

Book Review

The First Survivors of Alzheimer's: How Patients Recovered Life and Hope in Their Own Words by Dale Bredesen, Avery, 2021, 272 pp

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Pre-press 13 April 2022

There is an urgent need for generalizable treatments for Alzheimer's disease (AD). As many patients and families independently seek therapies, Dr. Dale Bredesen's latest best-selling book, "The First Survivors of Alzheimer's," offers solutions by describing "how patients recovered life and hope in their own words" [1]. The book comes in two parts, the first offering the testimony of seven patients who recount their "before and after" stories with Dr. Bredesen's individualized treatment protocol, and the second offering Dr. Bredesen's reflections on the program's wider implications, including use in other diseases.

The testimonies point to the tragic consequences of cognitive decline, including interpersonal and professional ruin. This evocative language will resonate with readers and contrasts sharply with the dry descriptions of clinical trials and surrogate endpoints following the US FDA's controversial accelerated approval of aducanumab, which was based on the successful removal of amyloid protein from the brains of AD patients, yet with safety concerns and questionable efficacy.

The research community is actively pursuing other therapeutic strategies, notably risk reduction through

lifestyle interventions for social, mental, and physical health [2]. The therapeutic rationale of Dr. Bredesen's program for reducing cognitive decline involves taking the logic of individual lifestyle intervention to the extreme, implicating dozens of variables such as vitamins, sleep hygiene, stress reduction, growth factors, and "toxins." Yet there currently are no sufficiently validated interventions for regular use that reduce cognitive decline. Dr. Bredesen's proposed solution is to combine multiple interventions with intuitive efficacy, making it a new non-validated intervention [3]. While we disagree with the strategy of combining potential treatments before validating them individually [4], the ethical guidelines of the Declaration of Helsinki allow for the use of unproven interventions for a serious disease with no alternative treatment [5].

However, these guidelines stipulate that unproven interventions must subsequently be made the object of research designed to evaluate their safety and efficacy, and that data derived from their usage be communicated in an unbiased way to the scientific and larger community, so as to avoid individual and public health harm due to widespread use of unsafe or ineffective non-validated interventions [6].

We argue that Dr. Bredesen's approach is therefore unsatisfying in three domains: clinical ethics, scientific communication, and public health impact [5]. Concerning clinical ethics, it is unclear if the

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involved patients in his publications were first offered the standard of care for AD management (cognitive, social, physical activity, with risk factor reduction) at no significant cost, in place of promoting his for-profit intervention. Dr. Bredesen's early articles did not mention the rejection of his proposed studies by institutional review boards (but he has mentioned this elsewhere). Concerning communication, the results he presents in his publications derive from methods that lack scientific rigor, and his financial conflicts of interest are not always reported [7]. Additionally, the language used is fulsome, which may cause readers to have a misleading impression of the protocol's efficacy. In all, this means that there is a need for extensive disclosure of these aspects of the protocol, without which hopeful patient stakeholders cannot undertake his protocol with informed consent. We think the therapeutic impact of the targets identified in the protocol should be tested individually before being combined [4]. Given its currently unproven nature and high initial costs (over \$1000 out of pocket, with additional monthly costs of hundreds for dietary supplements), the protocol would not be an efficient allocation of public health resources that Dr. Bredesen argues it to be. Nevertheless, our criticism is compatible with recognizing that certain readers may deem it prudent to undertake lifestyle changes, which can also be done at low or no cost, based on growing awareness of risk factors for dementia [2].

In conclusion, we argue that Dr. Bredesen has not yet sufficiently demonstrated that his therapeutic protocol is effective for regular use, and therefore is not yet a generalizable solution for AD. Such a solution can only be achieved through sound confirmatory clinical research [9]. The book's heartfelt testimonies, while compelling, unfortunately cannot replace data [7]. They serve as a reminder that the biomedical AD research community does need to listen more to the perspectives of people living with dementia and include them as equal partners in research [10]. Such involvement should go hand-in-hand with rigorous methods to find effective interventions and cures for AD.

ACKNOWLEDGMENTS

Thanks to Dr. Joanna Hellmuth for help in proof-reading the manuscript.

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