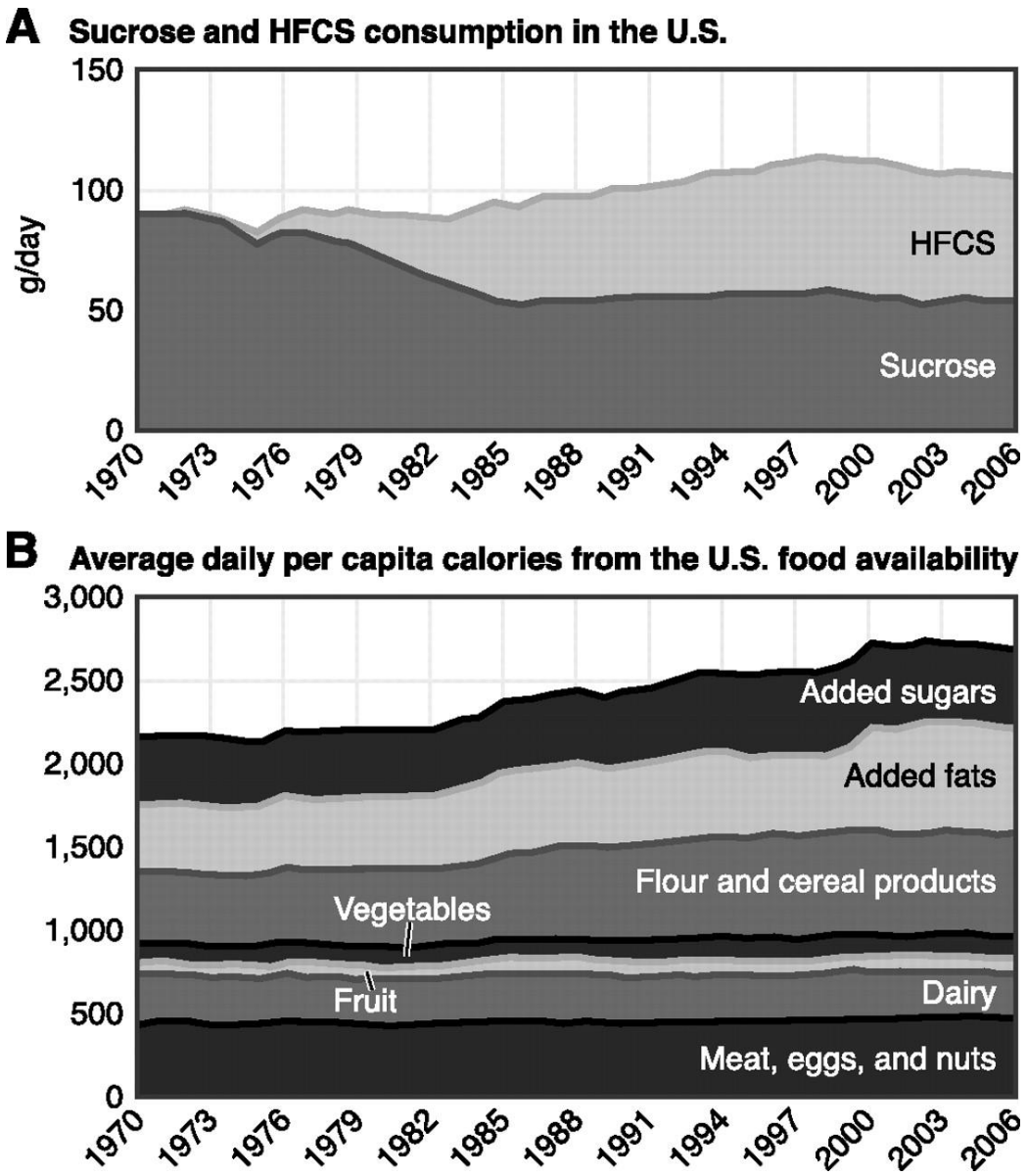

* VLCARB test meal significantly different from VLF and HUF test meals at week 0 and week 12, $P < 0.01$.

Noakes, Nutrition & Metabolism20063:7

Syllabus

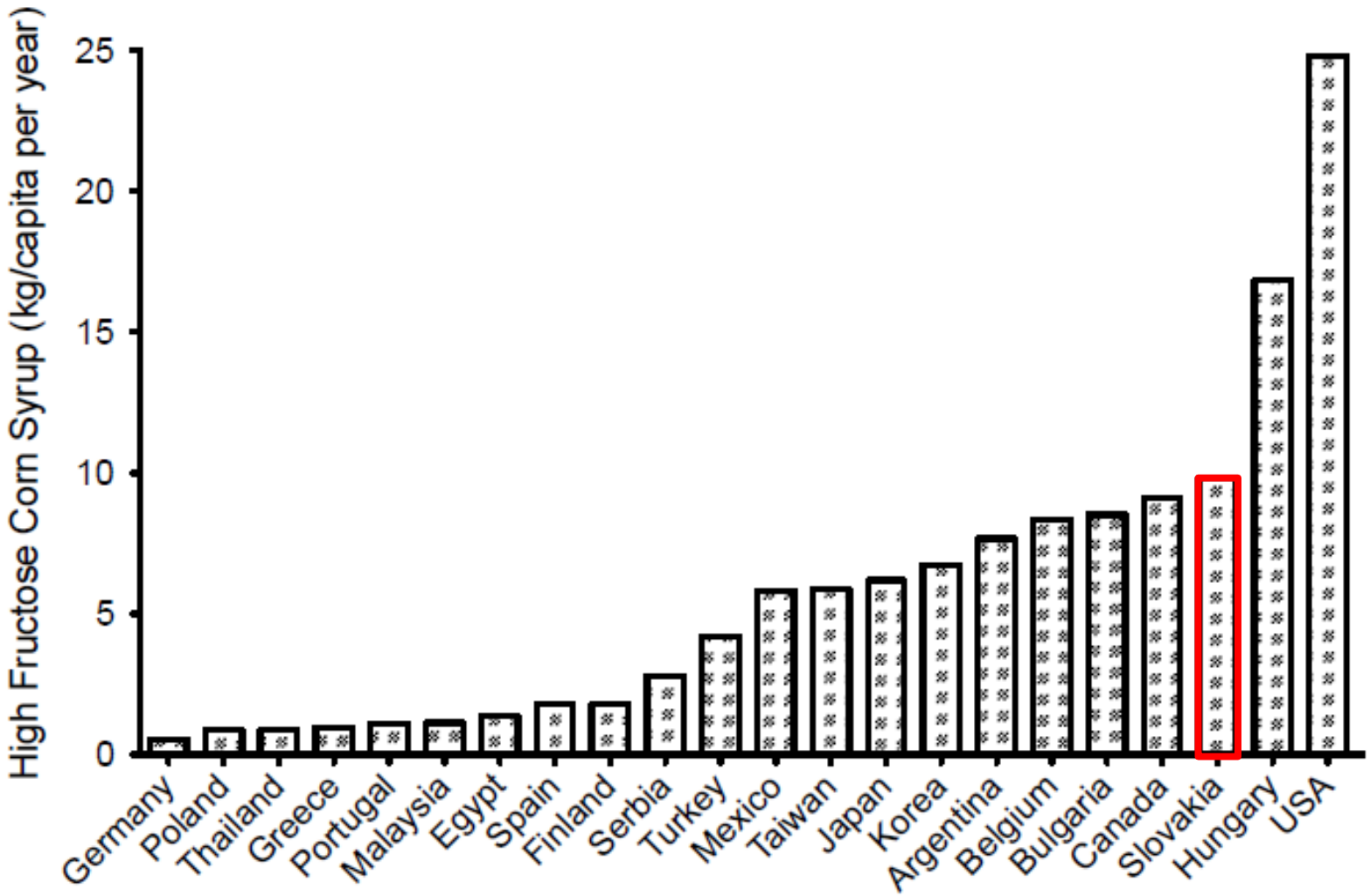
1. Úvod
2. Epidemiológia
3. Endokrinné disruptory
4. Pomer makroživín
5. **Sacharidy**
6. Tuky
7. Bielkoviny
8. Záver

**Evolution of the consumption of high-fructose corn syrup (HFCS) and sucrose in the United States between 1970 and present.**

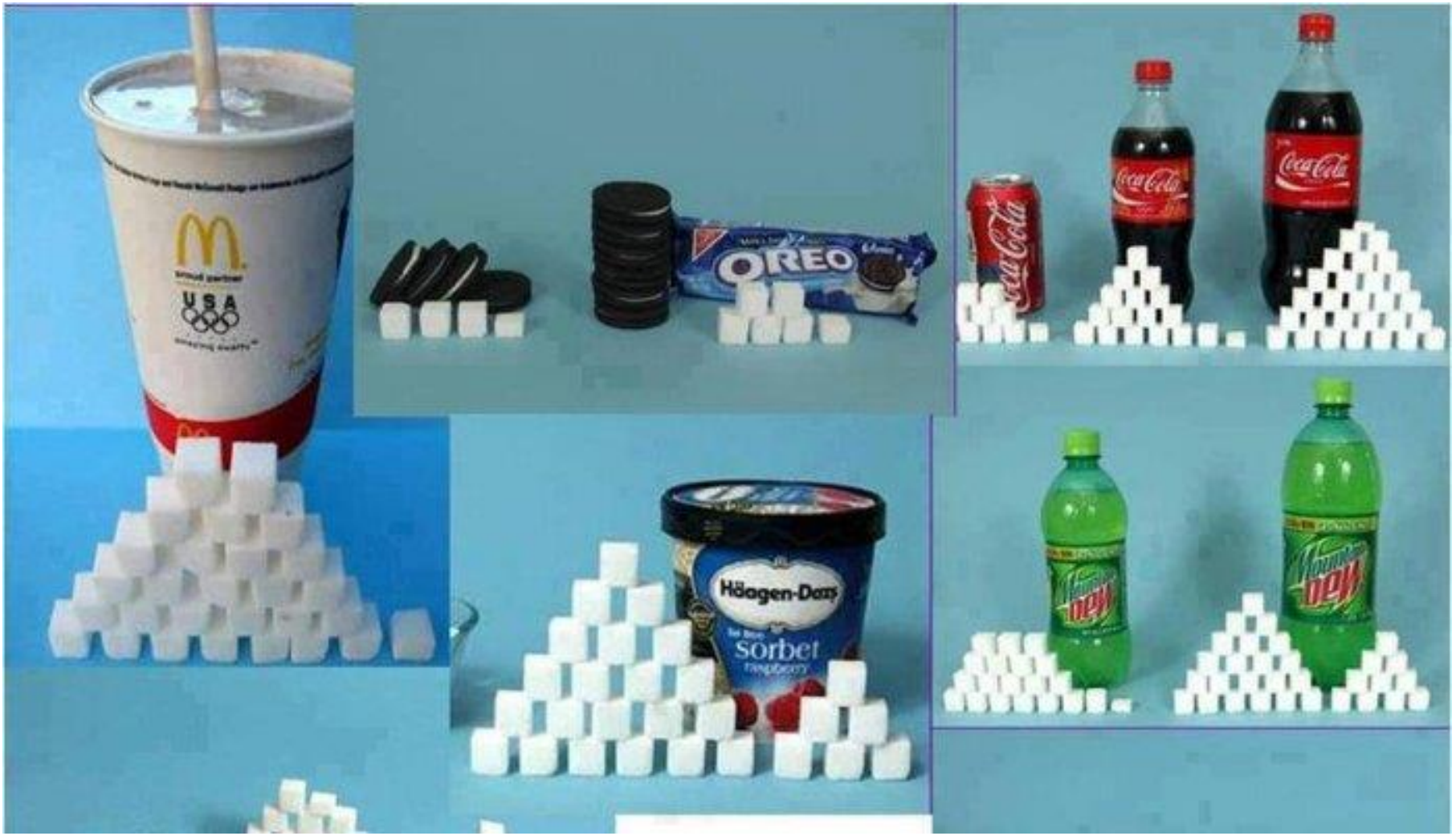



Luc Tappy, and Kim-Anne Lê Physiol Rev 2010;90:23-46

# Spotreba fruktózového kukuričného sirupu (kg/capita per ear) vo svete




Zero or < 0.5kg per capita/year: Australia, China, Cyprus, Czech Republic, Denmark, Estonia, France, India, Indonesia, Ireland, Italy, Latvia, Lithuania, Luxemburg, Malta, Netherlands, Romania, Slovenia, Sweden, United Kingdom, Uraguay

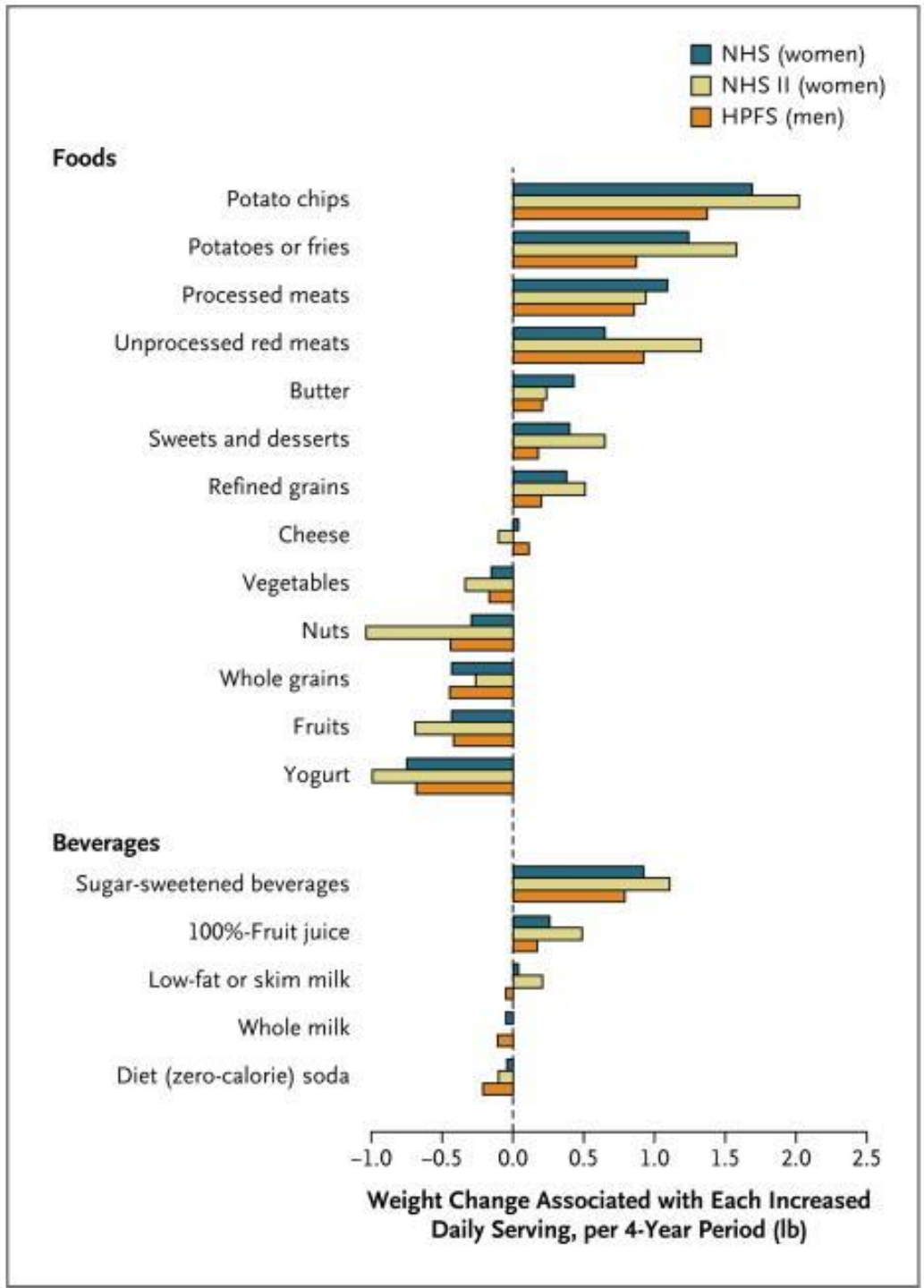

USA
OREO
Häagen-Dazs
sorbet
Mountain Dew
Mountain Dew

# Fructose-fed rhesus monkeys: A nonhuman primate model of insulin resistance, metabolic syndrome, and type 2 diabetes

We have successfully demonstrated that, like in humans, consumption of a high-fructose diet in rhesus monkeys produces many of components of the metabolic syndrome; the adverse metabolic changes also occur rapidly (within 6 to 12 months), making the model practical for both prevention and treatment studies. Moreover, a subset of monkeys on a high-fructose diet develop overt T2DM, permitting the ability to perform genotype-phenotype studies in a controlled fashion evaluating the genetic factors involved in β-cell failure.

**Bremer et al.**

**Ċlin Transl Sci. 2011; 4: 243–252**




# Changes in Diet and Lifestyle and Long-Term Weight Gain in Women and Men

Mozaffarian D et al.

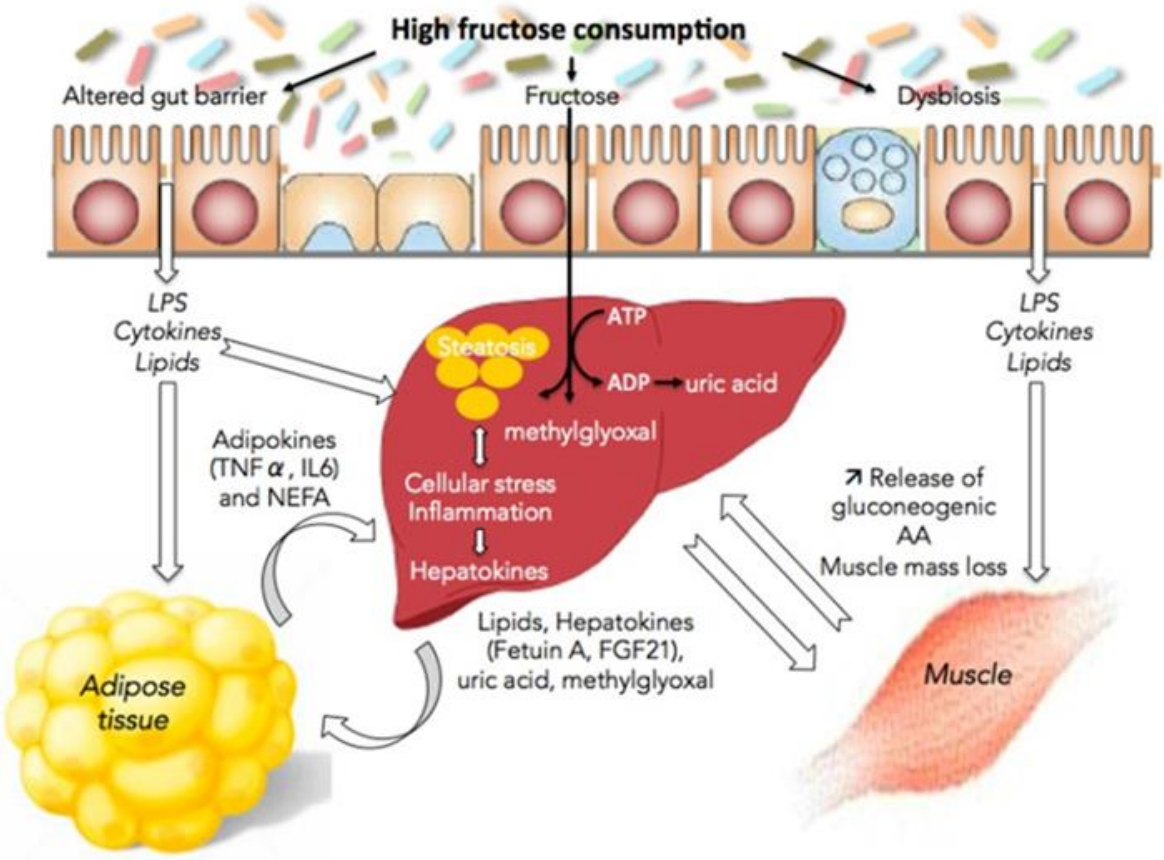
N Engl J Med. 2011;364: 2392–2404.

Relationships between Changes in Food and Beverage Consumption and Weight Changes Every 4 Years, According to Study Cohort

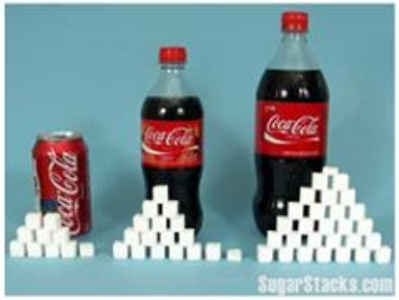
Study participants included 50,422 women in **the Nurses' Health Study (NHS),** followed for 20 years (1986 to 2006); 47,898 women in the **Nurses' Health Study II (NHS II),** followed for 12 years (1991 to 2003); and 22,557 men in the **Health Professionals Follow-up Study (HPFS),** followed for 20 years (1986 to 2006). The P value is less than 0.001 for all dietary factors with the exception of butter in the NHS II, cheese in the NHS and NHS II, low-fat or skim milk in the NHS and HPFS, diet soda in the NHS, and whole-fat milk in all three cohorts.

# KONZUMÁCIA SACHARIDOV A NAFLD: FRUKTÓZA AKO ZBRAŇ HROMADNÉHO NIČENIA

Carbohydrate intake and nonalcoholic fatty liver disease: fructose as a weapon of mass destruction
Basaranoglu M et al. Hepatobiliary Surg Nutr. 2015; 4(2): 109–116.






**Fructose and nonalcoholic fatty liver disease (NAFLD): the multifaceted aspects of fructose metabolism.** Excessive fructose consumption is associated with hepatic steatosis, cellular stress and inflammation. This is responsible for the release by the liver of lipids, methyglyoxal, uric acid, and hepatokines leading to alterations in the communication between the liver and the gut, muscles, and adipose tissue and to disease aggravation. acids.

Nutrients. 2017; 9(3): 230.

*BMJ* 2017;357:j1638 doi: 10.1136/bmj.j1638 (Published 2017 April 05)

# Coca-Cola's secret influence on medical and science journalists

A series of journalism conferences on obesity received covert funding from Coca-Cola. **Paul Thacker** investigates

Paul Thacker *freelance journalist*

For drinks manufacturers such as Coca-Cola the idea that consuming their products is fine as long as you exercise—reinforced with expensive advertising campaigns associated with sport—has been an important one. As Yoni Freedhoff, assistant professor of medicine at the University of Ottawa, told *The BMJ*, "For Coca-Cola the 'energy balance' message has been a crucial one to cultivate, as its underlying inference is that, even for soda drinkers, obesity is more a consequence of inactivity than it is of regularly drinking liquid candy."


Reklama na Coca-Colu

# Letter to the Editor

**Fruktóza redukuje hmonosť???**

*European Journal of Clinical Nutrition* (2012) **66,** 538; doi:10.1038/ejcn.2012.11; published online 15 February 2012

## Intake of cola beverages containing caffeine does not increase, but reduces body weight

P Celec[1,2,3]

In the published literature, there is a large body of evidence for the association of cola beverages intake and obesity. However, an interventional study in humans focused on this issue has not been published yet. Animal experiments conducted by our group and by others show the opposite —chronic cola intake DECREASES body weight in comparison with the control group and INCREASES insulin sensitivity, at least in rats (Park *et al.*, 2007; Celec *et al.*, 2010). Interestingly, there are indices that caffeine and the induction of uncoupling proteins in the muscle tissue might be the cause of this effect (Choi *et al.*, 2002).

Despite interspecies differences in metabolism, which are surely present, it can be anticipated that similar effects would be found in a human interventional study under controlled conditions. Evidence for the positive effect of caffeine directly in cola beverages is currently lacking. However, such an experiment comparing the effects of classic vs caffeine-free cola is under way in our lab. It might be that the associations found in epidemiological studies are secondary due to causative effects of food that is often rinsed down with cola, such as hamburgers and fries. Current efforts to raise taxes on cola beverages are not based on solid scientific evidence.

**No harmful effect of different Coca-cola beverages after 6 months of intake on rat testes.**

Tóthová L1, Hodosy J, Mettenburg K, Fábryová H, Wagnerová A, Bábíčková J, Okuliarová M, Zeman M, Celec P. Food Chem Toxicol. 2013 Dec;62:343-8


topky.sk

Slovenskí vedci nalievali pol roka potkanov Coca-Colou: Čo sa im podarilo zistiť?!

Opýtali sme sa Petra Celeca, šéfa výskumníkov, aby nám objasnil, o čo vlastne išlo. ***"Coca-Cola a podobné nápoje sú vo verejnej mienke jasne prezentované ako nezdravé. Väčšinou to vyplýva zo štúdií, ktoré ukázali asociáciu medzi pitím Coca-Coly a obezitou, diabetom apod. Lenže asociácia nemusí byť kauzálna. Je možné, že za obezitu a diabetes môže ten hamburger, ktorý Coca-Colou zapíjame, a samotná Coca-Cola s tým nič nemá,"*** prezradil nám Peter Celec z Ústavu molekulárnej biomedicíny lekárskej fakulty Univerzity Komenského.

***"Chceli sme vyťažiť z pokusu čo najviac informácií. A myslím, že práveže takto publikovaním aj negatívnych výsledkov, ktoré neboli primárnym cieľom, zabraňujeme v tom, aby sa zbytočne robili ďalšie pokusy. Je to zároveň príklad toho, ako aj základný výskum má veľký dosah na prax, lebo už v mnohých krajinách sa Coca-Cola zdaňuje a pritom evidentne podľa experimentov nemá negatívny a možno má aj pozitívny efekt na inzulínovú senzitivitu. Zrejme je to sprostredkované kofeínom a jeho účinkom na svaly, kde premieňa energiu napríklad aj z cukru v Coca-Cole na teplo. Takéto niečo sa nedá zistiť bez exeprimentov,"*** dodáva Celec.

# Acute caffeine ingestion reduces insulin sensitivity in healthy subjects: a systematic review and meta-analysis

Xiuqin Shi, et al. Nutr J. 2016; 15: 103.

**Results:** The search yielded 7 RCTs in which caffeine intake was the single variant. Compared with placebo, caffeine intake significantly decreased the insulin sensitivity index, with a standardized mean difference of −2.06 (95% confidence interval −2.67 to −1.44, I2 = 49%, P for heterogeneity = 0.06).

**Conclusion:** In the current meta-analysis, acute administration of caffeine reduced insulin sensitivity. Therefore, the inverse association between coffee and diabetes was not attributed to enhanced glucose control. Long-term trials investigating the role of caffeine in the anti-diabetic effect of coffee are needed.

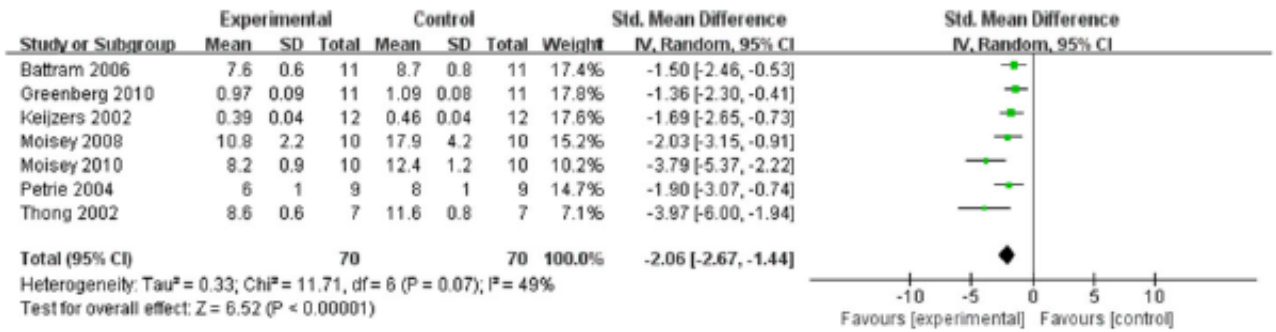
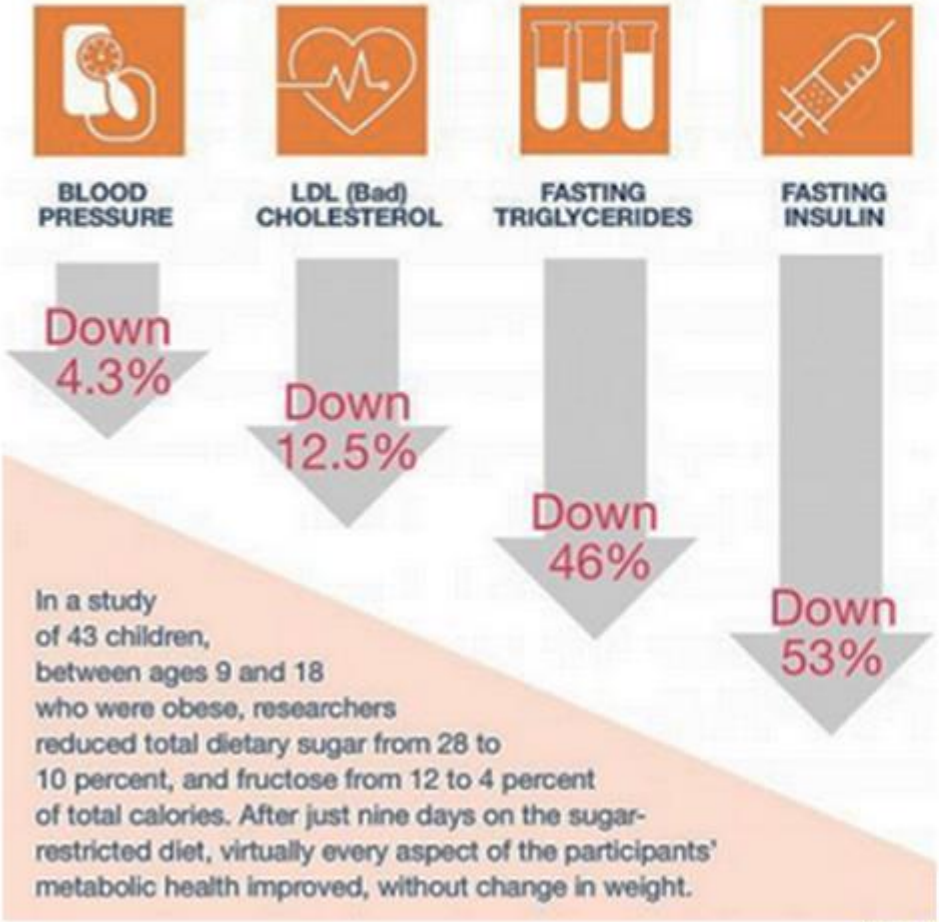



**Fig. 3** Forest plot showing the pooled standardized mean difference (SMD) and 95% confidence interval (CI) for insulin sensitivity for 7 randomized controlled trials. For each study of caffeine, the shaded square represents the point estimate of the intervention effect. The horizontal line joins the lower and upper limits of the 95% CI of these effects. The area of the shaded square reflects the relative weight of the study in the respective meta-analysis. The diamond at the bottom of the graph represents the pooled SMD with the 95% CI for the seven trials. Experimental: caffeine group; Control: control group; $I^2$: Inconsistency

# Isocaloric Fructose Restriction and Metabolic Improvement in Children with Obesity and Metabolic Syndrome

*Robert H. Lustig[1], Kathleen Mulligan[2,3], Susan M. Noworolski[4], Viva W. Tai[2], Michael J. Wen[2], Ayca Erkin-Cakmak[1], Alejandro Gugliucci[3], and Jean-Marc Schwarz[5]*

## What happens when you cut down sugar in a kid's diet for 9 days?



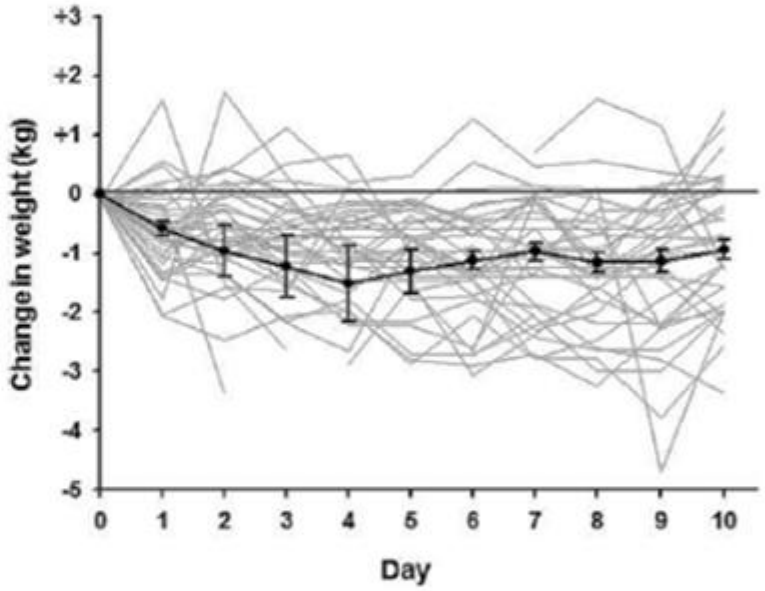




**Figure 1** Change in weight from baseline in the 43 participants over the 10 days of study. Individual weight change curves are in light gray, while means ± SEM for the entire cohort are in black.

*Obesity* (2016) **24**, 453–460. doi:10.1002/oby.21371

**U pacientov s nadváhou/obezitou a vysokou konzumáciou sladených nápojov, viedla náhrada za nápoje s umelými sladidlami počas 3 mesiacov k zníženiu intrahepatocelulárneho tuku o 74%. K poklesu ALT došlo iba u osôb s vyšším obsahom IHCL (>60 mmol/l). Výsledky RCT.**

# Sugar- and Artificially Sweetened Beverages and Intrahepatic Fat: A Randomized Controlled Trial

*Vanessa Campos[1], Camille Despland[1], Vaclav Brandejsky[2,3], Roland Kreis[2], Philippe Schneiter[1], Arnaud Chiolero[4], Chris Boesch[2], and Luc Tappy[1]*

**Objective:** To test the hypothesis that substituting artificially sweetened beverages (ASB) for sugar-sweetened beverages (SSB) decreases intrahepatocellular lipid concentrations (IHCL) in overweight subjects with high SSB consumption.

**Methods:** About 31 healthy subjects with BMI greater than 25 kg/m$^2$ and a daily consumption of at least 660 ml SSB were randomized to a 12-week intervention in which they replaced SSBs with ASBs. Their IHCL (magnetic resonance spectroscopy), visceral adipose tissue volume (VAT; magnetic resonance imaging), food intake (2-day food records), and fasting blood concentrations of metabolic markers were measured after a 4-week run-in period and after a 12-week period with ASB or control (CTRL).

**Results:** About 27 subjects completed the study. IHCL was reduced to 74% of the initial values with ASB ($N = 14$; $P < 0.05$) but did not change with CTRL. The decrease in IHCL attained with ASB was more important in subjects with IHCL greater than 60 mmol/l than in subjects with low IHCL. ALT decreased significantly with SSB only in subjects with IHCL greater than 60 mmol/l. There was otherwise no significant effect of ASB on body weight, VAT, or metabolic markers.

**Conclusions:** In subjects with overweight or obesity and a high SSB intake, replacing SSB with ASB decreased intrahepatic fat over a 12-week period.

*Obesity* (2015) **23**, 2335-2339. doi:10.1002/oby.21310

**Štúdie dokumentujúce, že aj pomerne malé množstvá fruktózy a sacharózy nepriaznivo ovplyvňujú inzulínovú senzitivitu a lipidový metabolizmus**


1. Aeberli I., et al. Moderate amounts of fructose consumption impair insulin sensitivity in healthy young men: A randomized controlled trial. Diabetes Care. 2013;36:150–156.
2. Tappy L., Lê K.A. Metabolic effects of fructose and the worldwide increase in obesity. Physiol. Rev. 2010;90:23–46.
3. Tappy L., Mittendorfer B. Fructose toxicity: Is the science ready for public health actions? Curr. Opin. Clin. Nutr. Metab. Care. 2012;15:357–361.
4. Lecoultre V., et al. Effects of fructose and glucose overfeeding on hepatic insulin sensitivity and intrahepatic lipids in healthy humans. Obesity. 2013;21:782–785.

# Strava s vysokým obsahom pridaných cukrov podporuje vznik inzulínovej rezistencie (1-5) a DM II (6-9).


1. Reiser S, et al. Isocaloric exchange of dietary starch and sucrose in humans. II. Effect on fasting blood insulin, glucose, and glucagon and on insulin and glucose response to a sucrose load. Am J Clin Nutr. 1979;32:2206–16.
2. Reiser S, et al. Effect of isocaloric exchange of dietary starch and sucrose in humans on the gastric inhibitory polypeptide response to a sucrose load. Am J Clin Nutr. 1980;33:1907–11
3. Stanhope KL, et al. Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. J Clin Invest. 2009;119:1322–34.
4. Stanhope KL, et al. Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. J Clin Invest. 2009;119:1322–34.
5. Hallfrisch J, et al. Effects of dietary fructose on plasma glucose and hormone responses in normal and hyperinsulinemic men. J Nutr. 1983;113:1819–26.
6. Reiser S, et al. Serum insulin and glucose in hyperinsulinemic subjects fed three different levels of sucrose. Am J Clin Nutr. 1981;34:2348–58.
7. Basu S, et al. The relationship of sugar to population-level diabetes prevalence: an econometric analysis of repeated cross-sectional data. PLoS One. 2013;8:e57873.
8. Goran MI, et al. High fructose corn syrup and diabetes prevalence: a global perspective. Global public health. 2013;8:55–64.
9. Gross LS, et al. Increased consumption of refined carbohydrates and the epidemic of type 2 diabetes in the United States: an ecologic assessment. Am J Clin Nutr. 2004;79:774–9.

# Ako pridané cukry podporujú vznik obezity A NAFLD prostredníctvom energeticko/nutričnej deplécie

- Nahrádzajú potraviny s vyššou nutričnou denzitou (2)
- Znižujú apetít na výživnejšie potraviny. (2)
- Spôsobujú depléciu živín v tele (za účelom uvoľnenia kalórii z cukru, ako aj na zvýšenie rastu baktérii a plesní (2)
- Poskytujú nulovú výživu (2 )
- Spôsobujú inzulínovú rezistenciu ( 27–30 ) , čo má za následok znížené využívanie glukózy ako energetického substrátu (znížený vstup do buniek) (47), ako aj porušenú oxidáciu MK na energiu (31-32)
- Zvýšené koncentrácie inzulínu tiež vedú k zvýšeným energetickým nárokom (33) a indukujú stav „vnútorného hladovania“ označovaný aj ako skryté bunkové semihladovanie (‘hidden cellular semistarvation’). 33 
- Znižujú absorbciu živín v dôsledku iritácie /poškodenia črevnej sliznice. (2,25)
- Zvyšujú exkréciu živín v dôsledku malabsorbcie fruktózy, čo vedie hnačkám (46).
- Spôsobuje poškodenie mitrochondrii a depléciu ATP. (8)
- Spôsobujú závislosť podobnú drogovej závislosti, čo vedie bludnému kruhu pokračujúceho sa prejedania a nutričnému a energetickému deficitu pri obezite.

DiNicolantonio JJ, Berger A. Open Heart 2016;3:e000469.

Syllabus

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6. Bielkoviny
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# Eperimentálne a intervenčné štúdie jednoznačne dokumentovali, že nasýtené tuky zvyšujú IR nalačno aj postprandiálne


1. El-Assaad W, et al. Saturated fatty acids synergizewith elevated glucose to cause pancreatic beta-cell death. Endocrinology. 2003;144:4154–63.
2. Mayer-Davis EJ et al. Dietary fat and insulinsensitivity in a triethnic population: the role of obesity. The Insulin Resistance Atherosclerosis Study (IRAS). Am J Clin Nutr. 1997;65:79–87.
3. Stein DT, et al. The insulinotropic potency offatty acids is influenced profoundly by their chain length and degree of saturation. J Clin Invest. 1997;100:398–403. [PMC free article]
4. Thomsen C, et al. Differential effects of saturated and monounsaturated fatty acids on postprandial lipemia and incretin responses in healthy subjects. Am J Clin Nutr. 1999;69:1135–43.

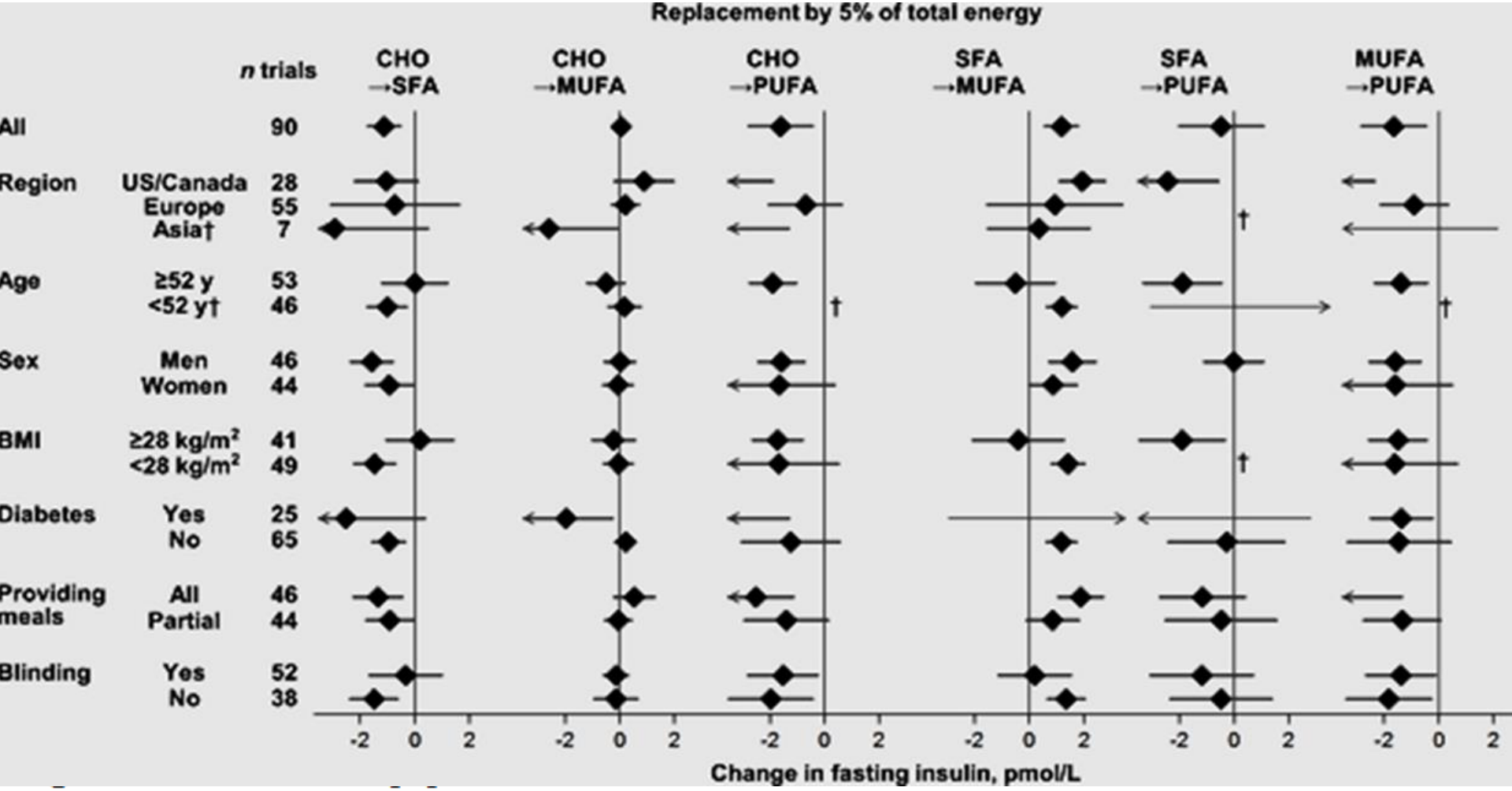
# Intervenčné štúdie jednoznačne dokumentovali, že nasýtené tuky zvyšujú IR nalačno aj postprandiálne

1. Náhrada nasýtených tukov za nenasýtené zlepšuje inzulínovú senzitivitu [1-2].
2. Niekoľko ďalších štúdii preukázalo, že nenasýtené tuky zlepšujú IR nalačno aj postprandiálne, ale mechanizmus nie je presne známy [3].
3. Štúdia PREDIMED preukázala, že nenasýtené tuky zlepšujú IR a znižujú incidenciu DM II. [4].


1. Vessby B, et al. Substituting dietary saturated for monounsaturated fat impairs insulin sensitivity in healthy men and women: The KANWU Study. Diabetologia. 2001;44:312–9.
2. Summers LKM (2002) Substituting dietary saturated fat with polyunsaturated fat changes abdominal fat distribution and improves insulin sensitivity. Diabetologia 45: 369–377
3. Wang X, Chan CB. n-3 polyunsaturated fatty acids and insulin secretion. J Endocrinol. 2015;224:R97–106.
4. Salas-Salvado J, et al. ; PREDIMED Study Investigators. Reduction in the incidence of type 2diabetes with the Mediterranean diet: results of the PREDIMED-Reus nutrition intervention randomized trial. Diabetes Care. 2011;34:14–9.

# Effects on fasting insulin of isocaloric replacements between carbohydrate (CHO), saturated fat (SFA), monounsaturated fat (MUFA), and polyunsaturated fat (PUFA) in randomised controlled feeding trials.

Imamura F, et al. PLoS Med 2016:13: e1002087.



# Pacienti s NASH mali vyšší príjem príjem SFA a chol a nižší príjem PUFA

HEPATOLOGY 2003;37:909-916

## Dietary Habits and Their Relations to Insulin Resistance and Postprandial Lipemia in Nonalcoholic Steatohepatitis

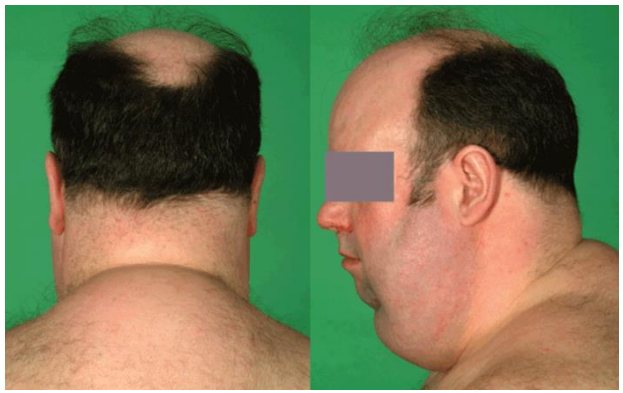
Giovanni Musso,[1] Roberto Gambino,[1] Franco De Michieli,[1] Maurizio Cassader,[1] Mario Rizzetto,[2] Marilena Durazzo,[1] Emanuela Fagà,[1] Barbara Silli,[1] and Gianfranco Pagano[1]

The relations of dietary habits to insulin sensitivity and postprandial triglyceride metabolism were evaluated in 25 patients with nonalcoholic steatohepatitis (NASH) and 25 age-, body mass index (BMI)-, and gender-matched healthy controls. After a 7-day alimentary record, they underwent a standard oral glucose tolerance test (OGTT), and the insulin sensitivity index (ISI) was calculated from the OGTT; an oral fat load test was also performed in 15 patients and 15 controls. The dietary intake of NASH patients was richer in saturated fat (13.7% ± 3.1% vs. 10.0% ± 2.1% total kcal, respectively, $P = .0001$) and in cholesterol (506 ± 108 vs. 405 ± 111 mg/d, respectively, $P = .002$) and was poorer in polyunsaturated fat (10.0% ± 3.5% vs. 14.5% ± 4.0% total fat, respectively, $P = .0001$), fiber (12.9 ± 4.1 vs. 23.2 ± 7.8 g/d, respectively, $P =$

The dietary intake of NASH patients was richer in saturated fat (13.7% ± 3.1% vs. 10.0% ± 2.1% total kcal, respectively, $P = .0001$) and in cholesterol (506 ± 108 vs. 405 ± 111 mg/d, respectively, $P = .002$) and was poorer in polyunsaturated fat (10.0% ± 3.5% vs. 14.5% ± 4.0% total fat, respectively, $P = .0001$), fiber (12.9 ± 4.1 vs. 23.2 ± 7.8 g/d, respectively, $P = .000$), and antioxidant vitamins C (84.3 ± 43.1 vs. 144.2 ± 63.1 mg/d, respectively, $P = .0001$) and E (5.4 ± 1.9 vs. 8.7 ± 2.9 mg/d, respectively, $P = .0001$).

**Saturated fatty acids in human visceral adipose tissue are associated with increased 11- β-hydroxysteroid-dehydrogenase type 1 expression.**

Petrus P et al. Lipids Health Dis. 2015 ;14:42.






**Hypotetická väzba medzi SFA a expresiou HSD11B1 (11-β-hydroxysteroid-dehydrogenáza typ 1), hlavného regulátora aktivity kortizolu.** SFAs môžu účinkovať ako signálne molekuly a alterovať HSD11B1. Zvýšená expresia HSD11B1 vo viscerálnom tuku (VAT) je spojená so zvýšenou expresiou proteínu enzýmu, čo vedie k zvýšenej konverzii kortizónu na kortizol. Kortizol sa viaže na glukokortikoidový receptor (GR), ktorý reguluje transkripciu , čo má za následok adipogenézu vo VAT, spojenú s o zvýšenou akumuláciou tuku v pečeni v dôsledku zvýšenej lipolýzy tukového tkaniva.

REKTOR
UNIVERZITY KOMENSKÉHO V BRATISLAVE
prof. RNDr. Karol Mičieta, PhD.
a
VEDECKÁ RADA UK

pozývajú

v rámci cyklu
celouniverzitných profesorských prednášok

**na profesorskú prednášku**

**prof. MUDr. Viliama Badu, CSc.**
z Lekárskej fakulty Univerzity Komenského v Bratislave

na tému

**AKO SA DÁ PREDCHÁDZAŤ CHOROBÁM SRDCA A CIEV**


dávka je 3 kg. Slovensko ***zaostáva za odporúčanou spotrebou masti o 0,5 kg, teda -16,7 %! Napriek tomu verejnosti dobre známy odborník na výživu tvrdí, že bravčovou masťou sa prekrmujeme!*** Zaostávanie v spotrebe masti popri intenzívnej antipropagácii je zrejme aj následok dramatického poklesu domáceho chovu ošípaných. Druhou sledovanou komoditou je spotreba masla. Na Slovensku dosahuje 2,9 kg/obyvateľ/rok, zatiaľ čo odporúčaná spotreba je 2,8 kg! Aj v tomto prípade odporúčanie prekračujeme o 0,1 kg. Keď si však na porovnanie zoberieme ***Francúzsko***, ktoré dlhodobo predstavuje v Európe jednu z vedúcich krajín z hľadiska nízkej srdcovo-cievnej úmrtnosti, konštatujeme, že spotreba masla ***vo Francúzsku***

PLoS One. 2016; 11(10): e0162368. PMCID: PMC5053538
Published online 2016 Oct 6. doi: 10.1371/journal.pone.0162368

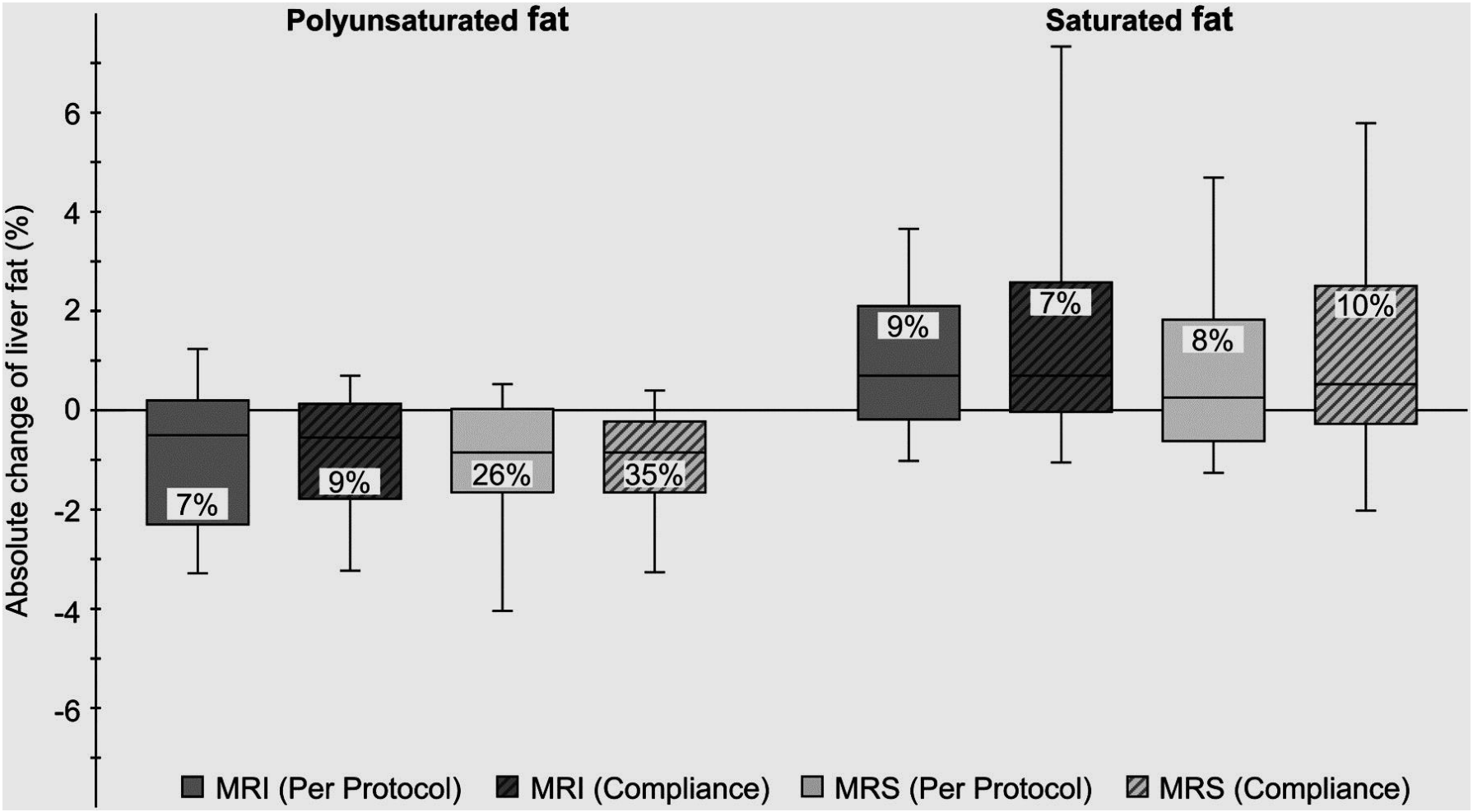
# Effectiveness of Omega-3 Polyunsaturated Fatty Acids in Non-Alcoholic Fatty Liver Disease: A Meta-Analysis of Randomized Controlled Trials

Xi-Xi He,[1] Xiao-Li Wu,[1] Ren-Pin Chen,[1] Chao Chen,[1] Xiao-Gang Liu,[2] Bin-Jiao Wu,[3] and Zhi-Ming Huang[1,*]

This analysis was a systematic review of RCTs investigating the efficacy of ω-3 PUFA in the treatment of NAFLD. Seven RCTs involving 227 patients in the experimental groups and 215 in the control groups were included in the analysis. Our results support the use of ω-3 PUFA supplementation as a practical and effective treatment for NAFLD, especially for reducing triglycerides. This conclusion is the same as that reached by Parker et al. [22] who first reported ω-3 PUFA supplementation in humans with NAFLD. In the analysis by Parker et al., ω-3 PUFA therapy had a significant beneficial effect on AST and a tendency toward a beneficial effect on ALT, but these effects were not significant after analysis of only RCT data. In this review, ω-3 PUFA therapy had a significant effect on liver fat, whether only RCT data (ES: −0.96, 95% CI: −0.43 to −1.48; $p<0.001$) or all the trials (ES: −0.97, 95% CI: −0.58 to −1.35; $p<0.001$) were included. In a previous meta-analysis (2010) [23], ω-3 PUFA also improved biochemical and radiological markers of NAFLD in a small subgroup of RCTs. Our review has clinical value as the results were extracted from RCTs. We also analyzed more markers, including primary results for ALT, AST, GGT, TC, TG, LDL-C and HDL-C and secondary results including fasting glucose, $HOMA_{IR}$, adiponectin, liver fat and fibrosis. We also analyzed subgroups according to the treatment time and the dose of ω-3 PUFA therapy.

# Effects of n−6 PUFAs compared with SFAs on liver fat, lipoproteins, and inflammation in abdominal obesity: a randomized controlled trial

Bjermo H et al. Am J Clin Nutr 2012;95:1003-1012




**Changes in absolute and relative liver fat content during the intervention.**

**Autori meta-analýzy konštatujú, že t.č. nie je možné robiť závery pre klinickú prax, lebo súčasné poznatky o tom, či zvýšený alebo znížený príjem PUFA ovplyvňuje riziko CVK a ich rizik. faktorov sú nedostačujúce**

## Omega 6 fatty acids for the primary prevention of cardiovascular disease (Review)

Cochrane Library
Cochrane Database of Systematic Reviews

Al-Khudairy L, Hartley L, Clar C, Flowers N, Hooper L, Rees K

Cochrane Database Syst Rev. 2015 Nov 16;(11):CD011094.

### Implications for practice

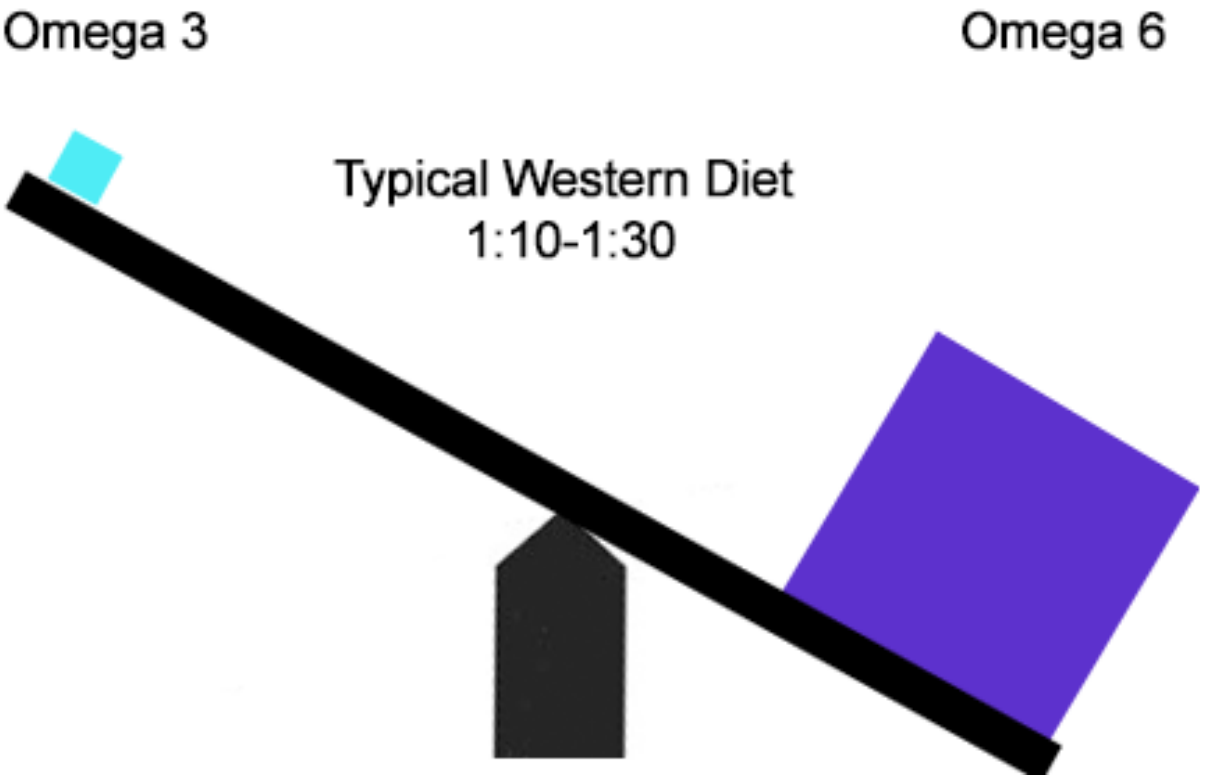
We have avoided making implications for practice as there is currently insufficient evidence for the effects of increased or decreased omega 6 intake on CVD events and CVD risk factors.

### Implications for research

Few trials met the inclusion criteria of this Cochrane review. All included trials were small, relatively short term, and at some risk of bias. None reported our primary outcomes. There is a need for large, well-designed, long term RCTs to assess the effect of increased or reduced omega 6 intake on cardiovascular events and risk factors to determine the effectiveness of either intervention for the primary prevention of CVD.

# Nutričná príčina tichého zápalu

1. Zvýšený príjem  rafinovaných sacharidov
2. Zvýšený príjem rastlinných olejov bohatých na n-6 PUFA
3. Znížený príjem n-3 PUFA



*Hepatology Research* 2015; 45: 533–539 doi: 10.1111/hepr.1238

***Original Article***

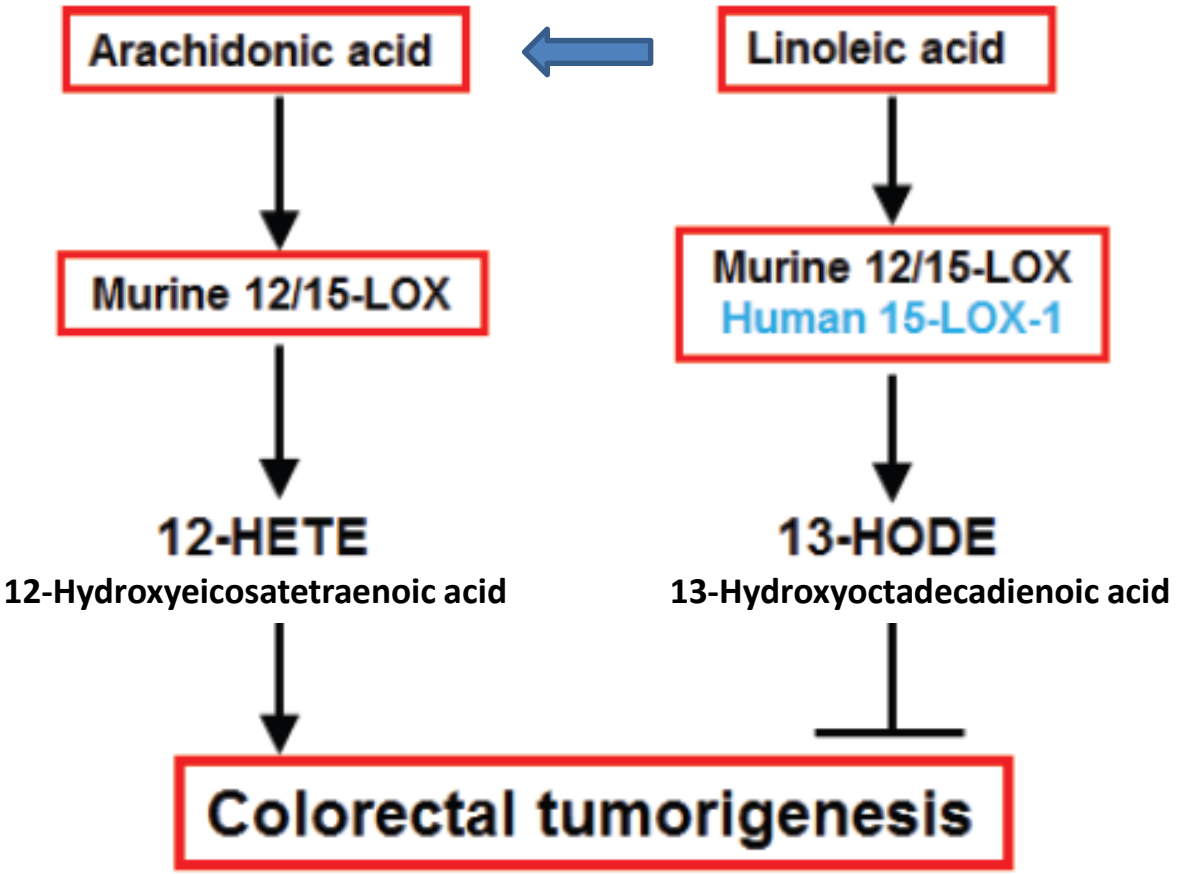
# Eicosapentaenoic acid/arachidonic acid ratio as a possible link between non-alcoholic fatty liver disease and cardiovascular disease

Tomokazu Ishitobi,[1] Hideyuki Hyogo,[1] Hiromi Kan,[1] Akira Hiramatsu,[1] Koji Arihiro,[2] Hiroshi Aikata[1] and Kazuaki Chayama[1]

*Conclusion:* EPA/AA ratio was lower in NAFLD, especially in younger NAFLD patients. Considering the high mortality from CVD in NAFLD patients, low EPA/AA ratio in young age may influence the increased prevalence of CVD in their older age. EPA/AA ratio is suggested to be a possible link between NAFLD and CVD, and would become a useful marker for CVD in NAFLD.

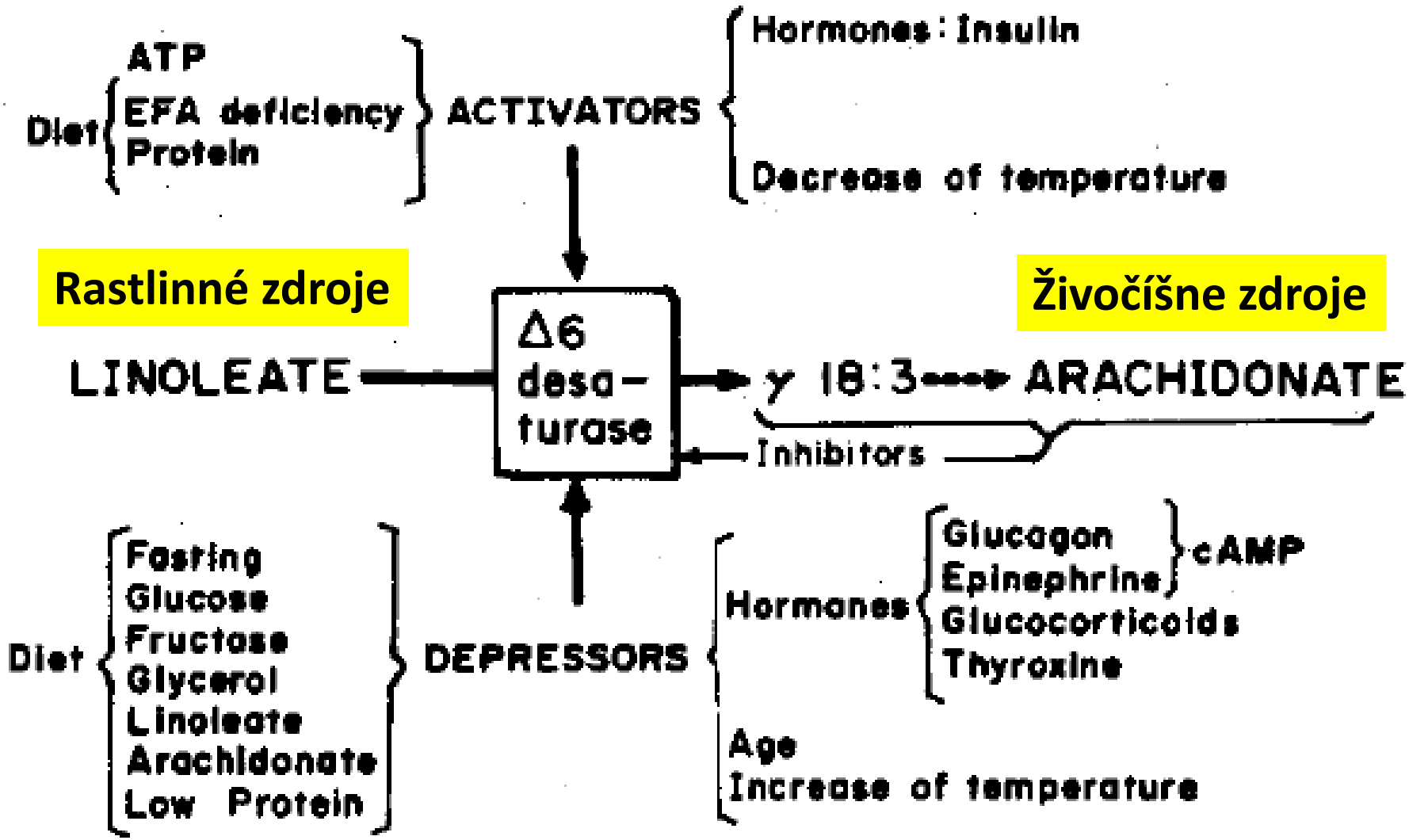
# 12/15 lipoxygenase regulation of colorectal tumorigenesis is determined by the relative tumor levels of its metabolite 12-HETE and 13-HODE in animal models

Jian Chang[1,3,*], Li Jiang[1,4,*], Yinqiu Wang[1], Bing Yao[1], Shilin Yang[1], Bixiang Zhang[3] and Ming-Zhi Zhang[1,2,5]




Oncotarget. 2015; 6: 2879–2888.

# Aktivátory a inaktivátory desaturácie esenciálnych MK




Brenner RR - Progress in lipid research, 1981

Syllabus

1. Úvod
2. Epidemiológia
3. Endokrinné disruptory
4. Sacharidy
5. Tuky
6. **Bielkoviny**
7. Záver

Journal of Hepatology 47 (2007) 711–717

# Long term nutritional intake and the risk for non-alcoholic fatty liver disease (NAFLD): A population based study☆

Shira Zelber-Sagi[1,3,†], Dorit Nitzan-Kaluski[2,3], Rebecca Goldsmith[2], Muriel Webb[1], Laurie Blendis[1], Zamir Halpern[1,3], Ran Oren[1,3,*]

[1]*The Liver Unit, Department of Gastroenterology, Tel Aviv Sourasky Medical Center, Tel Aviv 64239, Israel*
[2]*The Food and Nutrition Administration, Ministry of Health, 2 Ben Tabai St. Jerusalem, Israel*
[3]*The Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv 69978, Israel*

***Background/Aims*: Weight loss is considered therapeutic for patients with NAFLD. However, there is no epidemiological evidence that dietary habits are associated with NAFLD. Dietary patterns associated with primary NAFLD were investigated.**

***Methods*: A cross-sectional study of a sub-sample ($n$ = 375) of the Israeli National Health and Nutrition Survey. Exclusion criteria were any known etiology for secondary NAFLD. Participants underwent an abdominal ultrasound, biochemical tests, dietary and anthropometric evaluations. A semi-quantitative food-frequency questionnaire was administered.**

The results of this study show that a higher intake of soft drinks and of meat was significantly associated with an increased risk for NAFLD

Journal of Hepatology 47 (2007) 711–717

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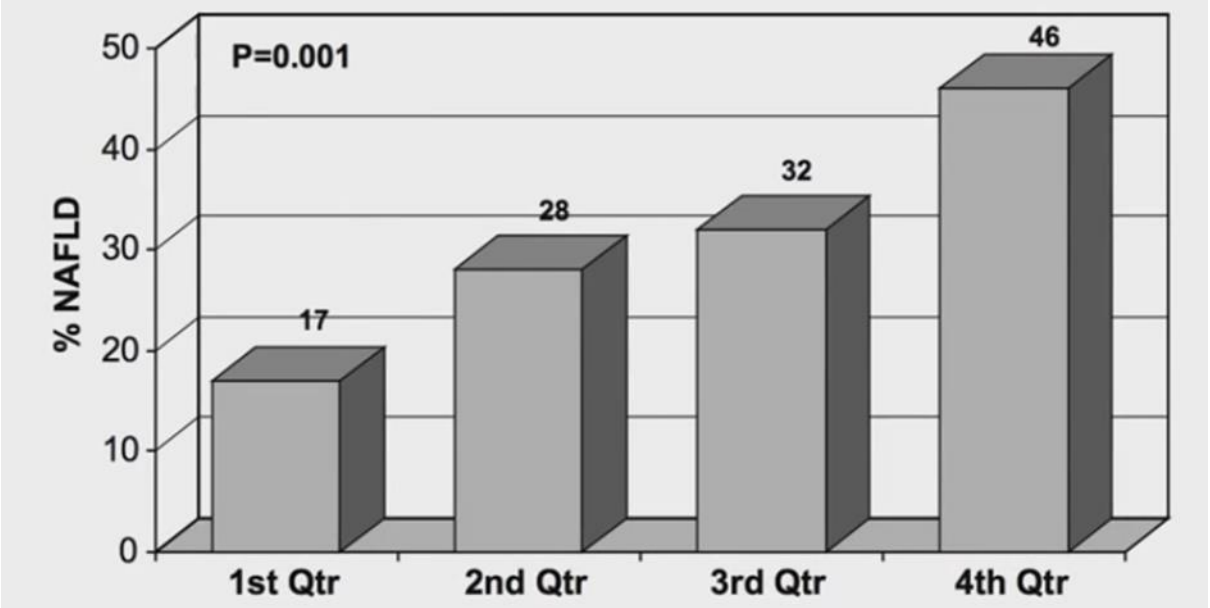
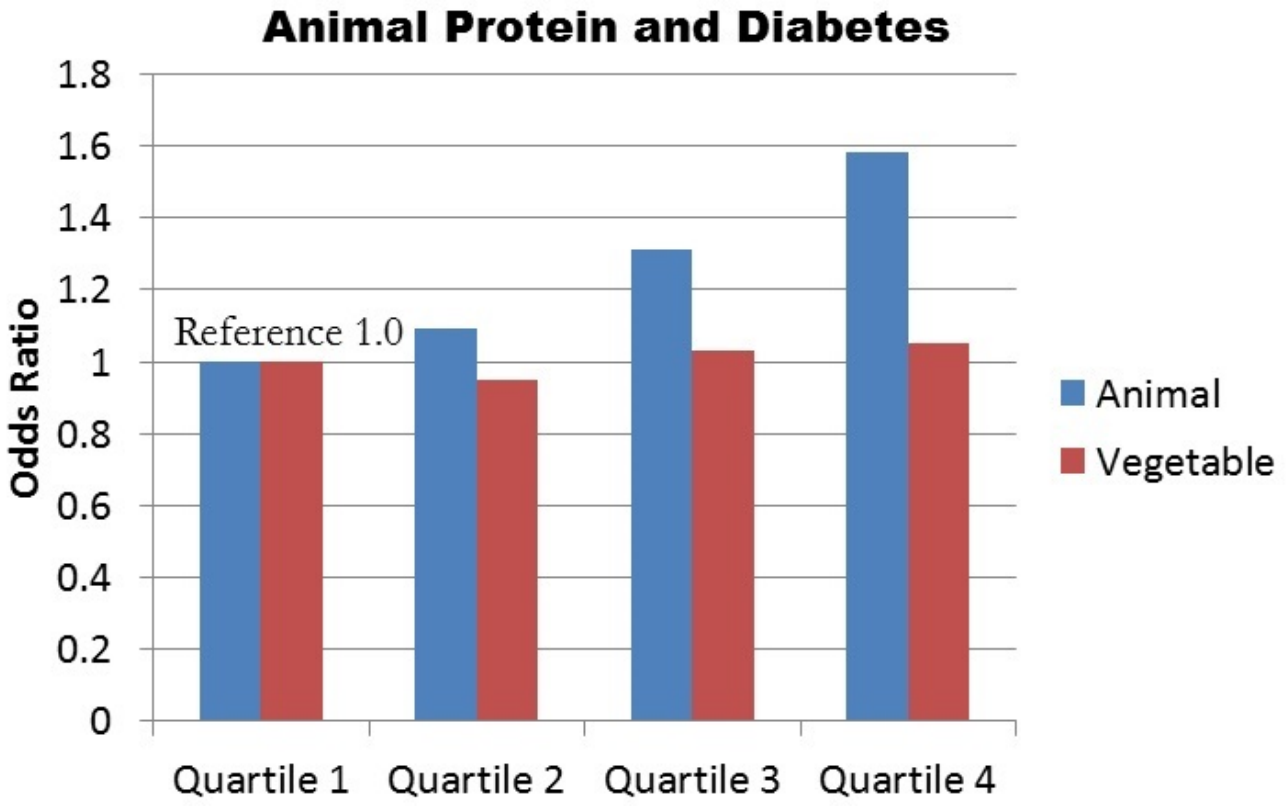



**Fig. 3. Percent of NAFLD diagnosed subjects according to quartiles of meat protein intake. The percent of subjects diagnosed as NAFLD in the fourth quartile of meat protein intake was 46% compared to 17% in the first quartile ($P = 0.001$).**

**Dietary intake of total, animal, and vegetable protein and risk of type 2 diabetes in the European Prospective Investigation into Cancer and Nutrition (EPIC)-NL study.**

Sluijs I et al. Diabetes Care. 2010 Jan;33(1):43-8.




CONCLUSIONS:Diets high in animal protein are associated with an increased diabetes risk. Our findings also suggest a similar association for total protein itself instead of only animal sources. Consumption of energy from protein at the expense of energy from either carbohydrates or fat may similarly increase diabetes risk. This finding indicates that accounting for protein content in dietary recommendations for diabetes prevention may be useful.

European Journal of Clinical Nutrition (2005) 59, 393–398

0954-3007/05 $30.00
www.nature.com/ejcn

# ORIGINAL COMMUNICATION

## High intakes of milk, but not meat, increase s-insulin and insulin resistance in 8-year-old boys

C Hop

[1]*Depart*

*Frederik*

*Advanc*

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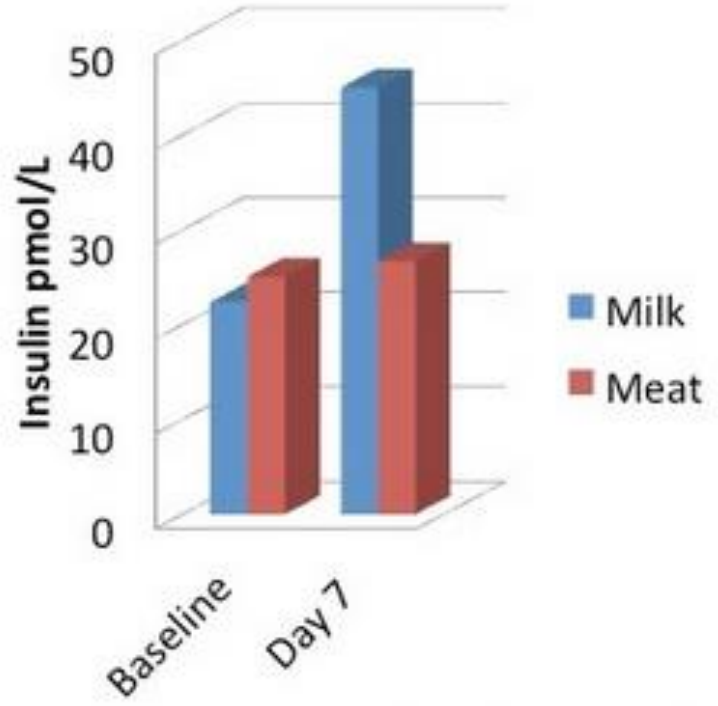
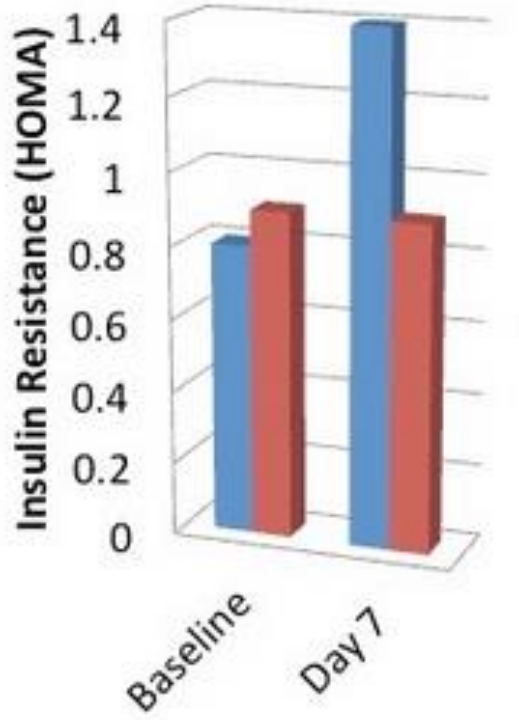
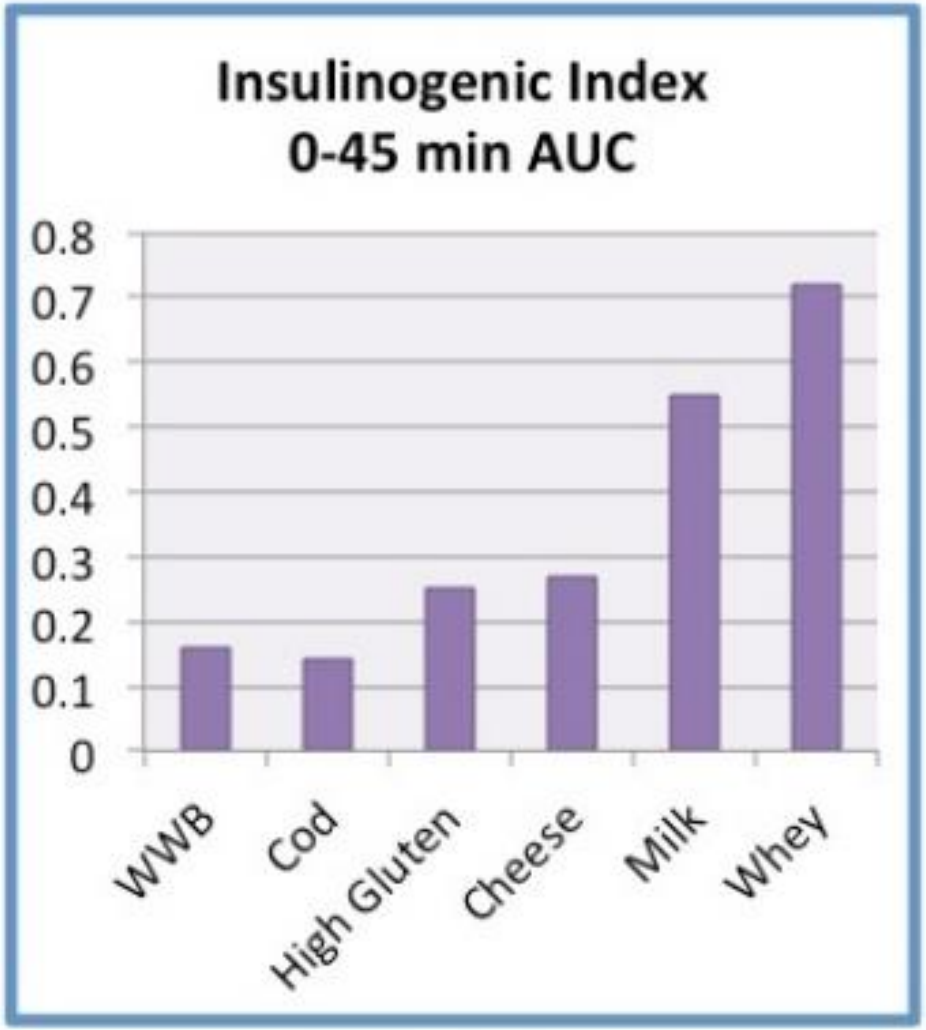


**Glycemia and insulinemia in healthy subjects after lactose-equivalent meals of milk and other food proteins: the role of plasma amino acids and incretins.**

Nilsson M et al. Am J Clin Nutr. 2004 Nov;80(5):1246-53.



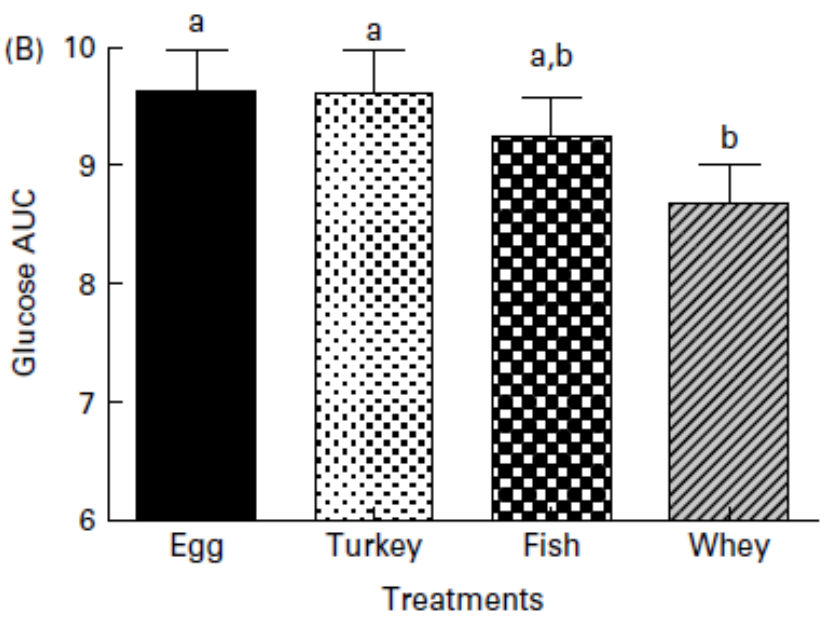

AmJ Clin Nutr 2004;80:1246 –53 Nilsson M

RESULTS: Reconstituted milk powder and whey had substantially lower postprandial glucose areas under the curve (AUCs) than did the bread reference (-62% and -57%, respectively). Whey meal was accompanied by higher AUCs for insulin (90%) and GIP (54%).

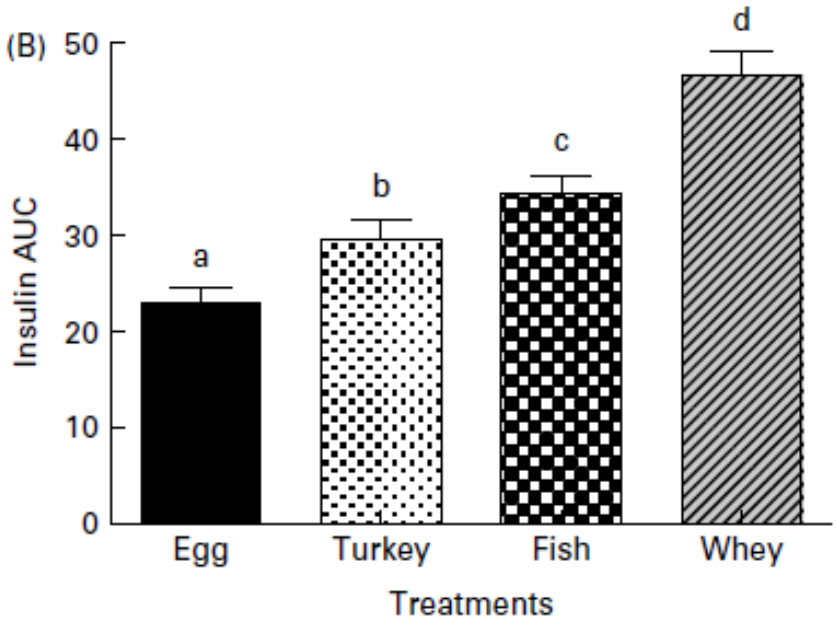
CONCLUSIONS: It can be concluded that food proteins differ in their capacity to stimulate insulin release, possibly by differently affecting the early release of incretin hormones and insulinotropic amino acids. Milk proteins have insulinotropic properties; the whey fraction contains the predominating insulin secretagogue.

# The acute effects of four protein meals on insulin, glucose, appetite and energy intake in lean men.

Pal S, Ellis V. Br J Nutr. 2010 Oct;104(8):1241-8.




**The effect of four different protein test meals on postprandial glucose.**




**The effect of four different protein test meals on postprandial insulin.**

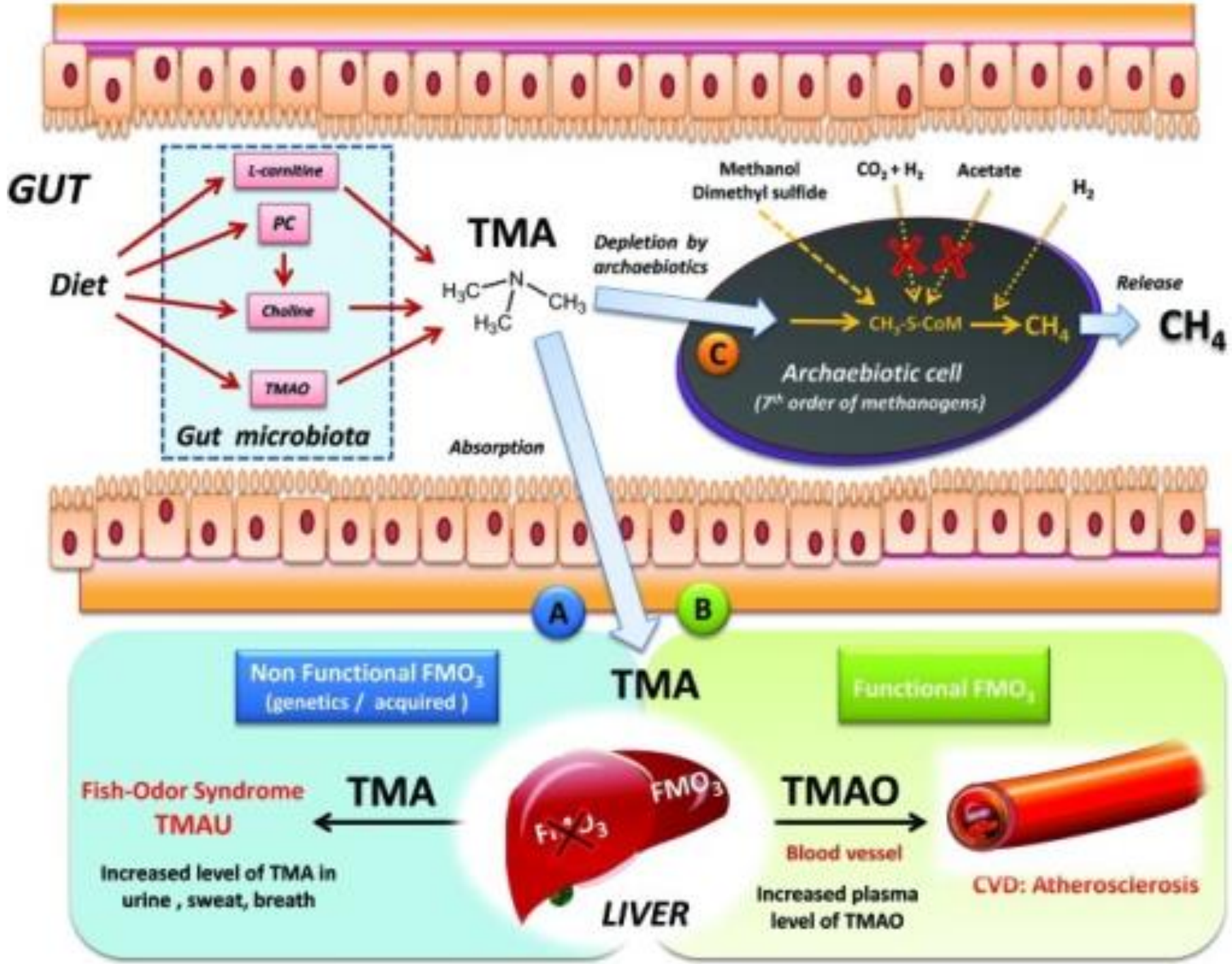
*Cell Rep*. 2016 July 12; 16(2): 520–530. doi:10.1016/j.celrep.2016.05.092.

# Decreased consumption of branched chain amino acids improves metabolic health

**Luigi Fontana**[#1,2,3], **Nicole E. Cummings**[#4,5,6], **Sebastian I. Arriola Apelo**[4,5], **Joshua C. Neuman**[4,5,7], **Ildiko Kasza**[8], **Brian A. Schmidt**[4,5], **Edda Cava**[1,9], **Francesco Spelta**[1,10], **Valeria Tosti**[1,10], **Faizan A. Syed**[4,5], **Emma L. Baar**[4,5], **Nicola Veronese**[1,11], **Sara E. Cottrell**[4,5,12], **Rachel J. Fenske**[4,5,7], **Beatrice Bertozzi**[1], **Harpreet K. Brar**[4,5], **Terri Pietka**[1], **Arnold D. Bullock**[13], **Robert S. Figenshau**[13], **Gerald L. Andriole**[13], **Matthew J. Merrins**[4,5,14], **Caroline M. Alexander**[8], **Michelle E. Kimple**[4,5,6,7,15], and **Dudley W. Lamming**[4,5,6,7,12]

## Abstract

Protein restricted, high carbohydrate diets improve metabolic health in rodents, yet the precise dietary components that are responsible for these effects have not been identified. Further, the applicability of these studies to humans is unclear. Here, we demonstrate in a randomized controlled trial that a moderately protein restricted (PR) diet also improves markers of metabolic health in humans. Intriguingly, we find that feeding mice a diet specifically reduced in branched chain amino acids (BCAAs) is sufficient to improve glucose tolerance and body composition equivalently to a PR diet, via metabolically distinct pathways. Our results highlight a critical role for dietary quality at the level of amino acids in the maintenance of metabolic health, and suggest that diets specifically reduced in BCAAs, or pharmacological interventions in this pathway, may offer a translatable way to achieve many of the metabolic benefits of a PR diet.


GUT
Diet
L-carnitine
PC
Choline
TMAO
Gut microbiota
TMA
Depletion by archaebiotics
Methanol
Dimethyl sulfide
$CO_2 + H_2$
Acetate
$H_2$
$CH_3$-S-CoM
$CH_4$
Release
$CH_4$
C
Archaebiotic cell
(7th order of methanogens)
Absorption
A
B
Non Functional $FMO_3$
(genetics / acquired )
TMA
Functional $FMO_3$
Fish-Odor Syndrome
TMAU
TMA
$FMO_3$
LIVER
TMAO
Blood vessel
Increased level of TMA in urine , sweat, breath
Increased plasma level of TMAO
CVD: Atherosclerosis

Syllabus

1. Úvod
2. Epidemiológia
3. Endokrinné disruptory
4. Pomer makroživín
5. Sacharidy
6. Tuky
7. Bielkoviny
8. **Záver**

# Sacharidy horšie, ako saturované tuky

**Reduction in saturated fat intake for cardiovascular disease.**

Hooper L et al , Cochrane Database Syst Rev. 2015;10;6:

- 15 RCT (spolu 59,000 účastníkov) zahrňujúcich rôzne intervencie zamerané na redukciu saturovaných tukov (SFA) v strave.

- **Náhrada SFA tukmi s vysokým obsahom nenasýtených mastných kyselín (PUFA) sa zdá byť užitočnou stratégiou, ale náhrada za sacharidy je horšou alternatívou.** Účinok MUFA bol nejasný, pretože zahrňoval iba jednu malú štúdiu.

- Rizikové skupiny by mali redukovať SFA v strave a čiastočne ich nahradiť PUFA.

- **Ideálny typ PUFA zatiaľ nie je jasný.**

# Mediteriánska strava zlepšuje NAFLD

Clinical Nutrition 33 (2014) 678–683

## Adherence to the Mediterranean diet is associated with the severity of non-alcoholic fatty liver disease☆

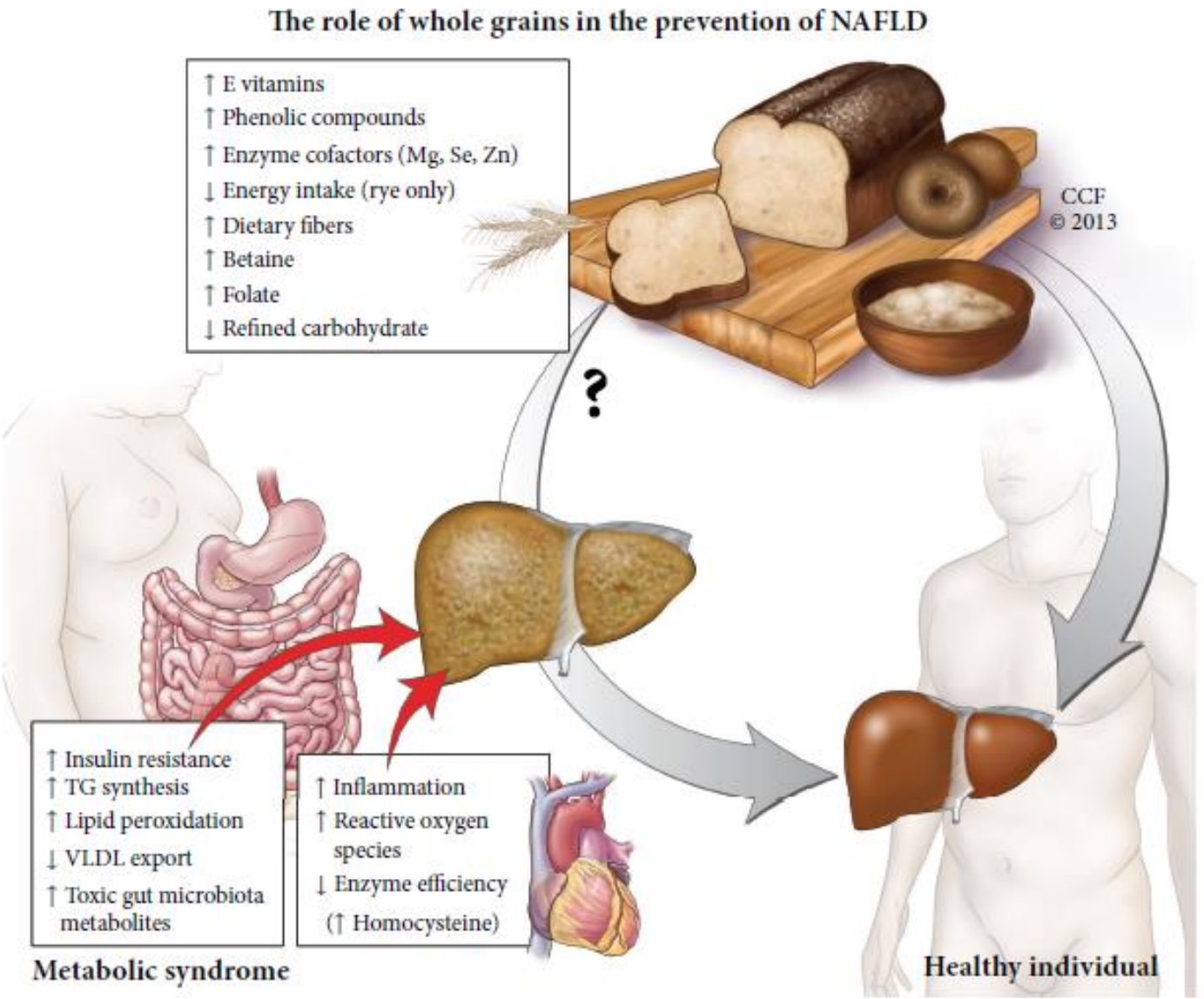
Meropi D. Kontogianni [a, *], Nafsika Tileli [a], Aikaterini Margariti [b], Michael Georgoulis [a], Melanie Deutsch [b], Dina Tiniakos [c], Elisabeth Fragopoulou [a], Rodessa Zafiropoulou [b], Yannis Manios [a], George Papatheodoridis [b]

Mediterranean diet, as described by the index used in the present study,[11] is a pattern characterized by high consumption of foods such as fruits, vegetables, non-refined cereals, legumes and potatoes

Mediterranean diet is a pattern with clear anti-inflammatory and anti-oxidant effects

# Increasing Whole Grain Intake as Part of Prevention and Treatment of Nonalcoholic Fatty Liver Disease

Alastair B. Ross et al. Int J Endocrionol 2013;2013



**Ďakujem za pozornosť**