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Abstract

Vitamin D and Cardiovascular Disease Risk: Using Outcomes to Guide Future Nutrition Science †

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Abstract: Despite positive associations between micronutrient intake, status, and health outcomes, many randomized controlled trials (RCT) of vitamins are null. Standards to establish causality in biological systems include the Bradford Hill criteria, the experimental component of which relies on and promotes RCT-centred approaches. Such criteria may need adaptations to the specificities of nutrition science. Our objective, as part of a broader FENS initiative to improve the science of nutrition, was to conduct a case study to assess the Bradford Hill criteria (BHC) applied to clinical studies of vitamin D and cardiovascular disease endpoints and evaluate strengths and pitfalls for this approach. We conducted a systematic review of the recent literature on CVD and vitamin D supplementation, including both RCT, cohort studies (CT), or systematic reviews within Medline, Web of Science, and Cochrane libraries. Studies had to be conducted in adults, including hard CVD-relevant endpoints with a minimum sample size of n = 500 for RCT and n = 10,000 for CT. CT had to utilize quality-assured, analytical methods for serum 25-hydroxyvitamin D assessment and include verified clinical outcomes. We also evaluated and proposed plausible biochemical and physiological mechanisms for vitamin D and CVD. We graded the evidence according to BHC for the establishment of causality in biological systems and the identification of strengths and pitfalls of this approach. The search yielded 4170 papers, and 31 met the predefined criteria. The criteria "strength of association", "consistency", "temporality", "biological gradient", "plausibility", "experiment", "specificity", "analogy", and "coherence" were analyzed and appraised. While the logical framework of the BHC is perceived as useful, its direct applicability to the nutritional context is partly open to interpretation and could be further specified. The Bradford Hill criteria for establishing causality need adaptation for the nutritional context and to the advances in biological and social sciences in the last decades. Insights gained and methodological paradigms identified may have broad application to nutrition science.

Keywords: Nutritional Science; Vitamin D; Cardiovascular Disease; Bradford Hill criteria

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