



DEEPCDIVE SUMMARIES

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Any Point to Dietary Supplements for Lowering LDL?

Laffin LJ, Bruemmer D, Garcia M, Brennan DM, McErlean E, Jacoby DS, Michos ED, Ridker PM, Wang TY, Watson KE, Hutchinson HG, Nissen SE. Comparative Effects of Low-Dose Rosuvastatin, Placebo, and Dietary Supplements on Lipids and Inflammatory Biomarkers. *J Am Coll Cardiol*. 2023 Jan 3;81(1):1-12.

Background

- It is now concretely established that LDL-cholesterol is the primary causal risk factor for the initiation, development, and progression of atherosclerosis in humans.
- However, there are some barriers to lowering LDL-C in clinical practice, specifically apprehension about starting pharmacotherapy and desire to try diet and lifestyle first.
- Dietary supplements lack quality evidence, but have rarely been compared against pharmacotherapy in a well-controlled intervention trial.

The Study

- The SPORT [Supplements, Placebo, or Rosuvastatin Study] trial was a single-blind RCT in participants aged 40–75-years with an LDL-C between 70–189mg/dL. Participants were randomly assigned to either rosuvastatin, fish oils, garlic extract, cinnamon, turmeric, red yeast rice [RYR], plant sterols, or placebo. The trial was 4-weeks in duration and primary outcome was changes in LDL-C.

Findings, Strengths & Limitations

- Over 28-days, rosuvastatin lowered LDL-C by 37.9%; fish oils by 3.4%; turmeric by 1.3%; plant sterols by 4.4%, and RYR by 6.6%. Garlic led to an increase in LDL-C of 5.1%, while LDL-C was unaffected by cinnamon. There was a 2.6% reduction in LDL-C in the placebo group.
- In comparing the magnitude of LDL-C lowering of rosuvastatin to the dietary supplements, rosuvastatin lowered LDL-C by 31.3–38.3% compared to the supplements.
- Strengths included the computer-generated randomisation, placebo control, and blinding of investigators. Limitations include the short duration which favoured the effects of the statin, and the fact that most supplements were underdosed and/or poorly formulated.

Context

- None of the dietary supplements significantly lowered LDL-C even compared against the placebo.
- However, overall the choices of dietary supplements have poor justifications, with weak rationale for some [e.g., turmeric and cinnamon], underdosing for others [e.g., omega-3 and plant sterols], or missing key information on active ingredients [e.g., RYR].
- While efficacy, effectiveness, and safety would all be strongly in favour of lipid-lowering drugs, however, this does not mean there is no potential role for nutritional interventions, but it would appear those interventions relate more to diet than supplements.

Application

- This is a rare study that stacks common dietary supplements against a frontline drug, which is highly relevant given statin hesitancy and the expression in survey data that patients may want to try diet, lifestyle, and natural supplement.
- The present study in fact lends support to the “food first” approach, and for lowering LDL-C specifically the most efficacious, effective, and safe dietary intervention is to replace saturated with unsaturated fats.

How Effective is Manipulating Energy Density to Reduce Energy Intake?

Robinson E, Khuttan M, McFarland-Lesser I, Patel Z, Jones A. Calorie reformulation: a systematic review and meta-analysis examining the effect of manipulating food energy density on daily energy intake. *Int J Behav Nutr Phys Act.* 2022 Apr 22;19(1):48.

Background

- To characterise this change in dietary composition and its potential influence on energy intake and bodyweight, the concept of energy density [i.e., the energy content divided by the weight of a food] has been a major focus of nutrition research.
- Experimental studies suggest that manipulating energy density may lead to reductions in energy intake from lowering energy density.
- The present study conducted a meta-analysis on this question.

The Study

- A systematic review and meta-analysis of interventions that investigated the effects of different energy densities on energy intake. Studies had to have manipulated energy density in at least one meal in a day, up to all meals. The primary outcome was total daily energy intake according to the energy density comparisons.

Findings, Strengths & Limitations

- Based on 31 studies, the lowest energy density was associated with significant reductions in energy intake with a large effect size. In studies that manipulated energy density in all meals/foods there was an average difference of ~700-855kcal less energy intake in the lower energy density conditions.
- In studies that manipulated one meal/foods or less than all meals/foods in a day, the magnitude of effect was ~200-237kcal less energy intake in the lower energy density condition.
- Strengths included the preregistration of the review and expansive literature search, and within-person designs of included studies [where each participant serves as their own control]. Limitations include the poorly defined inclusion criteria, reliance on single-day or meal studies, and unsuitability of combining the primary included studies.

Context

- Kevin Hall's metabolic ward study found that a low-fat diet with an energy density of 0.9kcal/g resulted in ~690kcal lower energy intake over 2-weeks compared to a low-carb diet with an energy density of 1.9kcal/g.
- The other meta-analysis on this topic published the same year as the present study also found in studies where energy density was manipulated in more than one meal, the lower energy density condition was associated with a 535kcal lower energy intake.
- However, previous analyses suggest that energy density primarily predicts short-term, not long-term, energy intake.
- Thus, we cannot assume that the magnitude of effect is truly as large as suggested in short-term interventions, including the outcomes of the present meta-analysis.

Application

- Over the longer-term, total energy intake is the most important factor in mediating bodyweight, and the influence of energy density in this context appears to relate to macronutrient variations and food-based differences
- Lower energy density foods also may provide a higher volume of total daily food intake, which appears to be a factor in enhancing satiety on lower energy density diets.

Is Breastfeeding a Risk for Infant Iodine Deficiency?

Næss S, Aakre I, Strand TA, Dahl L, Kjellevoid M, Stokland AM, Nedrebø BG, Markhus MW. Infant iodine status and associations with maternal iodine nutrition, breastfeeding status and thyroid function. *Br J Nutr.* 2023 Mar 14;129(5):854-863.

Background

- Iodine deficiency results in a spectrum of adverse effects on human growth and development, known collectively as 'Iodine Deficiency Disorders'.
- In developmental phases, both during gestation and into infancy, thyroid hormones are required for neuronal growth, which is dependent on adequate dietary intake of iodine.
- Consequently, maternal iodine intake is crucial. However, insufficient iodine intake is common in pregnant and lactating mothers, even in countries with mandatory policies of iodine fortifications in salt.

The Study

- The study was a secondary analysis of a randomised controlled trial [RCT] in 137 pregnant Norwegian women followed from 20-weeks gestation, and the mother-infant pairs underwent follow-up visits at 3, 6, and 11-months postpartum. Infants were classified according to whether they were exclusively breastfed, mixed-fed, or formula-fed. Iodine status was assessed in both mothers and infants.

Findings, Strengths & Limitations

- 61% of infants were under the WHO threshold of for iodine sufficiency at 3-months, which declined to 41% and 37% at 6 and 11-months, respectively. Breastfed infants were in the deficiency range, while formula-fed infants were iodine replete at each timepoint.
-]The average maternal breastmilk iodine concentration at 3-months postpartum was in the deficiency range. Neither infant urinary iodine concentrations nor maternal breast milk iodine concentrations were associated with infant thyroid status.
- Strengths include the multiple methods of assessing maternal iodine status, including breastmilk and urinary samples. Limitations include the secondary, observational nature of the analysis rather than direct test of the influence of maternal iodine intake on infant iodine and thyroid status.

Context

- While we must acknowledge the limitation that there were few infants in the mixed-fed and formula-fed categories at 3 and 6-months, respectively, which may limit the comparisons, ~80% of infants were exclusively breast-fed at these time points.
- For the exclusive breast-fed status of the infants with insufficient urinary iodine concentrations, this directly reflects inadequate maternal iodine intakes.
- The main relevance of the present study is that for exclusively breast-fed infants, maternal iodine intake is the primary factor influencing infant iodine status.

Application

- Note that the pregnancy and lactation recommendations are for ~200-250mcg/d total intake. It is possible to achieve iodine adequacy through a combination of supplements [as potassium iodide] and dietary intake.
- The most important consideration may be timing, as the evidence for adverse effects of maternal iodine deficiency on infant cognitive development relate specifically to first trimester deficiency. Pre-conception iodine sufficiency should be considered.

Allcott H, Diamond R, Dubé JP, Handbury J, Rahkovsky I, Schnell M. Food Deserts and the Causes of Nutritional Inequality. *The Quarterly Journal of Economics*. 2019 Nov; 134(4):1793–1844.

Background

- The term “food desert” seems to have first appeared in formal policy documents of a British government taskforce in the mid-1990’s and describes low-income communities where access to healthy, affordable foods is limited.
- “Food desert” may in fact be a proxy for other factors influencing dietary intake in low-income strata of society.
- The present study investigated the relationship between diet and income using food purchase data and data on food retail outlet locations from the United States.

The Study

- The study used retail scanner data, which records all packaged goods purchased from any retail store, and sales data, from a nationally representative survey of U.S. households and retail stores. The Healthy Eating Index [HEI], which is a diet quality index, was used to assess healthfulness of purchases.

Findings, Strengths & Limitations

- Households in the top income quartile purchased groceries that were significantly higher in HEI scores than households in the lowest quartile. Stores in higher income ZIP codes contained healthier options than stores in lower income ZIP codes. In low-income areas there were fewer supermarkets and more drug and convenience stores per capita.
- 7-12% of the relationship between income and nutrition was explained by “supply”, while 88-93% was explained by “demand”. Of this demand, 34% was explained by differences in education and nutrition knowledge.
- Strengths include the enormous dataset which encompassed a nationally representative sample of household consumers and income levels, and a long duration of data over 12-years. Limitations include the data only including grocery purchases, lack of thorough assessment of covariates, and only a limited number of potential mediators of the relationship between income and diet analysed.

Context

- In simple terms, the analysis suggested that if poor people exhibited the preferences and characteristics of wealthy people there would be no nutritional inequalities.
- The analysis of drivers of “demand” indicated that factors like education exert a strong contribution to the relationship between income and healthy grocery demands, which fundamentally alters the concept of “demand”.
- Economic modelling based on assumptions related to preferences and characteristics, with preferences defined by rationalist utility and reduced to a modelling equation, are an unrealistic model of human behaviour in the real world.

Application

- The present study builds on previous research by suggesting that “food deserts” may be too opaque a concept to capture income and neighbourhood disparities in healthy food access and diet quality.
- The fact that externalities such as education status and nutrition knowledge influence grocery purchasing is indicative of factors that underpin class-based disparities in diet quality and related health outcomes.