Plant sterols/stanols for cholesterol lowering and prevention of cardiovascular disease

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on behalf of the **International Plant Sterols and Stanols Association (IPSSA)**

Nutrition for management of NCDs
food matters live...
21 - 23 November 2017
ExCeL, London

International Plant Sterols and Stanols Association (IPSSA) – Introduction

- Established in 2015
- Based in and operating from Brussels, Belgium
- Founding (and current) members are leading international companies in plant sterols and stanols
  - Arboris
  - BASF
  - Cargill
  - Raisio
  - Unilever
- IPSSA covers all aspects of the plant sterols and stanols sector
  - B2B (producers of plant sterols, plant stanols, and their esters)
  - B2C (producers of foods with added plant sterols and stanols)
- IPSSA has a global focus

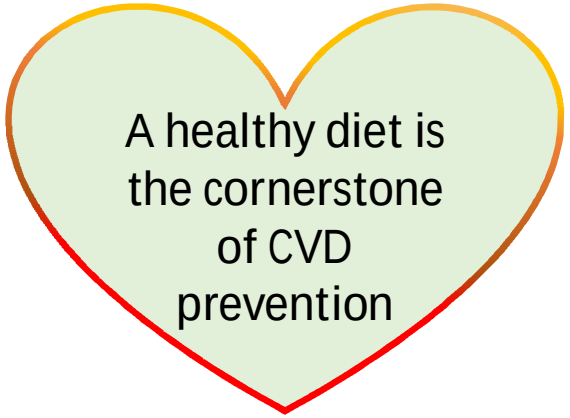
IPSSA - Our mission

1. To educate the **media** and the **public** about the role of a healthy diet and lifestyle in reducing the risk of heart disease
2. To demonstrate in a clear and concise manner how plant sterols and stanols have been **scientifically proven to lower blood LDL-cholesterol**
3. To inform **policymakers** and **influencers** about the safety of plant sterols and stanols as well as their efficacy in lowering blood LDL-cholesterol and thus, their contribution in reducing the risk of heart disease.

The burden of Cardiovascular Disease (CVD)

- CVD is worldwide the leading cause of death in adults
- In Europe, CVD accounts for 45% of all deaths*
- In 2015, there were just under 11.3 million new cases of CVD in Europe and more than 85 million people were living with CVD*
- CVD is a major burden on health care costs with estimated costs to the EU economy of 210 billion Euro per year

- There is however compelling evidence for diet and lifestyle playing an important role in CVD prevention
- With adequate changes in diet and lifestyle, at least 80% of (premature) CVD mortality may be prevented**



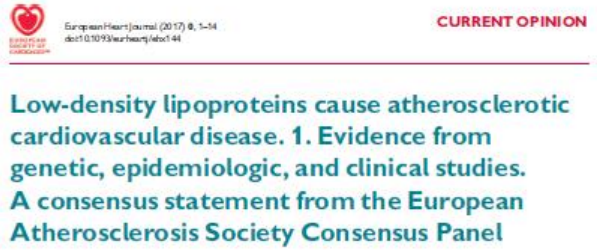
*European Cardiovascular Disease Statistics. 2017 Edition

**Piepoli et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice; Eur Heart J 2016.

Serum LDL-cholesterol - a causal CVD risk factor

- Elevated serum LDL-cholesterol is a known cause of atherosclerotic cardiovascular disease (ASCVD)*
- Causal relationship between LDL-cholesterol and ASCVD is supported by
  - genetic studies
  - epidemiological studies
  - Mendelian randomisation studies
  - randomized control trials
- LDL-cholesterol lowering irrespective of underlying mechanisms/intervention lowers CVD risk

Lowering LDL-cholesterol:
The *lower the better,* and the *earlier the better!*

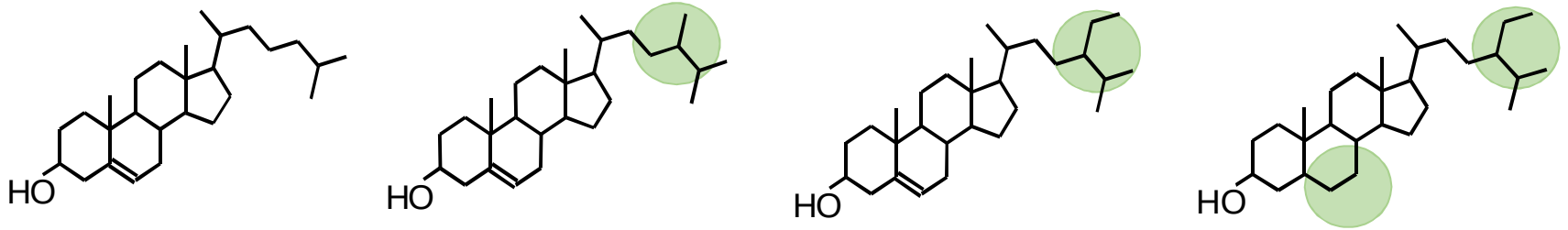


*Ference et al. Eur Heart J. 2017

Plant sterols and stanols are natural compounds in the human diet

- Plant sterols and stanols are found in foods of plant origin, e.g. grains, seeds, vegetable oils, nuts, legumes, fruit and vegetables
- The term ‘phytosterols’ comprises both plant sterols and stanols
- Average daily intake with habitual diets
  - 200 to 300 mg/day of naturally occurring plant sterols
  - ~50 mg/day of naturally occurring plant stanols
  - Up to 600 mg with vegetarian/vegan-type, plant-based diet

- Plant sterols and stanols are structurally similar to cholesterol with both different side chain configurations and lack of double bonds



cholesterol campesterol sitosterol sitostanol

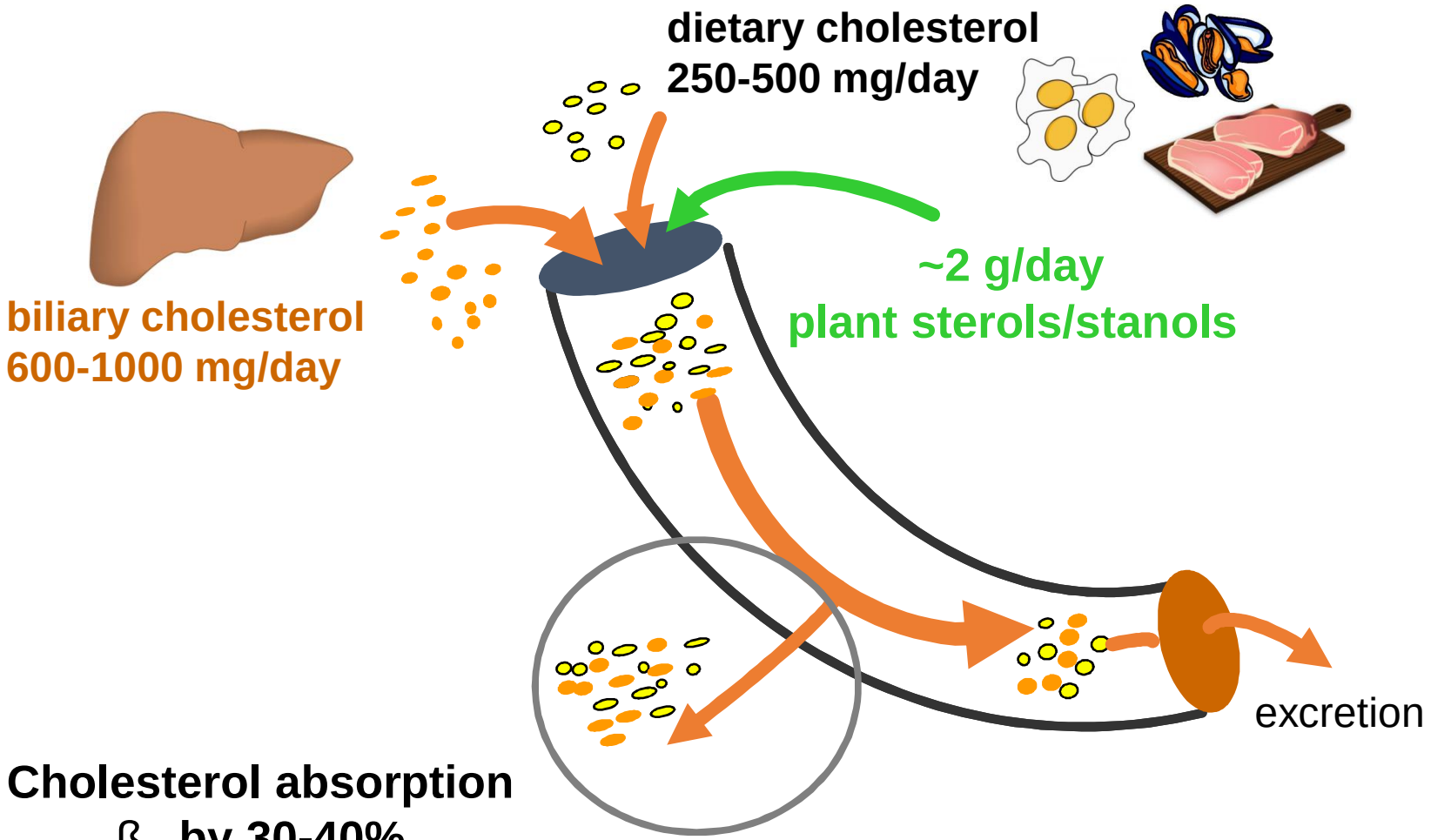
Long history of cholesterol-lowering effect of plant sterols/stanols

- Long history of knowing their cholesterol-lowering effect
  1st human study already published in **1953***
- Since mid/late 1990s, foods with added plant stanols/sterols commercially available, with wide range of different food formats and food supplements

- One of the most thoroughly studied dietary ingredients
  - To date **>120 randomised controlled trials** showing that plant sterols/stanols lower total and LDL-cholesterol without affecting HDL-cholesterol**
  - Plant sterols/stanols also modestly lower triglyceride (TG) esp. in individuals with high basal TG levels***

*Pollack, Circulation 1953
**Ras et al. Br J Nutr 2014
***Rideout et al. J AOAC International 2015

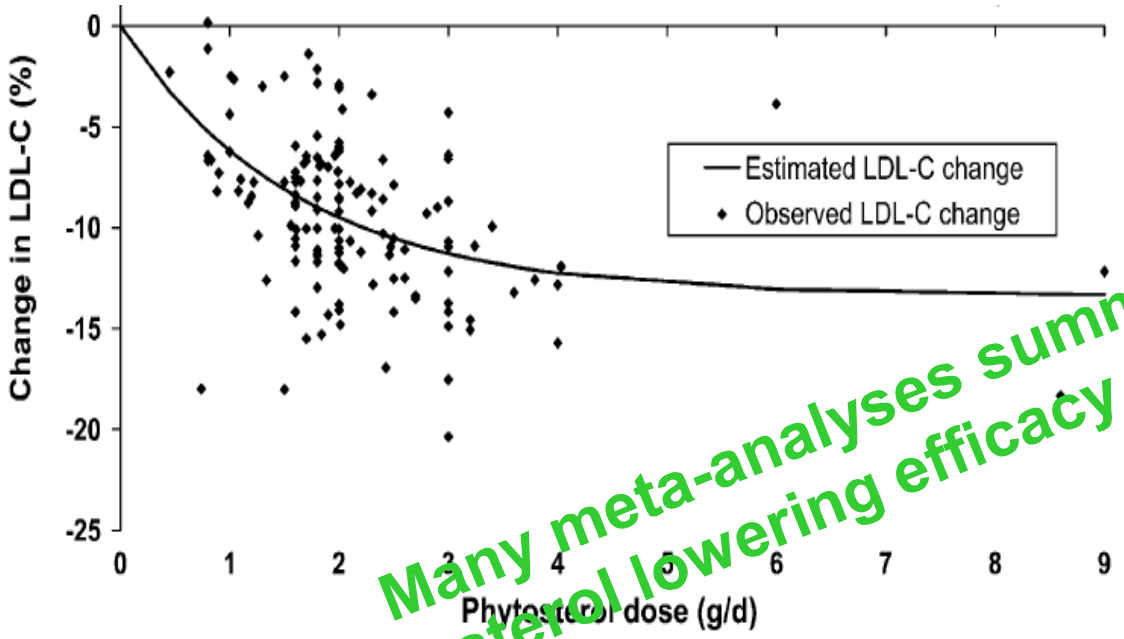
Plant sterols and stanols lower cholesterol by inhibiting cholesterol absorption from the gut



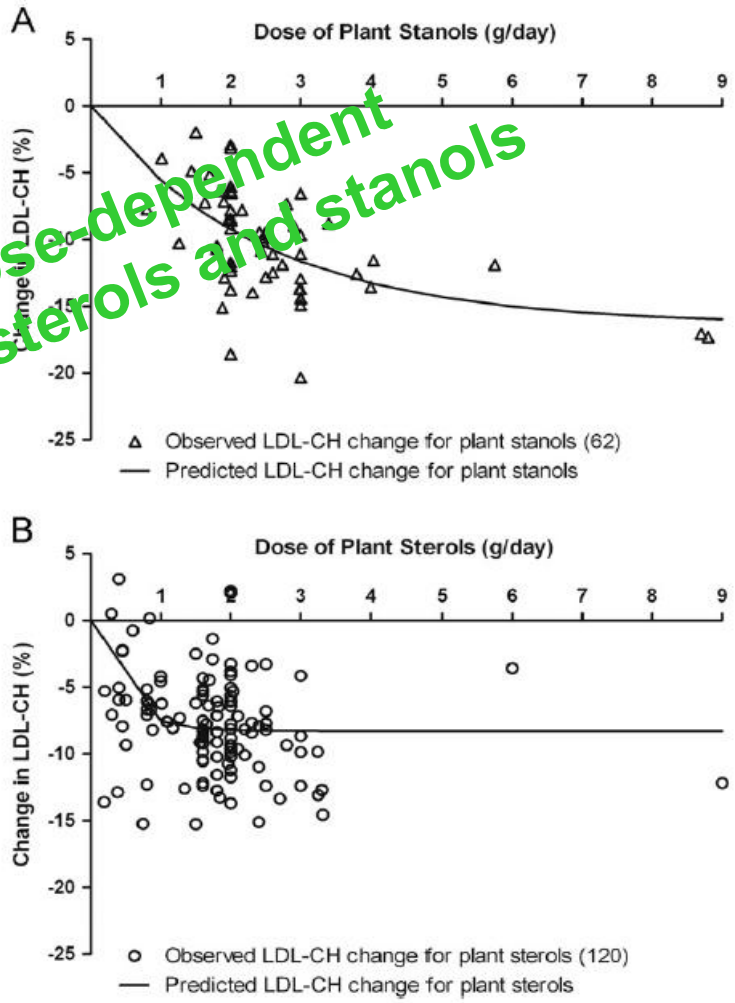
Cholesterol absorption
ß by 30-40%
Þ LDL-cholesterol ß

Continuous dose-response relationship of LDL-cholesterol-lowering with plant sterol/stanol intake

84 RCT with 141 strata; 6,805 study participants



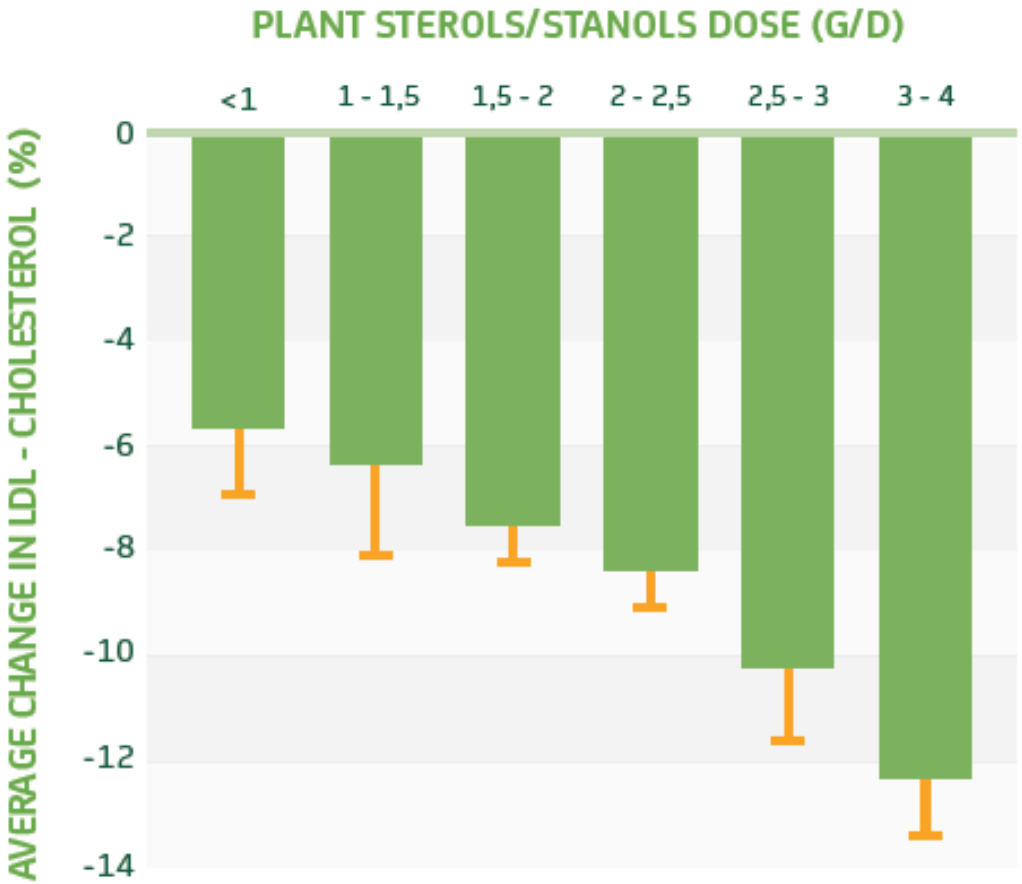
114 RCT with 182 strata



Many meta-analyses summarise dose-dependent cholesterol lowering efficacy of plant sterols and stanols

Demonty et al. J Nutr 2009; Musa-Veloso et al. PLEFA 2011

Most recent evidence: Cholesterol-lowering of plant sterols and stanols across different dose ranges



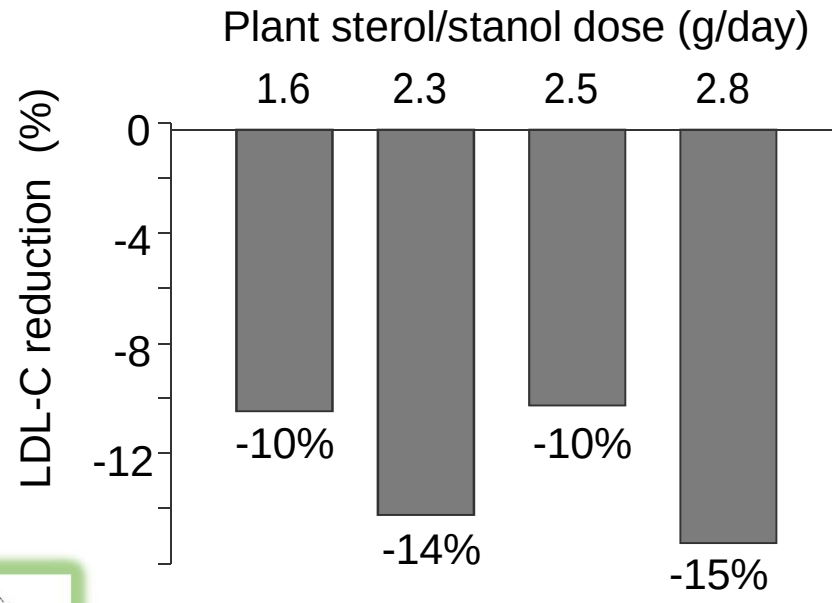
Meta-analysis based on 124 RCT with 201 strata;
9,692 study participants and variety of food formats

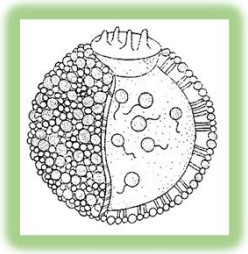
Plant sterol/stanol intakes of 1.5 - 3 g/day dose-dependently reduce LDL-cholesterol by 7 - 12.5%

Ras et al. Br J Nutr 2014

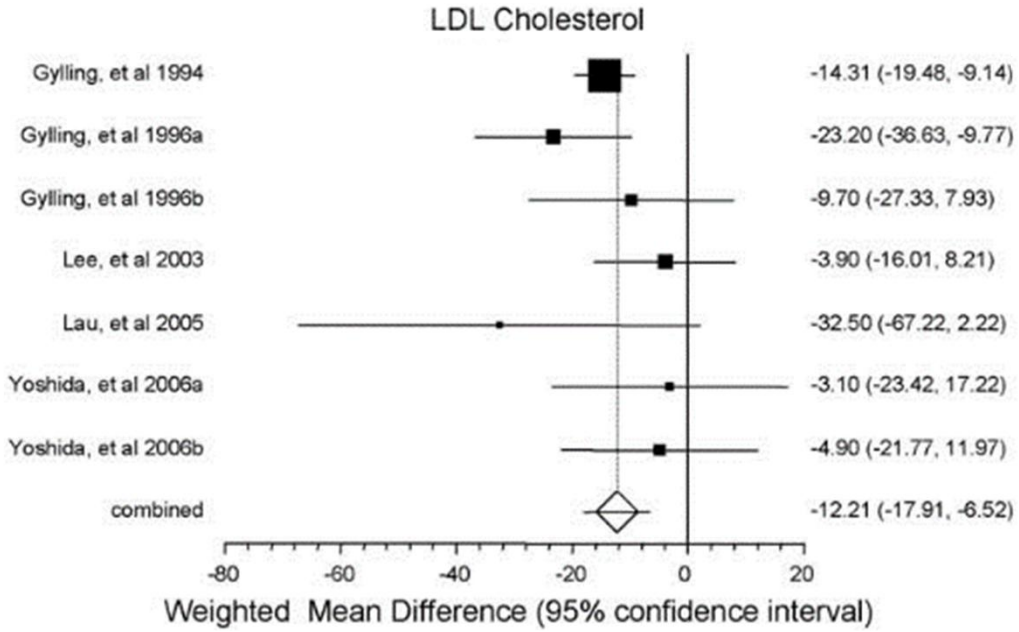
Cholesterol lowering benefit of plant sterols and stanols demonstrated in different populations

Meta-analysis with Familial Hypercholesterolemia (FH) patients*





Meta-analysis with individuals with Diabetes mellitus**

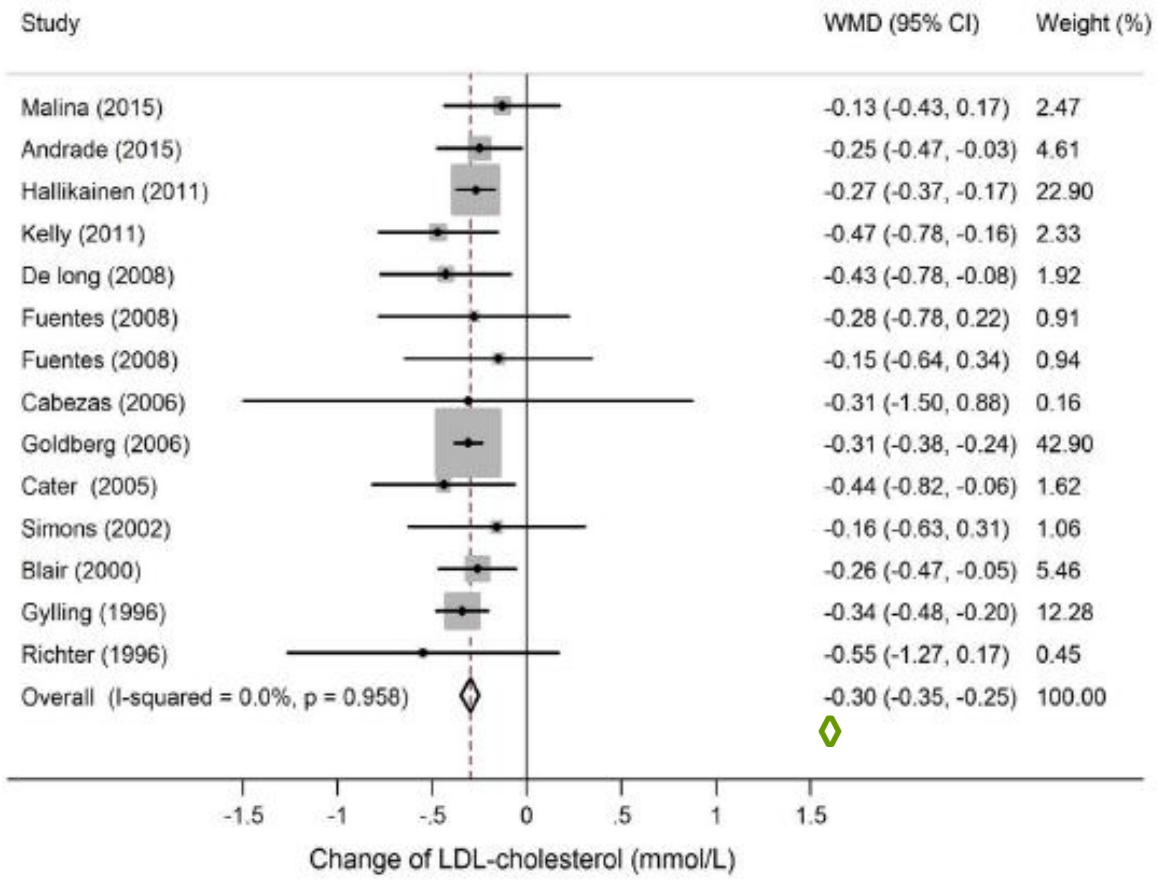


LDL-C lowering: 12 mg/dL
= 0.31 mmol/L (**~10%**)

*Moruisi et al. J Am Coll Nutr 2006; **Baker WL et al. Diabetes Res Clin Pract 2009

Additive effect of combining plant sterols and stanols with statins

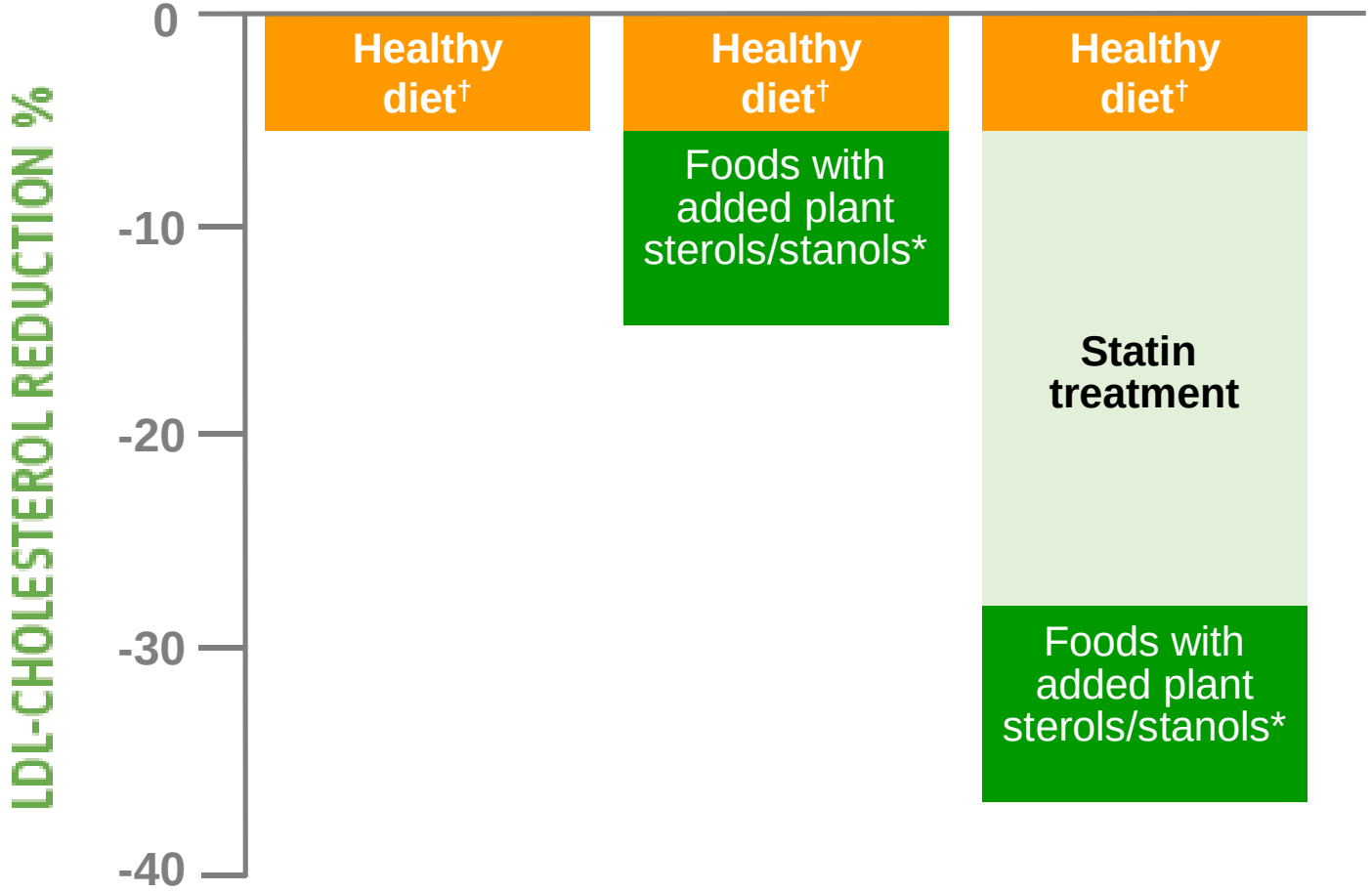
Meta-analysis of LDL-cholesterol effect of plant sterols/stanols in combination with statins
14 RCT (with 15 strata) with 500 participants



Plant sterols/stanols in combination with statins vs. statins alone lead to significantly stronger LDL-cholesterol reduction by 0.30 mmol/L (95% CI -0.35 to -0.25)

Han et al. Scientific Reports 2016

Additive effect of plant sterols and stanols combined with healthy diet and lipid-lowering drugs (statins)



†Low in saturated fat and dietary cholesterol

*1.5-3 g/day of plant sterols/stanols from foods with added plant sterols/stanols

Adapted from: Edwards & Moore, BMC Family Practice 2003; Cleghorn et al. Eur J Clin Nutr 2003; Chen et al. Lipids 2009, Katan et al. Mayo Clinic Proceed, 2003 ; Ras et al. Br J Nutr 2014

Cholesterol-lowering evidence forms basis for authorised EU Health Claim for plant sterols and stanols

Authorized Disease Risk Reduction claim:

- ‘Plant sterols and plant stanol esters have been shown to lower/reduce blood cholesterol.
- High cholesterol is a risk factor in the development of coronary heart disease.’

2-step claim with focus on the risk factor

EFSA Scientific Opinions: EFSA Journal (2008) 781, 1-12; EFSA journal (2008) 825, 1-13; EFSA Journal (2009) 1175, 1-9; EFSA Journal (2009) 1177, 1-12; Commission Regulations: EC 983/2009; EC 376/2010; EC 384/2010. *EFSA Journal (2012);10(5):2692; EFSA Journal (2012);10(5):2693; Commission Regulation (EU) No 686/2014*

Target population for foods with added plant sterols and stanols

- Individuals who need to lower their blood cholesterol
- Not intended for use of pregnant and breastfeeding women or children under 5 years of age
- However, studies show that children with Familial Hypercholesterolemia (FH) benefit from the cholesterol-lowering efficacy of plant sterols and stanols*

*Vuorio et al. Arterioscler Thromb Vasc Biol 2000; Amundsen et al. Am J Clin Nutr 2002; de Jongh et al. J Inherit Metab Dis 2003

European Atherosclerosis Society (EAS) Consensus Panel Paper recommends plant sterols and stanols and describes user groups

EAS Consensus Panel* conclusions and recommendations

- Foods with added plant sterols/stanols up to **2 g/day** are equally effective in **lowering LDL-cholesterol by up to 10%**
- Plant sterols/stanols can be **efficaciously combined with statins**

Foods with added plant sterols/stanols may be considered

- for **individuals with high serum cholesterol, but intermediate or low global CVD risk** who therefore do not (yet) qualify for drug treatment,
- as **adjunct to drug (statin) therapy**, in individuals who fail to achieve LDL-C targets or are statin-intolerant, in conjunction with other lifestyle interventions
- for **adults and children (>6 yrs.) with familial hypercholesterolaemia**

*Gylling et al. Atherosclerosis 2014
Catapano et al. 2016 ESC/EAS Guidelines for the management of dyslipidaemias Eur Heart J 2016 and Atherosclerosis 2016;

Recognition for foods with added plant sterols and stanols

Acceptance and support for safety and efficacy of plant sterols and stanols as dietary option for lowering LDL-cholesterol, a major risk factor of CVD

Regulatory bodies, *e.g.*

EU

efsa European Food Safety Authority

FDA

Health Canada Santé Canada

FOOD STANDARDS Australia New Zealand
Te Mana Kounga Kai – Ahitereiria me Aotearoa

Medical/scientific associations, *e.g.*

International Atherosclerosis Society

European Atherosclerosis Society

European Society of Cardiology

ESC/EAS GUIDELINES

British Heart Foundation

American Diabetes Association

eat right Academy of Nutrition and Dietetics

American Association of Clinical Endocrinologists ACE

JBS3

nla National Lipid Association

BDA The Association of UK Dietitians

Heart Foundation Australia

Canadian Cardiovascular Society
Leadership. Knowledge. Community.

Nederlandse Hartstichting

Conclusions

- Vast number of human intervention studies shows LDL-cholesterol lowering benefit of foods with added plant sterols and stanols
- **Intake of 1.5-3 g/day** lowers LDL-cholesterol dose-dependently by **7-12.5%**
- Plant sterols/stanols **are equally effective in all food formats and in food supplements**
- **Additive effect** to a heart healthy diet and to lipid-lowering medication (statins)
- **Approved health claims** by e.g. EU Commission, *FDA* (US), Health Canada
- Included in **recommendations** for diet and lifestyle approaches for management of dyslipidaemia as an additional adjunct to a healthy diet
  e.g. 2016 EAS/ESC guidelines on the management of dyslipidaemias

Voices of lowering cholesterol campaign

Thank you!

For more information on plant sterols and stanols visit http://www.ipssa-association.com and follow us on Twitter @IPSSAglobal

Downloadable Infographic