The Effects of Dietary Fat Intake on the Composition and Function of HDL in Relation to Cardiovascular Health

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Class: Issues in Nutrition and Health, NTR 338W

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Outline

Introduction:	History of the Diet-Heart Hypothesis and Dietary Guidelines, the Mediterranean Diet, meet the characters and the games they play
Hypothesis:	What is the main question being asked?
Methods:	How did I research this topic?
Results:	What did the research tell us?
Discussion:	What is the main storyline?
Conclusions:	What does the data suggest?
Future Research:	Which experiments to conduct next?

Introduction – How we got here!

- Ancel Keys – Seven Countries Study: tracked diet and disease-specific risk
- Diet-Heart Hypothesis – Dietary saturated fat, cholesterol and heart disease
- US Dietary Guidelines – Limit all fats, especially saturated fat and cholesterol
- Mediterranean Diet – predominant fat oleic acid, monounsaturated from EVOO
- Dietary fat choices – affect the composition and functionality of HDL
- Composition of the diet – pro or antioxidant environment

The Mediterranean Diet

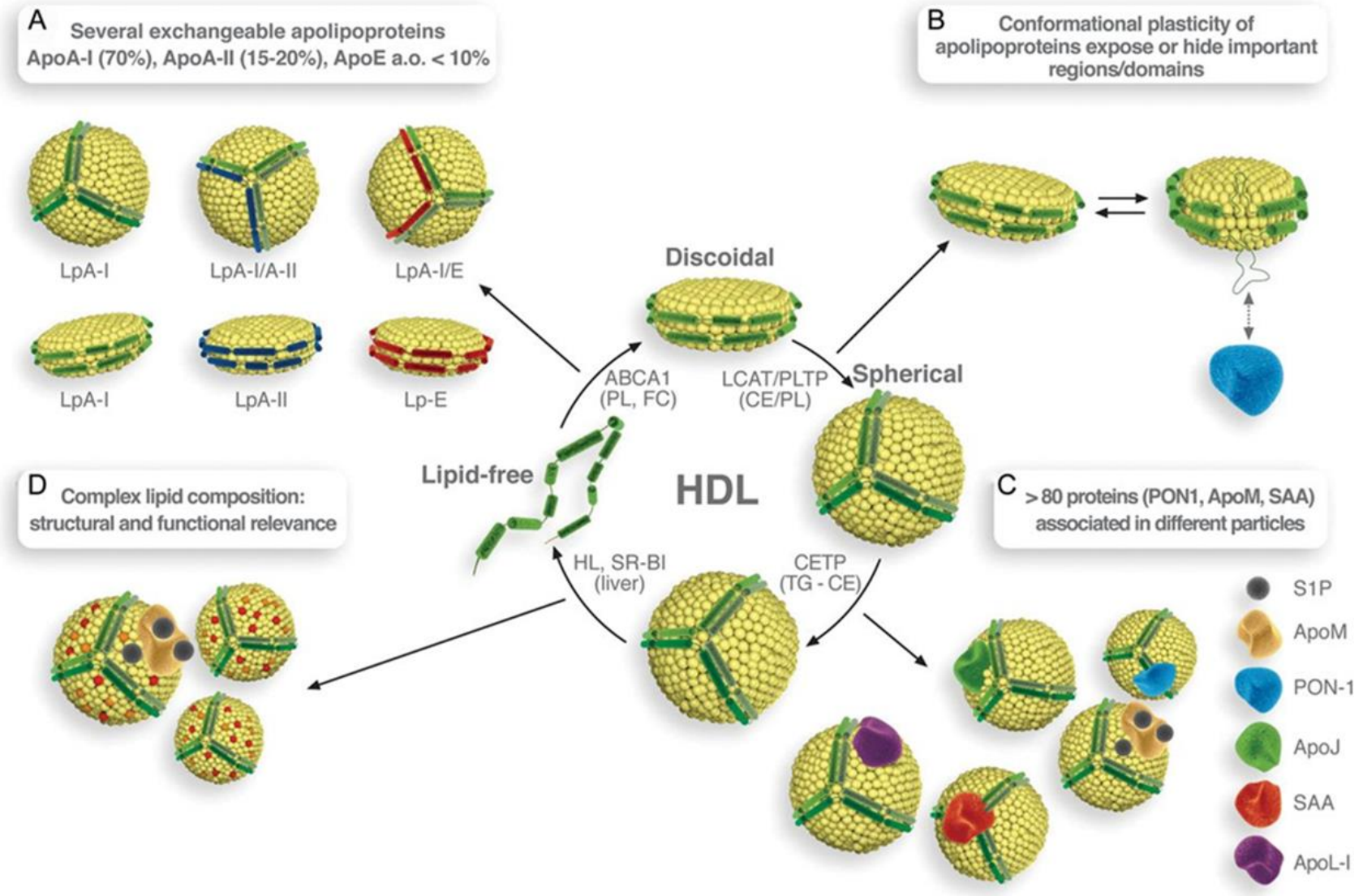
Eat less of the apex: whole grains, poultry, red meat, eggs, and dairy.

Eat more of the base: fruits, vegetables, nuts, seeds, EVOO, fish.

Introduction – Meet the players

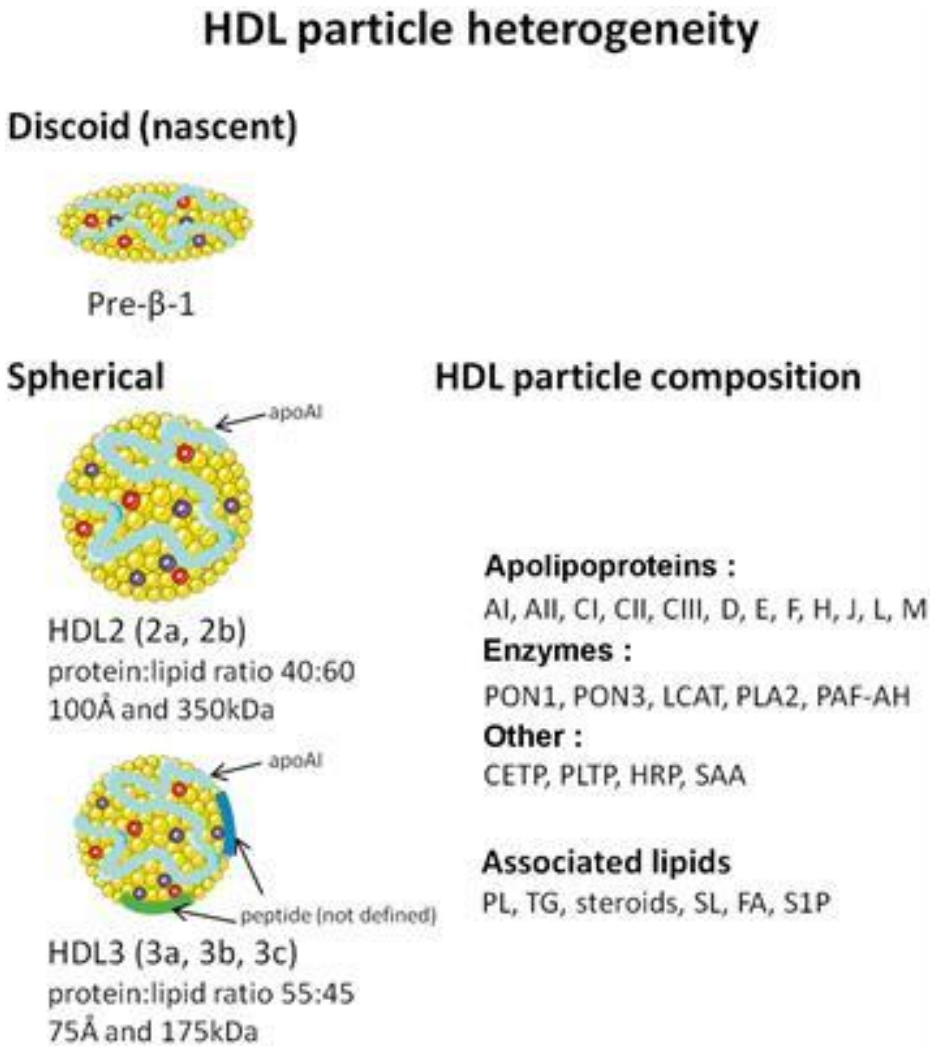
- Functions of lipoproteins and related enzymes:
  - HDL, MPO, PON1, *N*-Hcy
  - forward cholesterol transport (FCT) - dominated by LDL
  - reverse cholesterol transport (RCT) - dominated by HDL
  - cholesterol efflux capacity (CEC) - function of HDL
  - endothelial cell (EC) repair – impacted by HDL, MPO, PON1, *N*-Hcy

HDL – Dynamic Model



This is a dynamic system with exchangeable apolipoproteins and contents impacting the tertiary structure of HDL and its function.

HDL Composition



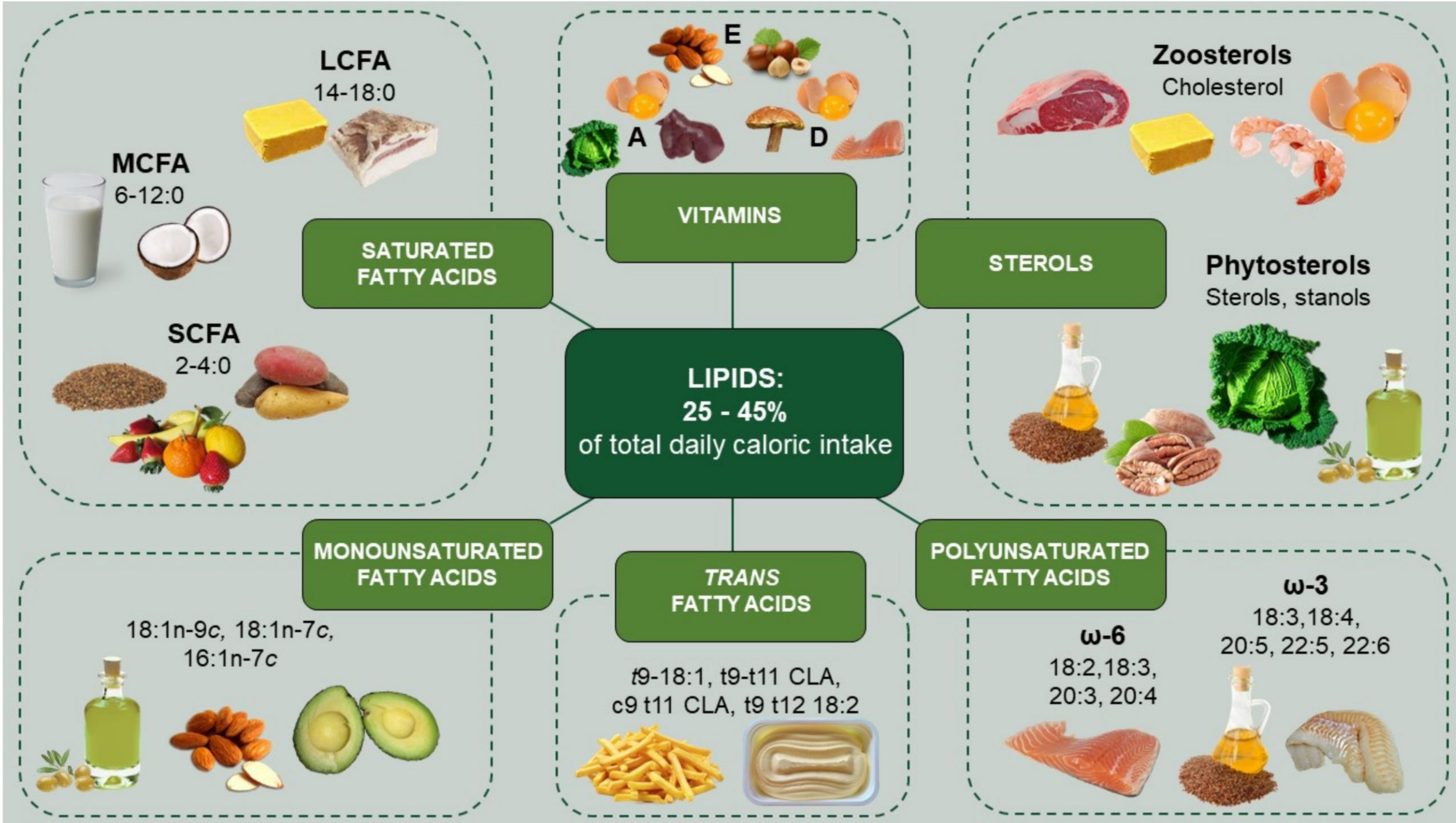
HDL is constantly changing. Diet and the oxidative environment are two drivers of HDL composition and function

Questions being asked

- Are HDL-C and LDL-C the primary drivers in CVD?
- Does HDL composition relate to its function?
- Does the oxidative environment play a pivotal role in HDL composition?
- How does HDL functionality affect RCT, CEC, and EC repair?
- Can CVR and CVD be prevented or reversed?

Hypothesis

Does fat consumption affect the composition of HDL altering its function and ability to perform RCT, CEC, and EC repair impacting CVR?


LIPIDS:
25 - 45%
of total daily caloric intake
SATURATED FATTY ACIDS
LCFA
14-18:0
MCFA
6-12:0
SCFA
2-4:0
VITAMINS
E
A
D
STEROLS
Zoosterols
Cholesterol
Phytosterols
Sterols, stanols
MONOUNSATURATED FATTY ACIDS
18:1n-9c, 18:1n-7c,
16:1n-7c
TRANS FATTY ACIDS
t9-18:1, t9-t11 CLA,
c9 t11 CLA, t9 t12 18:2
POLYUNSATURATED FATTY ACIDS
ω-6
18:2,18:3,
20:3, 20:4
ω-3
18:3,18:4,
20:5, 22:5, 22:6

Methods

- Paper selection
  - Inclusion criteria:
    - English language papers
    - Published within the last 5 years
    - Used PubMed database
    - Used specific keywords for each section
  - Exclusion criteria:
    - Non-English language papers
    - Published before 2016
    - Review papers

Methods

Study	Type	Title	Sample Size	M/F Age range Condition	Country
Guasch-Ferre et al.	Observational prospective cohort	Olive Oil intake and risk of cardiovascular disease and mortality in the PREDIMED study	N = 7216	Men, women at high CVR, 55-80 years old	Spain
Hernaez et al.	Two cross-sectional baseline samples from PREDIMED	Role of HDL function and LDL atherogenicity on cardiovascular risk: A comprehensive examination	N = 296	Men, women, HTN, diabetes, dyslipidemia, obese. Treated, untreated 35–74 years old	Spain
Otrante et al.	Quasi-experimental before and after design.	Extra Virgin Olive Oil prevents the age-related shifts of the distribution of HDL subclasses and improves their functionality	N = 84	Men, women, healthy, 27-67 years old	Canada
Girona et al.	Cross-sectional study	HDL triglycerdies: A new marker of metabolic and cardiovascular risk	N = 502	Men, women metabolic alteration, untreated, median age 61	Spain
Kameda et al.	In vitro wound healing assays	Effect of myeloperoxidase oxidation and *N*-homocysteinylation of high-density lipoprotein on endothelial repair function	N = 7	No gender or age data, varying levels of troponin I	Japan
Variji et al.	Cross-sectional study	The combined utility of myeloperoxidase (MPO) and paraoxonase (PON1) as two important HDL-associated enzymes in coronary artery disease: Which has a stronger predicative role?	N = 174	Men, women, CAD mean age 57.6 years old, non-CAD mean age 52 years old	Iran

Results

Guasch-Ferre et al.	
OO in highest tertile (mean 56.9g/d) decreased CVR	35% (HR; 0.65; 95% CI; 0.47 to 0.89)
EVOO in highest tertile (mean 56.9g/d) decreased CVR	39% (HR: 0.61: 95% CI; 0.44 to 0.85)
Each 10g/d EVOO consumed	Reduced CVD 10%, reduced CV mortality 7%
Highest tertile total OO at baseline	34% lower risk of major CV event

Hernaez et al.	
High CVR risk score group	low CEC, high HDL oxidation, high TG rich HDL core (P trend <0.05, all)
High CVR risk score group	low values of HDL2/HDL3 ratio (smaller HDL size) (P = 0.002)

Results

Otrante et al.	
Older age group (mean age: 70.72 ± 5.6 years) vs younger age group, (mean age: 31.81 ± 6.79 years)	lower levels of CEC at 11.12% ($p<0.001$)
After 12 weeks 25ml/d EVOO CEC	older age group increased approximately 8% ($p< 0.02$)
After 12 weeks 25ml/d EVOO CEC	significantly improved for all participants by 7.12% ($p< 0.03$)
Older age group, after 12 weeks 25 ml/d EVOO CEC	significantly lower (6.91%, $p< 0.03$) than younger age group
CEC significantly and negatively associated with age Correlation disappeared after 12 weeks 25 ml/d EVOO	($r = -0.28$ and $p< 0.003$) ($r = -0.012$ and $p< 0.24$)
Positive correlation between CEC and L-HDL levels Inverse correlation between CEC and S-HDL levels	($r = 0.35$, $p<0.001$) ($r = -0.27$, $p<0.01$)

Results

Girona et al.	
HDL-TG positively correlated with total TG	(r = 0.652, p<0.0001)
HDL-TG positively correlated with CETP	(r = 0.264, p<0.001)
HDL-TG negatively correlated with HDL-C	(r = -0.135, p<0.002)
CETP negatively correlated with HDL-C	(r = -0.110, p<0.022)
Patients with carotid plaques (32.8%) higher HDL-TG negatively correlated with HDL-C	(p<0.05) (p=0.05)

Results

Kameda et al.	
Normal HDL increased EC migration	123.4 ± 15.4% relative to control (p = 0.007)
MPO-oxidized HDL did not significantly alter EC migration	97.8 ± 17.5%, relative to control (p = 0.003)
MPO alone, EC migration	was unaffected
MPO-oxidized HDL decreased migration	78.9 ± 12.3% of normal HDL (p <0.05)
N-Hcy HDL significantly increased EC migration	at 1 and 10 nM relative to control by 144.8 ± 38.8% and 129.1 ± 25.5%, respectively (p <0.05)
HDL induced EC migration	162.0 ± 76.9% of the control value (p <0.05)
Patient HDL increased migration vs. healthy subjects	103.1 ± 12.1% of the control value (p = 0.052)
HDL from healthy subjects increased EC migration	120.9 ± 9.6% of the control value (p <0.05)

Results

Variji et al.	
PON1 activity was significantly lower in CAD patients	(p = 0.007)
CAD patients had a significantly higher MPO/PON1 ratio than non-CAD subjects	(p = 0.02)
Predictive values: PON1 and MPO/PON1 are better at detecting CAD patients than MPO alone	 (AUC = 61%, p = 0.003) (AUC = 60%, p = 0.01) (AUC = 50%, p = 0.42)

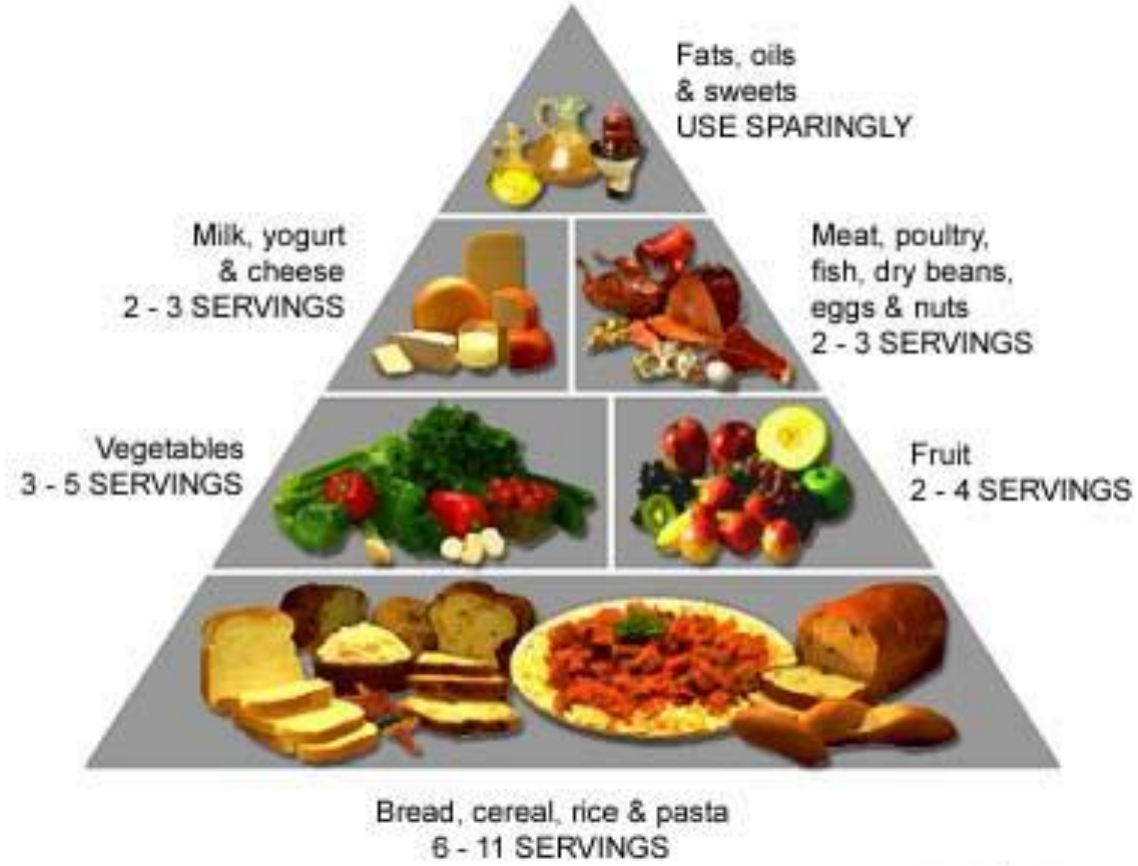
Discussion

- Type of fat intake has a compositional effect on HDL which is correlated with HDL function, RCT, and EC repair
- Increasing MUFAs from EVOO promote HDLs anti-atherogenic effects, leads to efficient CEC and EC repair
- EVOO promotes reversal of HDL composition due to ageing
- Oxidative environments, typically associated with diets high in processed foods and simple carbohydrates, diminishes HDLs anti-atherogenic efficiency and leads to a lack of EC repair and eventual plaque formation
- HDL-C appears to be a secondary consideration in CVR compared to HDL functionality, which is dictated by its composition

Conclusion

- Dietary fat composition → HDL composition change
- Dietary composition dictates oxidative environment in the vasculature
- HDL composition → functionality → CVD outcomes via EC repair
- EVOO reverses aging within HDL ↑ RCT, CEC and EC repair ↓ CVR and CVD
- The current Government Guidelines are not fully aligned with science
- We can take steps to minimize CVR and maximize health span

The USDA Food Pyramid



Future Research

- What is the impact of high LDL-P on the effectiveness of fully functional HDL?
- Can LDL be oxidized without affecting the oxidation status of HDL?
- Does LDL-ox create a more pro-atherogenic environment for HDLs that are participating in RCT, CEC and EC repair?

Citations

Guasch-Ferré M, Hu FB, Martínez-González MA, et al. Olive oil intake and risk of cardiovascular disease and mortality in the PREDIMED Study. *BMC Med*. May 13 2014;12:78. doi:10.1186/1741-7015-12-78

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Otrante A, Trigui A, Walha R, Berrougui H, Fulop T, Khalil A. Extra Virgin Olive Oil Prevents the Age-Related Shifts of the Distribution of HDL Subclasses and Improves Their Functionality. *Nutrients*. Jun 29 2021;13(7)doi:10.3390/nu13072235

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