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Time-restricted eating: What we know and where the field is going

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Time-restricted eating (TRE) is a temporal dietary intervention that restricts all dietary intake to a consistent 6- to 11-hour daily eating window with no effort to restrict diet quality or quantity required. TRE is unique in that is one of the few dietary interventions that was created to improve health by supporting the circadian system. Both the consistency of the daily eating window and the lack of prescribed caloric restriction are important differentiating factors between TRE and intermittent fasting.

The research that laid the groundwork for TRE started in rodent models in 2000, demonstrating that restricting feeding times uncouples circadian oscillators in peripheral tissues from those in the brain [1]. In 2007, it was observed that high-fat diets disrupt both behavioral and molecular circadian rhythms in mice [2]. Time-restricted feeding (TRF) as an overt dietary intervention to improve health was first performed in mice 10 years ago in 2012 by Satchidananda Panda's team [3]. This study demonstrated that, when mice on a high-fat diet ate within an 8-hour window, they did not gain weight and they had many health improvements compared with the mice that ate the same amount and quality of food without any time restrictions. These and many other seminal papers paved the way for the first studies to assess temporal eating patterns in humans. The first study to assess eating times was published in 2015 [4]. This study established that more than 50% of adults had an eating window of 14.75 hours or more. The study also included a pilot TRE trial demonstrating the potential for weight loss, improved sleep and energy, and decreased appetite. The first clinical trials assessing the health impacts of TRE found that TRE could improve glucose regulation and other cardiometabolic health factors independently of weight loss [5,6]. The term TRF was subsequently changed to TRE (feeding to eating) in future studies to make the terminology more appropriate for humans [7].

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CONFLICT OF INTEREST

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The field of TRE clinical trials is very new, and research on the topic has increased dramatically in the past 3 years, with many more studies under way. From 2015 to 2019, there were a total of 12 publications on clinical trials assessing TRE [8]. In the past 3 years (2020–2022), there have been 42 clinical trials published with the term TRE or TRF (PubMed search). Currently, Clinicaltrials.gov has 165 studies (all stages) that use the term "time-restricted."

The TRE clinical trials started with small, noninvasive studies in a population of generally healthy adults who frequently had overweight or obesity. The eating window of the TRE intervention of these studies typically ranged from 6 to 10 hours (with exceptions of 4 hours and 12 hours) and lasted for about 4 to 12 weeks [8]. A total of 4 hours did not show additional benefits but did have an increase in minor adverse events (e.g., headaches, moodiness, nausea) [9]. The 12-hour eating window did not yield health benefits [10]. Trials with an eating window of 6 to 10 hours found that TRE was generally safe and well received and that it had a variety of health benefits. Health benefits were dependent on the population and study outcomes and they included (but were not limited to) the following: weight loss [4,11-14], improved muscle performance [15], improved energy and restfulness [4,6,16], decreased hunger [4,17], improved glucose regulation [5,6,12,13,17-19], decreased blood pressure [5,6,11,14], and improved cholesterol [6,11].

More recent and ongoing studies are now typically randomized controlled trials (RCTs) with larger sample sizes. Now that safety has been established in smaller studies, clinical trials are focusing on populations with more complex health issues such as type 2 diabetes, cardiovascular disease, and cancer. A few also extended the duration of intervention to up to 1 year.

Although most studies have shown the benefits of TRE, albeit of small magnitude in some studies, some have found null results. This indicates that TRE may need more time to see changes, or that it may show benefits in only specific populations. It is very difficult to assess the role of TRE as part of a healthy lifestyle, to support health and prevent disease, rather than only as treatment for an already existing condition. Very large-scale and multiyear studies are needed to see changes in a currently healthy population. This may explain some null results in current studies. Conflicting outcomes may also be due to differences in research methods. A lack of eating window assessment, participants with short eating windows at baseline, and/or little to no monitoring or contact with participants throughout the study have occurred in multiple studies and they are functionally very different interventions. This leads to the inability to make conclusions about the outcomes of the intervention because the differences could be explained by the variation in methods alone.

It is important to note that, in addition to the approximately 54 clinical trials that have been published on TRE, there have also been 54 reviews published (note, this includes reviews published on animal models as well). Reviews can be extremely valuable to a field, especially to one evolving so rapidly and that encompasses researchers from so many fields. However, moving forward, the focus should be on original research.

In this special issue on TRE, we are excited to present some important new clinical and basic findings to help fill some of the gaps that exist in safety and efficacy as well as reviews to help put new findings into the context of what has been discovered in previous years. New insights include the following: (1) new or understudied populations, including breast cancer survivors, pre- and postmenopausal women, and nonhuman primates; (2) innovative methods and analysis, including transcriptomics in adipose tissue, myofibrillar protein synthesis rates, hormonal changes, and bone metabolism and health; (3) insight into changes in weight and fat, including mathematical modeling of the circadian phase of dietary consumption and comparisons of caloric restriction, protein pacing, and temporal eating pattern; (4) a RCT to assess glucose regulation in a population that has obesity; and (5) assessments of other dietary changes and behaviors, mood, and sleep when practicing TRE. Reviews in this special issue include a meta-analysis comparing the effectiveness of intermittent fasting and TRE, a review of energetics in mice, circadian regulation of cardiometabolic disorders in aging, and the feasibility of TRE in adults with overweight or type 2 diabetes.

We believe that this issue is timely, but it is just the beginning of a rapidly emerging field. There are many more questions to be answered about TRE. Future studies are needed to understand the feasibility, efficacy, safety, and mechanisms of TRE. Thus, future studies should be RCTs (in most cases), have larger sample sizes, be of an extended intervention duration (6 months to multiple years), include multisite trials, study novel populations, and, most importantly, ensure proper methods for assessing dietary intake and participant communication.O

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