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Reimagining Roles of Dietary Supplements in Psychiatric Care

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Abstract

Despite impressive pharmaceutical advances, mental illness remains a leading cause of suffering and disability. Although some dietary supplements appear to respond to some needs not met by prescription medications, several obstacles prevent their study or use. This article proposes government-supported review and safety monitoring of supplements' use in caring for patients with mental illness.

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Appeal of Supplements

Dietary supplements are regulated more like foods than pharmaceuticals under the Dietary Supplement Health and Education Act (DSHEA) of 1994.¹ Consequently, a number of companies have aggressively marketed their dietary supplements, often highlighting products' "natural" ingredients and implying vague yet appealing health benefits, such as "mood support." Although commercially successful, such marketing tactics invite skepticism, and some clinicians hesitate to consider dietary supplements in care plans.

Nevertheless, some dietary supplement ingredients do have credible scientific support as therapeutics. Acetyl-L-carnitine, for example, has been the subject of 12 randomized controlled trials and has been shown to significantly reduce depressive symptoms in older adults.² In addition, omega-3 fatty acids have shown benefit in populations at high risk of developing schizophrenia.^{3,4,5} These are important findings, given data from 1990 to 2015 suggesting that an increase in conventional pharmaceutical therapies did not decrease the prevalence and symptoms of mood and anxiety disorders in 4 English-speaking countries.⁶

The limitations of conventional pharmaceuticals create a dilemma for patients and clinicians. It would be ideal to subject promising dietary supplements to the types of clinical trials that would definitively assess their potential value. Yet there is little financial incentive to perform extensive (and expensive) definitive research on their therapeutic potential. We first discuss obstacles to supplement research and then

propose government-supported review and safety monitoring of supplements' use to promote the greater good and minimize suffering.

Obstacles to Research

Regulatory requirements. Under existing regulations of the US Food and Drug Administration (FDA), manufacturers are not required to supply the FDA with evidence of the safety and efficacy of a dietary supplement for treatment of any disease, as they are for pharmaceuticals. Within the ClinicalTrials.gov database, as of August 24, 2021, a search for the terms “acetyl-L-carnitine” and “depression” generated 3 results, while a search for “escitalopram” (a serotonin reuptake inhibitor) and “depression” generated 238 results.⁷ Fewer researchers are invested in studying the efficacy and safety profiles of supplements without this infrastructure. Furthermore, the DSHEA effectively proclaimed that supplements do not need to be registered or approved by the FDA for production and sale.¹

The DSHEA also has downstream effects. Lack of FDA registration or review is a disincentive for clinicians to consider dietary supplements in treating patients. Many prescribers look to the FDA for **guidance on safe treatment** and thus are wary and skeptical of the benefits of “off-label” interventions like dietary supplements. Without authoritative regulation, many supplements will be regarded by clinicians as unregulated and outside their scope of practice. Clinicians might feel uneasy about assessing the risks and benefits of dietary supplements without FDA review and approval, which, for drugs, often requires clear delineation of indications and risks.

Lack of incentives. It is uncommon for insurance companies to cover dietary supplements unless there is extensive scientific evidence of proven health benefits (eg, folic acid for prenatal care, calcium and vitamin D for osteoporosis).⁸ Pharmaceutical companies and researchers are not incentivized to prove the efficacy of dietary supplements due to limitations of patent law.⁹ Intellectual property rights are granted to pharmaceutical companies to hold a temporary monopoly on innovative drugs, which enables the company to **set prices high enough** to recover development costs, fund future research, and ensure the business survival of the company.⁹ The nature of dietary supplements, however, makes it difficult to label any composition as a true innovative discovery and for companies to gain intellectual property rights. A discovery within the supplement industry entails (1) isolation of an active ingredient from an already known food to create a supplement with a previously unknown beneficial effect or (2) production of a health-promoting supplement with a novel combination of active and/or inert ingredients in a previously unknown manner.¹⁰ The rarity of innovative discovery discourages manufacturers from conducting trials, and some studies of dietary supplements' ingredients are limited to case reports or small clinical trials typically conducted by independent research groups with limited funding.

More research should be directed toward elucidating the small amount of already existing data on supplements' adverse effects. Some ingredients, for example, can affect cytochrome P450 enzymes activity in the liver and alter serum levels of other pharmaceuticals, which in turn can affect the action of drugs with a narrow therapeutic index (blood thinners, for example).¹¹ Excessive intake of some nutrients, especially those in fortified foods, in conjunction with intake of nutraceuticals, may lead to toxic blood levels of bioactive ingredients—vitamins A and D, for instance.¹¹ Greater knowledge of supplements would promote well-informed prescribing practices.

Gaining Knowledge

Although large, systematic clinical trials on dietary supplements may be lacking, clinicians can gather knowledge about them from other sources. Case reports, retrospective or prospective trials, and open-label trials can provide some clues about the possible efficacy and risks of such products. Even a collection of case reports on a particular supplement might convince some clinicians to accept that use of that supplement is associated with particular side effects or health benefits. For example, the cessation of side effects once supplement use stops would support an association between the side effects and use of that supplement. Case reports and small studies, unlike trials sponsored by large institutions and companies, involve fewer significant conflicts of interest that can influence study design. Cases can also provide insights that might be lost or overlooked in randomized controlled trials.^{12,13,14} The Office of Dietary Supplements at the National Institutes of Health currently compiles fact sheets on dietary supplements and disseminates information about cases and small studies.^{15,16} When large-scale clinical trial data are lacking, it is still possible to evaluate a supplement.

Need for Review and Data

In what follows, we argue that establishing a review entity and prescribers' database would promote the greater good (ie, utility¹⁷) and minimize suffering. For dietary supplements with a stock of convincing evidence, a reviewing body could help achieve these goals by "certifying" widely available and low-cost dietary supplements to treat psychiatric ailments. A reviewing body with governmental authority would thus support the scientific legitimacy of companies' claims about dietary supplements that have been certified. Such a reviewing body would help consumers understand how dietary supplements can be used to improve mental health and how to make informed choices about dietary supplements. It would also provide patients a sense of security in knowing which dietary supplements were recognized by the group and for which supplements the benefits outweighed the risks in patient cases.

Germany has established such infrastructure to approve dietary supplements for medical use.¹⁸ German Commission E, a surveillance body that was founded in 1978, has helped supplements become integrated into conventional medicine. The commission is tasked with banning risky supplements from the market and compiling information on approved supplements into monographs for the public. By giving supplements official recognition like conventional treatments for psychiatric disorders, Germany has expanded the utility of dietary supplements for its citizens. Most notably, herbal supplements make up 30% of all pharmaceutical sales in Germany, more than half of which are paid for by health insurance.¹⁸ The system, however, is far from perfect, with critics lamenting that the monographs of herbal drugs lack scientific evidence to back claims.¹⁹

Other models for expanding the utility of supplements exist besides reviewing bodies. For example, a governmental agency could be empowered to create a "certified supplement" program following the model of the US Department of Agriculture's National Organic Program,²⁰ which sets standards for production and labeling of products. A third avenue would be for private third-party entities to set standards for the composition and production methods of supplements. In this model, natural product or supplement manufacturers would submit to inspection to receive third-party accreditation (like the Joint Commission model for hospital quality assurance²¹). Our ideal accreditation system would likely assume the third-party model of the Joint

Commission, which would have greater flexibility to change procedures and staff in comparison to government organizations. However, it was only 14 years after the Joint Commission's inception in 1951 that the government recognized that its accreditation practices met Medicare Conditions of Participation.²² Unlike a nonprofit organization such as the Joint Commission, a governmental reviewing body would have the recognized legitimacy even with early implementation. Finally, we would like dietary supplements to be of similar status to pharmaceuticals, in that manufacturers are required to provide evidence of a drug's safety and effectiveness to the FDA for approval. A governmental reviewing body would transfer the goal of adducing high-quality evidence from clinical and academic settings to the dietary supplement industry.

Conclusion

Current regulations for approval and marketing of pharmaceuticals in the United States exclude dietary supplements, thereby removing financial incentives for manufacturers to conduct the large, randomized controlled trials required for approval of pharmaceuticals. This paper has discussed regulatory changes that could assist patients and clinicians in making personalized health care decisions about the potential benefits and risks of dietary supplements as part of treatment. Despite breathtaking developments in psychopharmacology over the last 60 years, mental illness remains a leading cause of disability.²³ Considering this substantial unmet need, it is important for clinicians to consider all reasonable options when caring for patients and for policymakers likewise when reviewing regulations. Evidence-based psychotherapies are broadly underutilized,² and existing data suggest that some dietary supplements are potentially useful and relatively safe.^{2,3,4,5,24,25,26,27}

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