

THE IMPORTANCE OF EVIDENCE HIERARCHY IN NUTRITION SCIENCE

THE CASE OF LOW/NO CALORIE SWEETENERS

WHAT IS THE HIERARCHY OF EVIDENCE?

Hierarchy of evidence is a method used to assess the quality of available scientific evidence by ranking research according to the quality and reliability of their study design.¹



GRADE



The hierarchy of scientific evidence is frequently depicted in the form of a pyramid: **the higher the position on the pyramid, the stronger the evidence.**

CLINICAL PRACTICE GUIDELINES AND PUBLIC HEALTH RECOMMENDATIONS SHOULD BE BASED ON THE BEST-QUALITY SCIENTIFIC EVIDENCE. THEREFORE, EVALUATING THE STRENGTH OF AVAILABLE EVIDENCE IS KEY!

SYSTEMATIC REVIEWS WITH META-ANALYSIS OF RCTS ARE POSITIONED AT THE HIGHEST LEVEL IN THE HIERARCHY OF EVIDENCE AND SHOULD BE CONSIDERED AS A PRIMARY SOURCE OF INFORMATION IN SCIENCE-BASED PUBLIC HEALTH DECISIONS.



WHAT IS THE GRADE APPROACH?

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach is a method for rating the quality of, and certainty in, evidence and the strength of recommendations.^{2,3}

In the GRADE approach, study design is critical to the evaluation of the quality of evidence:



RCTS WITHOUT IMPORTANT LIMITATIONS PROVIDE HIGH QUALITY EVIDENCE



OBSERVATIONAL STUDIES WITHOUT SPECIAL STRENGTHS OR IMPORTANT LIMITATIONS PROVIDE LOW QUALITY EVIDENCE

However, the level of evidence of both RCTs and observational studies can be “downgraded” or “upgraded”, respectively, depending on their strengths and limitations.

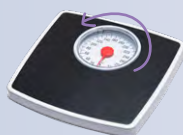
LOW/NO CALORIE SWEETENERS IN OBESITY AND DIABETES: INTERPRETING CURRENT SCIENCE IN LIGHT OF THE HIERARCHY OF EVIDENCE

Systematic reviews and meta-analyses of RCTs⁴⁻¹³:

Results consistently support the assertions that, being part of a healthy diet, low/no calorie sweeteners (LNCS) :



can help in calorie reduction



can assist with modest weight loss



do not affect glycaemia, lipidaemia and blood pressure



cause a lower rise in blood glucose levels when used instead of sugars

Systematic reviews and meta-analyses of observational studies¹²⁻¹⁵:

Results are inconsistent with studies reporting a positive, null or negative association between LNCS use and higher body weight or type 2 diabetes. **BUT association does not mean causation.**

Observational studies are prone to unmeasured confounding factors and reverse causality meaning that **“a positive association between LNCS consumption and weight gain in observational studies may be the consequence of and not the reason for overweight and obesity”**, as highlighted in WHO-supported research.^{4,12,13} Contrary to a lower-quality body of evidence from observational research, stronger evidence from RCTs, the gold standard in clinical and nutrition research, consistently support a useful role of low/no calorie sweeteners in obesity and diabetes.

References:

1. Burns PB, Rohrich RJ, Chung KC. The levels of evidence and their role in evidence-based medicine. *Plast Reconstr Surg*. 2011 Jul;128(1):305-310.
2. GRADE Handbook. Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach. Updated October 2015. Available at: <https://gdt.gradepro.org/app/handbook/handbook.html>
3. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008 Apr 26;336(7650):924-926.
4. Greyling A, Appleton KM, Raben A, Mela DJ. Acute glycaemic and insulinemic effects of low-energy sweeteners: a systematic review and meta-analysis of randomized controlled trials. *Am J Clin Nutr* 2020 Oct 1;112(4):1002-1014
5. Laviada-Molina H, Molina-Seguí F, Pérez-Gaxiola G, et al. Effects of nonnutritive sweeteners on body weight and BMI in diverse clinical contexts: Systematic review and meta-analysis. *Obesity Reviews* 2020;21(7):e13020
6. Lohner S, Toews I, & Meerpohl JJ. Health outcomes of non-nutritive sweeteners: analysis of the research landscape. *Nutr J* 2017; 16(1): 55
7. Lohner S, Kullenberg de Gaudry D, Toews I, Ferenci T, Meerpohl JJ. Non-nutritive Sweeteners for Diabetes Mellitus. *Cochrane Database of Systematic Reviews* 2020 May 25;5:CD012885.
8. McGlynn ND, Khan TA, Wang L, et al. Association of Low- and No-Calorie Sweetened Beverages as a Replacement for Sugar-Sweetened Beverages with Body Weight and Cardiometabolic Risk: A Systematic Review and Meta-analysis. *JAMA Network Open* 2022;5(3):e222092
9. Miller PE & Perez V. Low-calorie sweeteners and body weight and composition: a meta-analysis of randomized controlled trials and prospective cohort studies. *Am J Clin Nutr* 2014; 100(3): 765-777
10. Nichol AD, Holle MJ, An R. Glycemic impact of non-nutritive sweeteners: a systematic review and meta-analysis of randomized controlled trials. *Eur J Clin Nutr* 2018; 72: 796-804
11. Rogers PJ and Appleton KM. The effects of low-calorie sweeteners on energy intake and body weight: a systematic review and meta-analyses of sustained intervention studies. *Int J Obes* 2021; 45(3): 464-478
12. Toews I, Lohner S, Kullenberg de Gaudry D, Sommer H, Meerpohl JJ. Association between intake of non-sugar sweeteners and health outcomes: systematic review and meta-analyses of randomised and non-randomised controlled trials and observational studies. *BMJ* 2019;364:k4718
13. World Health Organization, Rios-Leyvraz, Magali & Montez, Jason. (2022). Health effects of the use of non-sugar sweeteners: a systematic review and meta-analysis. World Health Organization. <https://apps.who.int/iris/handle/10665/353064>. License: CC BY-NC-SA 3.0 IGO