

Dietary Supplements and Its Health Benefits: An Overview

Navneet Kumar Verma^{1*}, Asheesh Kumar Singh¹, Praveen Kumar Rao¹, Satysaran Singh¹, Swati Mishra¹, Janhvi Singh¹¹Buddha Institute of Pharmacy, GIDA, Gorakhpur, UP, India, Affiliated to Dr. APJ Abdul Kalam Technical University Lucknow, UP, IndiaDOI: [10.36347/sajp.2024.v13i05.007](https://doi.org/10.36347/sajp.2024.v13i05.007)

| Received: 04.04.2024 | Accepted: 11.05.2024 | Published: 17.05.2024

*Corresponding author: Navneet Kumar Verma

Buddha Institute of Pharmacy, GIDA, Gorakhpur, UP, India, Affiliated to Dr. APJ Abdul Kalam Technical University Lucknow, UP, India

Abstract

Review Article

Different nations define dietary supplements differently, and regulations are sometimes ambiguous and seem to prioritise corporate profits over the general welfare. Supplements may have direct negative effects or interact negatively with drugs or other supplements. It turns out that many supplements include heavy metals, and some of them don't have the expected amounts of active ingredients. Generally speaking, supplements are not necessary unless deficits are shown, and consuming excessive amounts of some nutrients may increase your risk of cancer. There are strong reasons to support the introduction of dietary recommendations for expecting mothers, such as those pertaining to iodine and folate. The most widely used nutritional supplements are amino acids and calcium, neither of which has much evidence to support their benefits for healthy teenagers. For competitive athletes who don't eat a balanced diet, nutritional supplements could be helpful if a specific dietary deficiency has been found. This assessment discusses possible dangers to the public's health related to dietary supplements and offers suggestions for upcoming legislative actions.

Keywords: Dietary supplement, Active Components, Nutritional Supplements.

Copyright © 2024 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

Medical study indicates that dietary supplements may be beneficial for a small subset of people—competitive athletes, for example—who don't consume a balanced diet [1]. In these cases, it is recommended to increase nutrient intake once a nutritional deficiency has been detected, either via diet or supplements. But supplement use is rising among kids who play sports or engage in physical activity.² The frequency of usage varies based on the type of exercise (bodybuilding and weightlifting are popular uses), cultural variables, age groups (adolescence is the most common), and sex (men are more likely to consume it) [3, 4]. Although the frequency, type, and amount of supplements taken have not been thoroughly investigated, it seems that recommended dosages are regularly exceeded [3]. A healthy diet and adequate sleep are essential for human survival and well-being; these factors can account for as much as 50% of disease burden [5, 6]. If a component satisfies the aforementioned criteria for a "dietary ingredient" and was not marketed as a dietary supplement in the US prior to October 15, 1994, it is considered a "new dietary ingredient" [7]. Directive 2002/46/EC is the primary piece of EU legislation pertaining to food supplements that contain

vitamins and minerals. "Supplements may be used to correct nutritional deficiencies or maintain an adequate intake of certain nutrients," the European Food Safety Authority [EFSA] continues. Maximum levels are required to guarantee the safety of vitamins and minerals because, in some situations, consuming too much of them may be hazardous or have unintended side effects. Utilization in dietary supplements [8] Over the world, more people are using dietary supplements. The yearly cost of dietary supplements used in the US was \$12 billion two decades ago [9]. Dietary supplements come in an almost infinite variety and composition, and even standard multivitamins are packed for different demographics based on factors like age, gender, physical condition, and degree of activity. According to Nowak, a typical US supermarket offers over 500 distinct dietary supplements; specialty shops have a much wider selection [10]. Furthermore, nearly 70% of Poles asked said using antioxidants stops the growth of cancer, and over 40% said taking vitamin and mineral supplements prevents diseases in healthy individuals [11, 12]. Food and the notions it holds about its importance to life form the basis of much human culture. Certain cuisines are presented on special occasions, while others signify life transitions, celebrations, or otherwise exceptional occasions. Encouraged for recovery. Furthermore, the

majority of our energy and the essential macro- and micronutrients come from staple foods; all cultures employ a range of flavors and condiments to improve our dining experience. These staple foods are typically categorized as foods; however they can also be sold as supplements, which raise definitional issues. For instance, kimchee is a must-have for any Korean dinner. Without it, probiotic-containing fermented meal [13].

DEFINITION OF DIETARY SUPPLEMENTS

The Dietary Supplement Health and Education Act (DSHEA) of 1994 contained the definition of a dietary supplement as defined by the US Food and Drug Administration (FDA) [14]. Anything that fits the description of a "dietary ingredient" above is considered a "new dietary ingredient." and before to October 15, 1994, was not offered for sale as a dietary supplement in the United States [7]. Orally administered compounds used to address a particular nutritional deficiency are referred to as dietary supplements. They are frequently marketed as ergogenic drugs, meaning they can boost or enhance athletic performance [15]. It is challenging to categorize dietary supplements into distinct classes due to the vast quantity of items, their diverse contents, and the range of side effects and actions. [16]. Definitions have evolved over time, as seen in the National Health and Nutrition Examination Survey (NHANES) [16], making comparisons of intake challenging. The phrases "supplement," "supplementary food," or "complementary food," as an alternative, are frequently utilized for nursing infants. Although there are dangers associated with adding nutritional supplements or additives to infant formula, this review does not address these since formula additions are controlled differently [17].

CLIMATE CHANGE AND SUPPLEMENTS

Climate change is becoming a major concern for public health since it could have an impact on the manufacturing and makeup of supplements derived from crops as well as how heat affects users of particular supplements [18]. An often used dietary supplement is creatine for bodybuilders and athletes, and it is currently the most popular dietary supplement utilized by the armed forces [19]. It may be connected to heatstroke deaths in hot conditions [20, 21], though this finding has been contested [22]. Supplements to Diet in Developing Countries the potential of vitamin and mineral supplementation relies on if there is a shortage of that element in the diet [6]. For the prevention and treatment of malnutrition in groups at high risk for the illness, dietary supplements have been frequently used. High energy and protein supplements are typically offered strengthened with additional minerals and vitamins. For instance, children with moderate acute malnutrition in Mali saw improved growth rates when they were given dietary supplements based on lipids [23]. Other examples of supplementation in the poor world abound; many of these are from the 1960s and 1970s and were effective in lowering severe malnutrition, especially in emergency

scenarios [24-27]. In Africa, Asia, and South America, trials using multiple micronutrient powder (Sprinkles) have proven effective in addressing deficiency in children and expectant mothers [28-31]. In the developing world, the need for supplements would decrease with an improved food supply and a wider variety of nutrient-dense foods. Dietary supplements as well as immoral actions for some, the lure of becoming well-known and wealthy through the creation of dietary supplements that address serious nutritional issues has proven to be too strong. There is one particularly dishonest instance in which the chair of the World Nutrition Congress, a well-known nutrition scientist, and the president of a national society asserted that "nutritional supplementation can, for elderly people, protect against infection and greatly improve memory and ability to learn, and delay or even reverse dementia" [32]. Chandra has withdrawn other papers as well, although in 2016 his works were still being cited [33].

FUTURE PUBLIC HEALTH REGULATION OF DIETARY SUPPLEMENTS

Most nations have lax rules that prioritize company profit and market access over the interests of the general public's health. Japan and the EU both have more stringent policies than other nations or international organizations. Whenever possible, the difficulties of Evaluating and managing up to 100,000 goods would be excessive for any given system. The US\$180 billion industry merits stricter regulation and supervision over product labeling, warnings of side effects (banning if considerable), and efficacy (if health claims are made), given its risk of problems and side effects. Dietary supplements taken on medical advice and as part of clinical practice guidelines for particular life phases ought to be controlled independently. Examples in pregnancy and newborns include folate, iodine, iron, vitamin D, and vitamin K. These suggestions are made in Australia by the National Institutes of Health and Medicine, and are included into clinical rules. Between food and drugs is a no-man's land where dietary supplements reside. Putting rules for dietary supplements in the same vein as pharmaceuticals would just not be feasible the idea of completing or assessing 100,000. It is unbelievable that randomized controlled trials exist. Although enforcement levels differ between jurisdictions, the food sector uses direct regulation, market-based incentive mechanisms, post-market surveillance, and legal liability incentives as safety measures [34]. Foods cannot be advertised as such unless they closely adhere to compositional and purity criteria, such as the Australian Food criteria [35]. The content of certain foods is typically strictly regulated. Using the EU's Food Supplements Directive as an example, Nowak suggests that the US Congress pass more proactive legislation [10]. Other nations might also utilize the Directive as a template and for the development of Codex guidelines.

DIETARY SUPPLEMENT REGULATION WOULD INCLUDE SEVERAL MINIMUM REQUIREMENTS

1. A list of drugs that are allowed first based on substances that have been safely sold. When a product's toxicity is confirmed, all sales must end as soon as possible. It is necessary to monitor interactions and problems more closely. The application for each hospital admission, nutritional supplements and alternative therapies should be documented. Two factors should be taken into consideration when deciding whether to begin a review of a dietary supplement: [a] the frequency and severity of adverse events; and [b] the likelihood that the supplement will be used.
2. All products should have a registration system with clear guidelines on acceptable compositional variation.
3. The establishment of a license and inspection system for manufacturing plants.
4. Using the top bounds of RDIs and nutritional reference values to get the highest possible concentration of vitamins and minerals.
5. Product labels contain ingredient facts that are more educational. It would seem obvious that compositional labels that are clear, accurate, and thorough are necessary. As a result, analyses have to be performed by a recognized laboratory within predetermined tolerances and with conventional procedures. Since many supplements contain botanicals, which naturally vary in composition, these tolerances are necessary. In order to prevent allergies, labeling is necessary. Even with precise labeling, it would not be feasible for the majority of knowledgeable epidemiologist and pharmacologist to help with decision-making for roughly 50,000–100,000 items. Some products are even harder to grasp because they contain up to 50 ingredients. For the general public, guidance ought to be supplied by only accepting verified health claims, even when randomized controlled trials are necessary to assess efficacy. For examples, visit the FDA website [36]. On the other hand, comprehensive testing, effectiveness assessment, and sufficient claim substantiation would be highly expensive.
6. Advise against using off-label medication.
7. Limiting the usage of solely commercially produced goods. Plants that are just picked from the forest are hard to recognize [37].
8. Removing prohibited items from supplements, such as endangered animal species.
9. These prohibitions ought to be upheld everywhere, not only in some places.
10. The use of uniform classifications and criteria when monitoring usage and complications. The Codex is working to ensure that definitions used

in international trade and registration is uniform.

11. Improving the International Regulations (Codex) in light of the dietary supplement trade as it exists now. Many nations lack the resources and knowledge necessary to create their own regulatory frameworks.
12. Better oversight of internet sales of dietary supplements. A lot of people utilize the Internet to market and sell a large number of unproven dietary supplements. There is minimal regulation over the sale of supplements made online. It will take an international task group to address this new problem.

DIETARY SUPPLEMENTS IN THE DEVELOPING WORLD

The potential of vitamin and mineral supplements depends on whether or not that component is lacking in the diet [6]. In groups that are significantly at risk for malnutrition, dietary supplements have been used extensively for both prevention and treatment of this condition state. Typically, the supplements offered are high-energy, protein-fortified, and vitamin and mineral-enriched. For instance, nutritional supplements based on lipids increased the growth rates of kids suffering from moderate acute malnutrition in Mali [23]. There are many more instances of supplements being given in underdeveloped countries, many from the 1960s and 1970s, that have been shown to be effective in lowering severe malnutrition, especially in emergency situations [24–27]. Several micronutrients In Africa, Asia, and South America, powder (Sprinkles) has been effectively used to supplement deficits in children and expectant mothers [28–31]. In the developing world, a greater variety and quality of food would eliminate the need for supplements.

DIETARY SUPPLEMENTS AND UNETHICAL BEHAVIOUR

For some, the lure of becoming well-known and wealthy through the creation of dietary supplements that address serious nutritional issues has proven to be too strong. One particularly notable instance of fraud involves a well-known nutritionist, the head of a national organization, and the president of "Nutritional supplementation can, for elderly people, protect against infection and greatly improve memory and ability to learn, and delay or even reverse dementia," according to a World Nutrition Congress [32]. Chandra has withdrawn other papers as well, although in 2016 his works were still being cited [33].

CALCIUM

Numerous essential bodily processes depend on the mineral calcium [38, 39]. The impacts of either dietary calcium or calcium supplements have been directed towards other health outcomes, even though research on the role of calcium has traditionally concentrated on bone health results recently. An

observation from the 1980s brought attention to the connection between preeclampsia/eclampsia during pregnancy and calcium intake [40]. This came about as a result of an analysis of the Mayan diet in Guatemala, which involved soaking and heating corn in limewater before grinding it, and finding that a low incidence of preeclampsia/eclampsia was linked to a high intake of calcium as a result [41]. This article's goal is to provide an update on the many health benefits of calcium, as evidenced by results from random controlled trials (RCTs) taking into account its availability and intake, and make recommendations for tactics to ensure sufficient intake.

SOURCE OF CALCIUM

Due to their high calcium content, dairy products like milk, yogurt, and cheese are typically consumed in conjunction with other foods. Dairy products, particularly hard cheese, which has a calcium content of 1 g per 100 g, are high in calcium. In contrast, milk and yogurt don't contain calcium is able to supply 100 mg to 180 mg per 100 g. Cereals typically contain 30mg per 100 g, but if they are fortified, that number can rise to 180 mg. Additionally high in calcium are nuts and seeds, particularly chia, sesame, and almonds, which can give 250–600 mg per 100 g. Kale, broccoli, and watercress are vegetables high in calcium, with 100–150 mg per 100 g [42]. Still, the effect that these items have on the population's overall calcium intake is dependent upon the dietary habits of that community. Dairy products make up about 14% of the total dietary energy intake in wealthy nations, whereas in underdeveloped nations, they only make up about 4% [6]. In this sense, even though they also consume far less calcium overall, certain Asian nations acquire a larger percentage of their total calcium intake from non-animal foods like grains, legumes, and vegetables than from dairy products [43]. Dairy products provide 72 and 58% of the calcium supply in the United States and Holland, respectively. In China, however, the majority of calcium intake comes from vegetables (30.2%) and legumes (16.7%) [44-46] foods that have been fortified such as juices and cereals, can also develop into significant calcium sources. For certain people, supplements are an excellent dietary supply of calcium as well. Up to 1000 mg of calcium can be found in some over-the-counter calcium supplements, meeting the dietary needs of the majority of adults. Still, supplement usage differs from nation to nation. About 40% of adults in the US and Canada were reported to have taken calcium supplements in the month before to the interview; this percentage rose to 70% in the group of older women [40, 43, 47]. However, very few women reported taking calcium supplements in Holland and Argentina, even during pregnancy [42, 48, 49].

PROTEIN

One of the most important nutritional aspects for maintaining independence is getting enough protein, mostly because it helps prevent frailty, sarcopenia, and

related comorbidities in later age by reducing the loss of muscle mass and strength [50, 51, 52].

DAILY QUANTITY

0.8 g of protein per kilogram of body weight (bw) is the current worldwide Recommended Dietary Allowance (RDA) for protein, irrespective of age [53, 54]. The Reference Nutrient intake (RNI) in the United Kingdom is 0.75 g/kg/bw [55]. These suggestions are based on the bare minimum amount necessary to preserve the nitrogen balance and are not tailored to the degree of physical activity (PAL). In contrast to individuals who are active, people with poor PAL have lower rates of nitrogen retention, which means they require more protein to maintain muscle tissue [65]. Given that physical activity levels decline with aging [57], this is a crucial consideration when assessing protein requirements. Moreover, an adult's body experiences several physiological changes as they age that affect how proteins are used and, consequently, what's needed (such as insulin and anabolic resistance). reduced IGF-1 levels, resistance, inflammation, and poor digestion [51, 58, 59, 60]. The suitability of the existing guidelines for proteins has also been questioned due to possible methodological errors. First, there's a chance that the nitrogen-balance approach, which was employed in most pooled research, is inaccurate since nitrogen input and outflow pathways may not have been tracked [51, 61]. The requirement for nitrogen-balance investigations to be conducted in a regulated clinical setting is a second constraint, meaning that the evaluation of protein requirements is comparatively brief [61]. A priority area for academic research is the lack of data on long-term assessments of protein requirements in aging people using new, more precise assessment methods [62, 63].

AMINO ACID

The fundamental components of proteins, amino acids provide the nitrogenous framework for molecules such as hormones and neurotransmitters. An amino acid is an organic molecule in chemistry that has both a carboxylic acid (-CH₂) and an amino acid (-NH₂). The term "amino acid" comes from the COOH) functional group. Proteins are either lengthy chains or polymerization of alpha-amino acid polymers, a particular class of amino acids. Because the functional groups of amino and carboxylic acids are separated by just one carbon atom—typically a chiral carbon—alpha-amino acids are special. In this piece, we'll only concentrate on the alpha-amino acids found in proteins [64, 65].

The 20 to 22 amino acids that comprise proteins include:

- Alanine
- Arginine
- Asparagine
- Aspartic Acid
- Cysteine

- Glutamic acid
- Glutamine
- Glycine
- Histidine
- Isoleucine
- Leucine
- Lysine
- Methionine
- Phenylalanine
- Proline
- Serine
- Threonine
- Tryptophan
- Tyrosine
- Valine
- Selenocysteine
- Pyrrolysine (not used in human protein synthesis) of these 20 amino acids, nine amino acids are essential.
- Phenylalanine
- Valine
- Tryptophan
- Threonine
- Isoleucine
- Methionine
- Histidine
- Leucine
- Lysine

You can cut out the non-essential amino acids—also referred to as dispensable amino acids—from your diet. Only the essential amino acids are needed by the human body to synthesis these other amino acids. In a healthy adult, the nine amino acids listed above are the most common just the necessary amino acids. However, because the body is unable to synthesize some amino acids in sufficient amounts during specific physiological times of growth, such as pregnancy, teenage growth, or the healing process following damage, certain amino acids, such as histidine and arginine, may be regarded as conditionally necessary [66].

CONCLUSION

You may make sure you get "enough" micronutrients each day and treat vitamin and mineral shortages using dietary supplements. Additionally, there is evidence that some supplements can improve health and lessen the symptoms of some disease circumstances. Ongoing study, though, is being done on the effectiveness of supplements. People mistakenly believed that a substance labeled as "natural" was risk-free and safe. Being natural does not, in reality, imply constant safety. The safety of food supplements is contingent upon various aspects, including but not limited to their chemical composition, method of manufacture, mode of action, and dosage administered.

REFERENCES

1. Scofield, D. E., & Unruh, S. (2006). Dietary supplement use among adolescent athletes in central Nebraska and their sources of information. *The Journal of Strength & Conditioning Research*, 20(2), 452-455.
2. Calfee, R., & Fadale, P. (2006). Popular ergogenic drugs and supplements in young athletes. *Pediatrics*, 117(3), e577-e589.
3. Maughan, R. J. (2004). King, DS. Lea, T. *Dietary supplements. Journal of Sports Sciences*, Abingdon, 22(1), 95-113.
4. Pereira, R. F., Lajolo, F. M., & Hirschbruch, M. D. (2003). Consumo de suplementos por alunos de academias de ginástica em São Paulo. *Revista de nutrição*, 16, 265-272.
5. Glob. Burden Dis. Risk Factors Collab., Forouzanfar, M. H., Alexander, L., Anderson, H. R., & Bachman, V. F. (2015). Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*, 386, 2287–323.
6. Willett, W. C., & Stampfer, M. J. (2013). Current evidence on healthy eating. *Annual review of public health*, 34, 77-95.
7. US FDA [Food Drug Adm.]. (2017). What is a dietary supplement. Updated Jan. 13. US FDA, Silver. <https://www.fda.gov/food/dietarysupplements/usingdietarysupplements/ucm480069.htm#whatis>
8. Eur. Food Saf. Auth. 2015. Food supplements. Eur. Food Saf. Auth., Parma, Ital. <http://www.efsa.europa.eu/en/topics/topic/food-supplements>
9. Burdock, G. A. (2000). Dietary supplements and lessons to be learned from GRAS. *Regul Toxicol Pharmacol*, 31, 68–76.
10. Nowak, R. E. (2010). DSHEA's failure: why a proactive approach to dietary supplement regulation is needed to effectively protect consumers. *Univ. Ill. Law Rev*, 1045-1081.
11. Karbownik, M. S., Horne, R., Paul, E., Kowalczyk, E., & Szemraj, J. (2021). Determinants of knowledge about dietary supplements among polish internet users: Nationwide cross-sectional study. *Journal of medical Internet research*, 23(4), e25228. doi: 10.2196/25228
12. Wierzejska, R., Jarosz, M., Siuba, M., & Rambuszek, M. (2014). Assessing patients' attitudes towards dietary supplements. *Roczniki Państwowego Zakładu Higieny*, 65(4), 317–323.
13. Park, K. Y., Jeong, J. K., Lee, Y. E., & Daily III, J. W. (2014). Health benefits of kimchi (Korean fermented vegetables) as a probiotic food. *Journal of medicinal food*, 17(1), 6-20.
14. Dietary Supplement Health and Education Act of 1994, Public Law No. 103-417 [1994].

- <https://www.fda.gov/regulatoryinformation/lawsenforcedbyfda/significantamendmentstotheftdaact/ucm148003.htm#sec3>
15. Hallak, A., Fabrini, S. P., & Peluzio, M. D. C. G. (2007). Avaliação do consumo de suplementos nutricionais em academias da zona sul de Belo Horizonte, MG, Brasil. *Revista Brasileira de Nutrição Esportiva*, 1(2), 55-60.
 16. Yetley, E. A. (2007). Multivitamin and multiminer dietary supplements: definitions, characterization, bioavailability, and drug interactions. *The American journal of clinical nutrition*, 85(1), 269S-276S.
 17. Abrams, S. A. (2015). Is it time to put a moratorium on new infant formulas that are not adequately investigated?. *The Journal of Pediatrics*, 166(3), 756-760.
 18. Myers, S. S., Smith, M. R., Guth, S., Golden, C. D., Vaitla, B., Mueller, N. D., ... & Huybers, P. (2017). Climate change and global food systems: potential impacts on food security and undernutrition. *Annual review of public health*, 38, 259-277.
 19. Havenetidis, K. (2016). The use of creatine supplements in the military. *BMJ Military Health*, 162(4), 242-248.
 20. Bailes, J. E., Cantu, R. C., & Day, A. L. (2002). The neurosurgeon in sport: awareness of the risks of heatstroke and dietary supplements. *Neurosurgery*, 51(2), 283-288.
 21. Lopez, R. M., & Casa, D. J. (2009). The influence of nutritional ergogenic aids on exercise heat tolerance and hydration status. *Current sports medicine reports*, 8(4), 192-199.
 22. Lopez, R. M., Casa, D. J., McDermott, B. P., Ganio, M. S., Armstrong, L. E., & Maresh, C. M. (2009). Does creatine supplementation hinder exercise heat tolerance or hydration status? A systematic review with meta-analyses. *Journal of athletic training*, 44(2), 215-223.
 23. Ackatia-Armah, R. S., McDonald, C. M., Doumbia, S., Erhardt, J. G., Hamer, D. H., & Brown, K. H. (2015). Malian children with moderate acute malnutrition who are treated with lipid-based dietary supplements have greater weight gains and recovery rates than those treated with locally produced cereal-legume products: a community-based, cluster-randomized trial. *The American journal of clinical nutrition*, 101(3), 632-645.
 24. Gordon, J. E., & Scrimshaw, N. S. (1972). Field trial of a newly developed food for prevention of malnutrition. *World Rev Nutr Diet*, 15, 256-288.
 25. Scrimshaw, N. S. (2007). Fifty-five-year personal experience with human nutrition worldwide. *Annu. Rev. Nutr.*, 27, 1-18.
 26. Scrimshaw, N. S., & Viteri, F. E. (2010). INCAP studies of kwashiorkor and marasmus. *Food and nutrition bulletin*, 31(1), 34-41.
 27. UNICEF. 2015. Management of Severe Acute Malnutrition in Children. UNICEF Progr. Guid. Doc. New York: UNICEF.
 28. https://www.unicef.org/eapro/UNICEF_program_guidance_on_management_of_SAM_2015.pdf
 28. Cardoso, M. A., Augusto, R. A., Bortolini, G. A., Oliveira, C. S., Tietzman, D. C., Sequeira, L. A., ... & ENFAC Working Group. (2016). Effect of providing multiple micronutrients in powder through primary healthcare on anemia in young Brazilian children: a multicentre pragmatic controlled trial. *PLoS One*, 11(3), e0151097.
 29. De-Regil, L. M., Suchdev, P. S., Vist, G. E., Walleser, S., & Peña-Rosas, J. P. (2013). Home fortification of foods with multiple micronutrient powders for health and nutrition in children under two years of age. *Evidence-Based Child Health: A Cochrane Review Journal*, 8(1), 112-201.
 30. Oliveira, C. S., Sampaio, P., Muniz, P. T., Cardoso, M. A., & ENFAC Working Group. (2016). Multiple micronutrients in powder delivered through primary health care reduce iron and vitamin A deficiencies in young Amazonian children. *Public Health Nutrition*, 19(16), 3039-3047.
 31. Pena-Rosas, J. P., De-Regil, L. M., Rogers, L. M., Bopardikar, A., & Panisset, U. (2012). Translating research into action: WHO evidence-informed guidelines for safe and effective micronutrient interventions. *The Journal of nutrition*, 142(1), 197S-204S.
 32. Margetts, B. (2006). Stopping the rot in nutrition science. *Public health nutrition*, 9(2), 169-173.
 33. White, C. (2015). Ranjit Chandra: how reputation bamboozled the scientific community. *BMJ*, 351.
 34. Brewster, N. A. T., & Goldsmith, P. D. (2007). Legal systems, institutional environment, and food safety. *Agricultural Economics*, 36(1), 23-38.
 35. Food Stand. Aust. N. Z. (2016). Food standards code. Food Stand. Aust. N. Z., Canberra. <http://www.foodstandards.gov.au/code/Pages/default.aspx>
 36. US FDA [Food Drug Adm.]. (2017). Dietary supplement products and ingredients. Updated Aug. 1. US FDA, Silver Spring, MD. <https://www.fda.gov/Food/DietarySupplements/ProductsIngredients/>
 37. Van Breemen, R. B., Fong, H. H., & Farnsworth, N. R. (2008). Ensuring the safety of botanical dietary supplements. *The American journal of clinical nutrition*, 87(2), 509S-513S.
 38. World Health Organization. Vitamin and Mineral Requirements in Human Nutrition. 2nd ed. WHO; Geneva, Switzerland: 2004.
 39. Ross, A. C., Manson, J. E., Abrams, S. A., Aloia, J. F., Brannon, P. M., Clinton, S. K., ... & Shapses, S. A. (2011). The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. *The Journal of Clinical Endocrinology & Metabolism*, 96(1), 53-58. doi: 10.1210/jc.2010-2704
 40. Belizan, J. M., & Villar, J. (1980). The relationship between calcium intake and edema-, proteinuria-,

- and hypertension-gestosis: An hypothesis. *Am J Clin Nutr*, 33, 2202–2210. doi: 10.1093/ajcn/33.10.2202
41. Bressani, R., Turcios, J. C., & de Ruiz, A. S. C. (2002). Nixtamalization effects on the contents of phytic acid, calcium, iron and zinc in the whole grain, endosperm and germ of maize. *Food science and technology international*, 8(2), 81-86. doi: 10.1177/1082013202008002574. CrossRef] Google Scholar]
 42. US Department of Agriculture, Agricultural Research Service, Nutrient Data Laboratory USDA National Nutrient Database for Standard Reference, Release 28 [Slightly Revised] [accessed on 12 July 2019]; Version Current: May 2016. Available online: <http://www.ars.usda.gov/ba/bhnrc/ndl>
 43. Silanikove, N., Leitner, G., & Merin, U. (2015). The interrelationships between lactose intolerance and the modern dairy industry: global perspectives in evolutionary and historical backgrounds. *Nutrients*, 7(9), 7312-7331. doi: 10.3390/nu7095340.
 44. Dietary Reference Intakes. Recommended Dietary Allowances and Adequate Intakes, Element. [accessed on 11 July 2019]; Available online: http://nationalacademies.org/hmd/~media/Files/Report%20Files/2019/DRI-Tables-2019/2_RDAIIVVE.pdf?la=en
 45. Huang, F., Wang, Z., Zhang, J., Du, W., Su, C., Jiang, H., ... & Wang, H. (2018). Dietary calcium intake and food sources among Chinese adults in CNTCS. *PLoS One*, 13(10), e0205045. doi: 10.1371/journal.pone.0205045.
 46. Willemse, J. P., Meertens, L. J., Scheepers, H. C., Achten, N. M., Eussen, S. J., van Dongen, M. C., & Smits, L. J. (2020). Calcium intake from diet and supplement use during early pregnancy: The Expect study I. *European journal of nutrition*, 59, 167-174. doi: 10.1007/s00394-019-01896-8.
 47. Bailey, R. L., Dodd, K. W., Goldman, J. A., Gahche, J. J., Dwyer, J. T., Moshfegh, A. J., ... & Picciano, M. F. (2010). Estimation of total usual calcium and vitamin D intakes in the United States. *The Journal of nutrition*, 140(4), 817-822. doi: 10.3945/jn.109.118539
 48. Ministerio de Salud de la Nación *Encuesta Nacional de Nutrición y Salud*; 2007. [accessed on 11 July 2019]; Presidencia de la Nación. Available online: <http://www.extensioncbc.com.ar/wp-content/uploads/ENNyS-2007.pdf>
 49. Cormick, G., Zhang, N. N., Andrade, S. P., Quiroga, M. J., Di Marco, I., Porta, A., ... & Belizán, J. M. (2014). Gaps between calcium recommendations to prevent pre-eclampsia and current intakes in one hospital in Argentina. *BMC Research Notes*, 7, 1-6. doi: 10.1186/1756-0500-7-920
 50. Wolfe, R. R. (2012). The role of dietary protein in optimizing muscle mass, function and health outcomes in older individuals. *British Journal of Nutrition*, 108(S2), S88-S93. doi: 10.1017/S0007114512002590.
 51. Bauer, J., Biolo, G., Cederholm, T., Cesari, M., Cruz-Jentoft, A. J., Morley, J. E., ... & Boirie, Y. (2013). Evidence-based recommendations for optimal dietary protein intake in older people: a position paper from the PROT-AGE Study Group. *Journal of the American Medical Directors Association*, 14(8), 542-559. doi: 10.1016/j.jamda.2013.05.021.
 52. Bradlee, M. L., Mustafa, J., Singer, M. R., & Moore, L. L. (2018). High-protein foods and physical activity protect against age-related muscle loss and functional decline. *The Journals of Gerontology: Series A*, 73(1), 88-94. doi: 10.1093/geron/glx070.
 53. Food and Nutrition Board [FNB] of the Institute of Medicine. Dietary Reference Intakes for Energy, Carbohydrate, Fibre, Fat, Fatty Acids, Cholesterol, Protein and Amino Acids [Macronutrients] The National Academies Press; Washington, DC, USA: 2005.
 54. World Health Organisation [WHO]. Dietary Reference Intakes for Energy, Carbohydrate, Fibre, Fat, Fatty Acids, Cholesterol, Protein and Amino Acids [Macronutrients] World Health Organisation [WHO]; Geneva, Switzerland: 2007. [WHO Technical Report Series 935].
 55. Committee on Medical Aspects of Food and Nutrition Policy [COMA]. Report of the Panel on Dietary Reference Values of the Committee on Medical Aspects of Food Policy. H.M. Stationery Office; London, UK: 1991. Dietary reference values for food energy and nutrients for the United Kingdom; pp. 1–210.
 56. Butterfield, G. E., & Calloway, D. H. (1984). Physical activity improves protein utilization in young men. *British Journal of Nutrition*, 51(2), 171-184. doi: 10.1079/BJN19840021
 57. Hallal, P. C., Andersen, L. B., Bull, F. C., Guthold, R., Haskell, W., & Ekelund, U. Lancet Physical Activity Series Working Group Global physical activity levels: Surveillance progress, pitfalls, and prospects., 2012, 380, 247–257. doi: 10.1016/S0140-6736[12]60646-1
 58. Wolfe, R. R., Miller, S. L., & Miller, K. B. (2008). Optimal protein intake in the elderly. *Clinical nutrition*, 27(5), 675-684. doi: 10.1016/j.clnu.2008.06.008
 59. Deutz, N. E., Bauer, J. M., Barazzoni, R., Biolo, G., Boirie, Y., Boly-Weber, A., ... & Calder, P. C. (2014). Protein intake and exercise for optimal muscle function with aging: recommendations from the ESPEN Expert Group. *Clinical nutrition*, 33(6), 929-936. doi: 10.1016/j.clnu.2014.04.007
 60. Phillips, S. M., Chevalier, S., & Leidy, H. J. (2016). Protein “requirements” beyond the RDA: implications for optimizing health. *Applied Physiology, Nutrition, and Metabolism*, 41(5), 565-572. doi: 10.1139/apnm-2015-0550

61. Millward, D. J. (2001). Methodological considerations. *Proceedings of the Nutrition Society*, 60(1), 3-5. doi: 10.1079/PNS200064
62. Rand, W. M., Pellett, P. L., & Young, V. R. (2003). Meta-analysis of nitrogen balance studies for estimating protein requirements in healthy adults. *The American journal of clinical nutrition*, 77(1), 109-127. doi: 10.1093/ajcn/77.1.109
63. Stokes, T., Hector, A. J., Morton, R. W., McGlory, C., & Phillips, S. M. (2018). Recent perspectives regarding the role of dietary protein for the promotion of muscle hypertrophy with resistance exercise training. *Nutrients*, 10(2), 180. doi: 10.3390/nu10020180
64. LaPelusa, A., & Kaushik, R. (2022). StatPearls Internet. StatPearls Publishing; Treasure Island [FL]: Nov14, 2022. Physiology, Proteins.
65. Wu, G. (2009). Amino acids: metabolism, functions, and nutrition. *Amino acids*, 37(1), 1-17.
66. De Koning, T. J. (2013). Amino acid synthesis deficiencies. *Handbook of Clinical Neurology*, 113, 1775-1783.