

## Letter to Editor

# Intermittent Fasting and Adding More Days to Life

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## Letter to Editor

With over 50% of the adult population in the UK currently classified as overweight or obese, accompanied by an increased risk of type 2 diabetes and cardiovascular disease, finding more effective strategies to manage these conditions remains imperative [1]. In 2016, World Health Organization (WHO) reported that more than 1.9 billion people in the world were overweight and over 650 million people were obese which has tripled in number since 1975 [2]. To date, the most robust intervention efficient in warding off the aforementioned cellular markers of aging is Calorie Restriction (CR) that involves the administration of a well-balanced, nutrient-dense diet that reduces calorie intake by 20% to 40% without malnutrition [3]. It is the only non-genetic intervention that has consistently been found to extend both mean and maximal life span across a variety of species [4]. Randomized trials demonstrate that intentional weight loss reduces type 2 diabetes, retards aging-related functional decline; and increases cognitive and physical function; and increases lifespan [5]. Modest weight losses of 5%-10% have been associated with significant improvements in cardiovascular disease risk factors (i.e., decreased HbA1C levels, reduced blood pressure, increase in HDL cholesterol, decreased plasma triglycerides) in patients with T2D [6]. In addition to the weight loss effects and metabolic improvements, several other beneficial effects of therapeutic fasting have been described including improvements in lipid profiles, osteoarthritis, healing of thrombophlebitis, healing of refractory dermal ulcers and tolerance of elective surgery [7]. Recent findings indicate that meal timing is crucial, with both intermittent fasting and adjusted diurnal rhythm of feeding improving health and function, in the absence of changes in overall intake. Lowered intake of particular nutrients, rather than of overall calories, is also key, with protein and specific amino acids playing prominent roles [8]. Importantly, long-term exposure to a CR diet might also cause substantial side effects like amenorrhea, osteoporosis, decreased fertility and libido (due to reduced testosterone in men), impaired wound healing and increased susceptibility to infections [9,10]. Fasting is distinct from Caloric Restriction (CR), in which daily caloric intake is chronically reduced by up to 40%, but meal frequency is maintained [11]. The cellular and molecular mechanisms by which

Intermittent Fasting (IF) improves health and counteracts disease processes involve activation of adaptive cellular stress response signaling pathways that enhance mitochondrial health, DNA repair and Autophagy [12]. IF regimens that induce the metabolic switch have the potential to improve body composition in overweight individuals. Moreover, IF regimens also induce the coordinated activation of signaling pathways that optimize physiological function, enhance performance, and slow aging and disease processes [7]. Current evidence suggests that as little as 10 min of high intensity exercise can improve metabolic health and aerobic capacity and alternative day fasting can reduce obesity-associated changes in body composition, fasting insulin and glucose concentrations [12]. Studies in rodents have demonstrated that restricting the availability of food to the normal night time feeding cycle improves metabolic profiles and reduces the risk of obesity and obesity-related conditions, such as nonalcoholic fatty liver disease, and chronic diseases, such as diabetes and cancer [13]. Fasting periods with various patterns are found in most religions. In fact, this ascetic practice is referenced in the Old Testament, as well as other ancient texts such the Koran and the Mahabharata. Muslims, for example, fast from dawn until dusk during the month of Ramadan, while Christians, Jews, Buddhists, and Hindus traditionally fast on designated days or periods. For instance, Ramadan intermittent fasting was linked with improvements in cardio metabolic risk factors [14,15]. Studies reported that Total Cholesterol (TC), Low-Density Lipoprotein (LDL), High Density Lipoprotein (HDL) and blood glucose have been improved after Ramadan compared to before Ramadan among athletes [16]. Rahbar et al. [17] 2019 concluded that fasting in Ramadan independent of anthropometric measures decreases IGF-1, IL-2, and serum lipid levels. As Smocking has been forbidden during fasting of Ramadan, studies revealed a significant reduction in second-hand smoke levels in public places. Even with no advice on lifestyle changes, there are consistent-albeit transient-reductions in weight and fat mass with the Ramadan fast, especially in people with overweight or obesity [18]. Ramadan intermittent fasting might be associated with decrease in sexual desire, frequency of sexual intercourse and serum FSH level [19]. Remarkably, IF during early adult hood, and also during mid-life, was sufficient to extend lifespan, indicating a “memory” effect Hormesis is a phenomenon by which “low-level” toxic stress elicits response mechanisms that protect against similar but higher-level stresses associated with aging. Given that intermittent starvation in early life led to increased post-IF starvation resistance in addition to increased lifespan, hormesis could play a role [20]. One of metabolic effects of intermittent fasting is intermittent ketosis known for its appetite suppression effect resulting in voluntary calorie reduction. In terms of meal timing, skipping breakfast is similar to intermittent fasting [21]. Although several studies reported associations between breakfast skipping and fatigue at noon, worsens memory and higher body mass index as well as increased prevalence of obesity-related chronic illness; deficient in total energy, vitamins and minerals, increased risk of central

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adiposity, and risk of insulin resistance and cardio-metabolic disorders [22]. There are two basic varieties of the IF diet. The most popular variation is time-restricted feeding. It may be used in three variants: 16/8, 18/6 and 20/4. 16/8, consisting of a 16-h fast, and then an 8-h nutritional window. Another protocol consists of a 24-h fasting period, alternated with a 24-h eating period, repeated two or three times a week. There are two possible systems, 5:2 or 4:3. In the 5:2 system, in which caloric restriction is used for two days a week and a regular diet for 5 days [23]. However, intermittent fasting should not be used by children, pregnant women, and people performing heavy physical work [24]. Intermittent fasting would be a useful tool in distressful condition to improve learning and memory by down regulation of the putative molecular factors involved in neuro-inflammation, although chronic stressors are generally well-known for adverse effects on the body particularly cognitive decline [25]. To improve health, the goal should be to lose weight by reducing the total amount of calories consumed, rather than focusing on when those calories are consumed [26], 4-h to 8-h time restricted feeding reduces caloric intake (without calorie counting) and significantly decreases fat mass without changing lean mass in young resistance trained men. Gabel et al. [27] revealed that 8-h time restricted feeding produces mild caloric restriction and weight loss, without calorie counting. It may also offer clinical benefits by reducing blood pressure. Altering body composition in such a manner may be advantageous to the athlete for various biomechanical, aesthetic, and locomotive reasons, thereby increasing the likelihood of competitive success in a target weight-class (e.g., combat sports, weight lifting), weight-sensitive sports (e.g., endurance events, ski jumping), or aesthetically judged sports (e.g., gymnastics and bodybuilding) [28]. IF regimens may be a promising approach to lose weight and improve metabolic health for people who can tolerate intervals of not eating, or eating very little, for certain hours of the day or days of the week. If proven to be efficacious, these eating regimens may offer promising non pharmacologic approaches to improving health at the population level with multiple public health benefits [29].

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