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LETTER

Are trailblazing trials for reducing cognitive decline putting the cart before the horse?

McEwen et al.'s PREVENTION trial published in this journal[1] is "designed to evaluate the efficacy of a personalized, predominantly remote-based, multimodal intervention for the treatment of early stage cognitive decline due to AD neuropathology" (p. 8). The logic behind the trial is as follows: "Because monotherapies have failed to prevent or ameliorate AD, interventional studies should deploy multiple, targeted interventions that address the dysfunctional systems that give rise to AD" (p. 1). There are three issues with their study that undermine the authors' efforts to use the study to "develop an evidence-based framework for a clinical implementation model of reducing cognitive decline" (p. 8).

First, a recent Cochrane review on multi-domain interventions for dementia risk reduction "found no evidence that multi-domain interventions can prevent incident dementia,"[2] so multi-domain interventions are still non-validated treatments. Second, when non-validated treatments are combined before being validated, it becomes increasingly difficult to identify where treatment effects come from because of possible interactions between treatment components. This is one of the problems of the work of Dr. Dale Bredesen, whom McEwen et al.[1] cite as having "trailblazed the field of clinical, multicomponent, precision medicine for the treatment of cognitive decline with promising results" (p. 2). Unfortunately, his results based on "metabolic enhancement protocols," are far from promising because of lack of methodological rigor in producing them—no controls, no consistent measurements, unmeasured language and disregard of publication norms, no methods section and low generalizability, and financial gain from marketing the protocols in best-selling books.[3,4] While the PREVENTION trial does not suffer from these striking drawbacks and is a randomized controlled trial (RCT), what is actually being randomized—and therefore tested—is not the multi-domain treatment itself but rather "health coaching": "Participants are assigned randomly to a personalized, multimodal lifestyle intervention with or without health coaching"[1] (p. 3). Those in the coaching group, beyond extensive contact with a health coach, are also "provided with the resources to carry out … recommendations" (p. 5). Health coaching is thought to "encourage, inspire, and empower patients to reach their maximum potential" (p. 8).

But is the availability of health coaching a major priority for dementia research? Individualistic midlife interventions focusing on motivation and protocol adherence should not distract from the need to study the physical, mental, and social environment of individuals and communities across the lifetime.[5] This is because the wealth–brain health link is a double-edged sword: socio-economic deprivation not only increases dementia risk[6] but also reduces participation in multi-domain interventions aiming at risk reduction like the PREVENTION trial.[7]

In conclusion, McEwen et al. have a laudable goal of bringing rigor to the application of precision medicine to cognitive decline, which has been tarnished by previous pseudoscientific efforts. But their study design undermines the objective of building an evidence base for risk reduction, because it can only provide evidence of the effects of coaching and resources to improve participation in a currently non-validated, individualized protocol, for only these elements separate the study groups. Moving forward, and given the growing literature on health disparities for dementia affecting significant portions of the population, the extent to which individual health coaching should be a priority for dementia research should be the subject of a larger democratic debate around priority setting within the divided research community.[8]

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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