

# The Association of Different Types of Intermittent Fasting with Mental Health: A Protocol for Systematic Review

## Abstract

The high prevalence of depression, stress, and anxiety imposes a high cost on society. Recently, intermittent fasting (IF) has attracted a great deal of attention regarding the improvement in physical and psychological health. Due to insufficient information in this field, our study will review systematically the effect of different types of IF including religious and nonreligious fasting on mental health. We will search MEDLINE/PubMed, Scopus, and Web of Science for papers published from the inception until the end of September 2024. All clinical trial studies that report the effect of intervention through intermittent fasting on mood disorders, stress, depression, and anxiety, in all countries, with their full text available in the English and Persian languages, will be included. Cochrane Risk of Bias Tool for Randomized Controlled Trials will be used to evaluate the quality of evidence in the domains of random sequence generation, allocation concealment, selective reporting, other bias, blinding of participants and personnel, blinding of outcome assessment, and incomplete outcome data. We will conduct the study in accordance with the guideline of the Preferred Reporting Items for Systematic Review and Meta-analyses Protocols. Our systematic review will clarify the answer of some important questions like “Does fasting interventions have any effectiveness on stress, anxiety and depression?” and “Are there differences between the effects of Ramadan fasting and other types of fasting on mental health?” It is hoped that the results can provide a new treatment for the most prevalent mental disorders.

**Keywords:** Anxiety, depression, intermittent fasting, Ramadan fasting, stress

## Introduction

Major depression is the most debilitating mental disorder in the world and the second most common mental disorder after anxiety.<sup>[1,2]</sup> According to the report of the World Health Organization in 2022, the prevalence of this disorder was 28% in the world.<sup>[3]</sup> The high prevalence of these disorders imposes a high cost on society. Although drug and psychotherapy interventions are the main treatments for depression, these approaches mostly do not achieve the expected results and about 50% of these patients do not respond to the current treatments.<sup>[4,5]</sup> This issue encourages researchers to find new therapeutic interventions. Recent evidence has suggested lifestyle factors, especially nutritional behaviors, as the main factors involved in depression, to the extent that the role of genetic factors in this field is limited to only 30 to 40%.<sup>[6,7]</sup> Therefore, the field of psychonutrition has expanded in parallel with the recognition of the protective role

of healthy and anti-inflammatory diets in the treatment of depression.<sup>[8,9]</sup> Developing individual treatments for mental disorders and improving their complications is one of the main challenges of recent research.

Recently, intermittent fasting (IF) has attracted a great deal of attention regarding the improvement in physical and psychological health.<sup>[10]</sup> IF refers to a dietary pattern that restricts food intake for a predetermined period of time so that the body can enter a period of fasting.<sup>[11,12]</sup> There are different protocols for IF, including alternate-day fasting (ADF, consuming no calories on fasting days), alternate-day modified fasting (ADMF, consuming less than 25% of baseline energy needs on fasting days), time-restricted fasting (TRF, restricting food intake to specific time periods of the day), and periodic fasting (PF, fasting only 1–2 days per week).<sup>[13]</sup>

The beneficial effects of fasting may be exerted through conserved nutrient-sensitive pathways that control circadian rhythms of appetite and energy expenditure and stress

**How to cite this article:** Rabiei S, The association of different types of intermittent fasting with mental health: A protocol for systematic review. *Int J Prev Med* 2025;16:43.

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10.4103/ijpvm.ijpvm\_312\_24

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response pathways that regulate cellular defenses such as antioxidant enzymes. Fasting may trigger adaptive cellular stress responses that prime host defense to confront with upcoming severe stress and counteract pathogenesis. Dietary restriction can stimulate the body surveillance system through activation of immune response or induction of autophagy to strengthen the immune system. The available evidence shows the positive effect of these types of diets on serum glucose and liver glycogen depletion. Shifting fuel from glycolysis to ketogenesis is another positive effect of these diets. During prolonged periods of food unavailability, metabolism is enhanced by the production and utilization of ketones derived from fatty acids, which are essential for maintaining brain and muscle functions, as well as by increasing the recycling of nutrients at the cellular level through autophagy and conversion to a storage mode.<sup>[14]</sup> Induction of cell repair, suppression of inflammation, an increase in neurotrophin production, and modulation of  $\gamma$ -mercaptobutyric acid (GMBA) are other possible mechanisms regarding the potential physiological effects of IF.<sup>[15-18]</sup> On the other hand, the gastrointestinal system-brain axis has attracted a great deal of attention due to the role of microbiota on depression and anxiety.<sup>[19,20]</sup> Fasting improves gut microbiota disturbances and inflammation by reducing the intake of inflammatory foods and reducing blood flow devoted to food digestion.<sup>[21]</sup>

As mentioned above, the idea that the less the eating frequency, the more the healing effect on mental health has become the focus of researchers to this area. Some researchers suggest that religious fasting affects spiritual progress and stress as an emotional variable too. Ramadan fasting is a kind of fasting that involves people abstaining from eating and drinking during the time between sunrise and sunset for 30 days (Ramadan month).<sup>[22-24]</sup> However, researchers have shown that physiological changes occurring during Ramadan fasting might be different from those during the other kinds of IF. According to the findings of Riat *et al.*'s<sup>[25]</sup> study, the level of brain-derived neurotrophic factor (BDNF) decreased during 1 month of Ramadan fasting and returned to its normal level 1 month after Ramadan. This change is significantly related to mood improvement. In addition, the significant relationship between the level of BDNF and body composition parameters indicates the positive effects of Ramadan fasting on the physical and mental health. In addition to BDNF, other neuropeptides such as neuropeptide Y and Orexin increase during fasting periods, which is associated with mood improvement.<sup>[26]</sup> Some studies indicate the negative or insufficient effects of these types of diets on improving mood and depression.<sup>[21,27]</sup>

Despite several clinical studies regarding the metabolic effects of IF on various mental health indicators, a few systematic reviews have been conducted in this field,<sup>[28,29]</sup> and furthermore, there is no comparison between the effects of Ramadan fasting and other types of fasting on

psychological aspects. There is still no consensus regarding the effect of IF on mood, depression, stress, and anxiety. Meanwhile, knowing the effects of IF regimes may open a new window toward the treatment of the most common mental disorders such as stress, anxiety, and depression. Therefore, the aim of this study will be to review systematically the association of different types of IF with mental health. In addition, Ramadan fasting and other types of fasting regimes will be compared in terms of their effect on mental health status.

## Methods

This protocol is prepared in accordance with the PRISMA-P (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols) guideline, which is favored for outlining components of systematic view and meta-analysis protocols.<sup>[30]</sup> Since it is a literature-based study, ethical approval is unnecessary. The present protocol has been registered in the PROSPERO database under registration number CRD42024558725.

## Search strategy

The primary source of literature is a structured search of major electronic databases including Web of Science, PubMed, and Scopus. These databases will be searched for relevant articles by combining Medical Subject Headings (MeSH) such as “intermittent fasting”, “fasting”, “Islamic fasting”, “Ramadan fasting”, “time restricted fasting”, “alternate day fasting”, “religious fasting”, “mood”, “depression”, “depressive”, “major depression”, “stress”, “anxiety”, “mood disorders”, “mental health”, “mental disorders”, “Randomized controlled trial”, “Quasi experimental study”, “Randomized clinical trial”, “Semi experimental study”, “RCT”, and “Cluster randomized trial”. Search terms will be adapted according to the requirements or individual databases. Selected keywords are shown in Table 1. The search will be limited to publications that were written in the English or Persian language from their inception until September 30, 2024. References of retrieved articles and relevant reviews will be scanned for potentially eligible studies.

## Types of participants/target group

Data related to all adults over 18 years old from both sexes who are assessed for depression, stress, anxiety, or mood disorders without any comorbidity from any countries will be examined.

## Primary outcome

Statuses of mental health, including mood disorders, stress, anxiety, and depression, of those who received any type of IF (Ramadan fasting or other types of fasting) were compared with those of the control group who received a low-calorie diet or no calorie restriction and will be considered as the primary outcomes in general and if available by sex and type of IF. Furthermore, the

comparison between Ramadan fasting and other types of fasting with regard to mental health will be evaluated.

### Selection criteria

Studies that meet the following criteria will be considered for inclusion in the study:

All clinical trial studies (without restriction to specific groups) including cluster randomized, quasirandomized, and nonrandomized controlled trials (CCTs) (including controlled before and after studies (CBAs)) that report the effect of intervention through IF (all types such as Ramadan and other types of fasting) on mood disorders, stress, depression, and anxiety recognized by validated questionnaires, in all countries, with their full text available in the English and Persian languages, will be included.

### Exclusion criteria

Studies designed as cross-sectional, cohort, and case-control, in addition to studies which reported the findings with specific conditions such as comorbidity of any other diseases like diabetes or other psychological disorders, will be excluded from this study. The studies which assessed the effect of intervention (defined in this study) in patients with COVID-19 will also be excluded. Any studies that presented findings solely related to children under the age of 18 or specific settings will also be excluded in this study. Studies will also be excluded if there is no access to the full text version.

### Data management and selection process

Two members of our research team independently will assess the relevant studies based on the inclusion and exclusion criteria. Each reviewer will scan the titles and abstracts of all potential articles to determine eligibilities. Disagreements will resolve consensually by a third researcher in the team. Then, two independent reviewers will read all eligible full texts and summarize relevant

content. All information on the phases of the selection process is identified in Figure 1 based on PRISMA.

### Data extraction

Table 2 shows data abstraction forms which will be used for extraction steps. The same two reviewers will perform the data extraction, independently. Reviewers will come to an agreement to address any discrepancies, and if there are any remaining differences, a third reviewer will step in to settle them. If any changes are required in the data extraction form, they will made during this stage.

### Quality assessment of included studies

In order to determine the quality of evidence, Cochrane Risk of Bias Tool for Randomized Controlled Trials will be used. This system helps to evaluate the quality of evidence

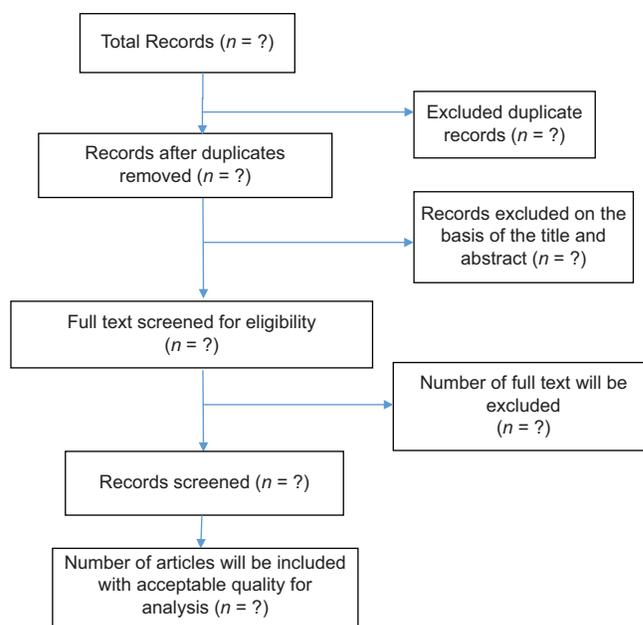


Figure 1: PRISMA flowchart of study selection

Table 1: Selected keywords

| Database       | Search strategy   |
|----------------|---|
| PubMed         | ((mood[Title/Abstract] OR depres*[Title/Abstract] OR stress[Title/Abstract] OR anxiety[Title/Abstract] OR "mood disorders"[Title/Abstract] OR "mental health"[Title/Abstract] OR "mental disorders"[Title/Abstract]) AND ("intermittent fasting"[Title/Abstract] OR fasting[Title/Abstract] OR "Islamic fasting"[Title/Abstract] OR "Ramadan fasting"[Title/Abstract] OR "time restricted fasting"[Title/Abstract] OR "alternate day fasting"[Title/Abstract] OR "religious fasting"[Title/Abstract]) AND ("Randomized controlled trial"[Title/Abstract] OR "Quasi experimental study"[Title/Abstract] OR "Randomized clinical trial"[Title/Abstract] OR "Semi experimental study"[Title/Abstract] OR "Cluster randomized trial"[Title/Abstract] OR RCT[Title/Abstract])) |
| Web of Science | AB=(mood OR depres* OR stress OR anxiety OR "mood disorders" OR "mental health" OR "mental disorders") AND ("intermittent fasting" OR fasting OR "Islamic fasting" OR "Ramadan fasting" OR "time restricted fasting" OR "alternate day fasting" OR "religious fasting") AND ("Randomized controlled trial" OR "Quasi experimental study" OR "Randomized clinical trial" OR "Semi experimental study" OR "Cluster randomized trial" OR RCT)  |
| Scopus         | ((TITLE-ABS-KEY ("mood OR depres* OR stress OR anxiety OR "mood disorders" OR "mental health" OR "mental disorders"))) AND (TITLE-ABS-KEY ("intermittent fasting" OR fasting OR "Islamic fasting" OR "Ramadan fasting" OR "time restricted fasting" OR "alternate day fasting" OR "religious fasting")) AND (TITLE-ABS-KEY ("Randomized controlled trial" OR "Quasi experimental study" OR "Randomized clinical trial" OR "Semi experimental study" OR "Cluster randomized trial" OR RCT)))   |

**Table 2: Characteristics of the studies on the effect of IF on mental health**

| Author (s)/year | Country | Sample size | Gender | Age | Psychological disorder | Measurement methods | Intervention | Control group | Duration of the study | Results | Any explanation if needed |
|-----------------|---------|-------------|--------|-----|------------------------|---------------------|--------------|---------------|-----------------------|---------|---------------------------|
|-----------------|---------|-------------|--------|-----|------------------------|---------------------|--------------|---------------|-----------------------|---------|---------------------------|

in the domains of random sequence generation, allocation concealment, selective reporting, other bias, blinding of participants and personnel, blinding of outcome assessment, and incomplete outcome data through three categories: “high risk”, “low risk”, and “unclear risk”.

### Software to be used

Searched articles will be exported to EndNote X20 for consequent scanning and extracting steps.

Data will be evaluated qualitatively to find which type of IF has the most effect on mental health. Obviously, the type of IF (religious fasting, nonreligious fasting) and type of mental disorders (stress, depression, anxiety) will be considered at the time of interpretation.

### Discussion

The prevalence of depression, stress, and mood disorders has become a significant global health concern in recent years among various populations.<sup>[31]</sup> The impacts of these mental disorders on productivity and economics are considerable.

Recently, different studies have suggested that IF may be a nutritional intervention potentially beneficial to mental health<sup>[15]</sup> by reducing symptoms of depression and anxiety in both clinical and preclinical studies.<sup>[28,32]</sup> So, the impact of IF on the prevalence of depression and stress globally is a topic of ongoing research and debate.

The association between IF and depression, stress, and mood disorders is less well studied but warrants further investigation.<sup>[32]</sup> Some proposed mechanisms by which IF could improve mood include switching metabolism from glucose to ketone bodies, inducing anti-inflammatory, antioxidative, and stress resistance effects, improving microbiota disturbances and intestinal inflammation through decreased inflammatory foods and blood flow to digestion,<sup>[28]</sup> and increasing neurotransmitter availability and neurotropic factors in the brain.<sup>[32]</sup> Furthermore, IF appears to enhance inhibitory GABA signaling, modulate excitatory glutamate pathways, increase neurotropic BDNF, increase serotonin levels by activating the HPA axis, and activate key metabolic sensors in the brain. These neurotransmitter and neuroplasticity changes may underlie some of the cognitive benefits of IF observed in animal studies. However, more research is needed to fully elucidate the effects of different fasting regimens on the human brain.<sup>[33-35]</sup> Furthermore, the effects of IF on mood appear to be mixed, in such a way that individual differences and potential negative effects,

especially for those with a history of eating disorders or mental health conditions, may lead to different findings.<sup>[36]</sup>

On the other hand, religious fasting, a type of periodic fasting, has some similarities to IF diet.<sup>[10,37]</sup> Studies have reported varying effects of Ramadan fasting on mental health and different hormones. Depression improvement may occur due to not only due fasting but also other lifestyle modifications during Ramadan month. For example, Ramadan fasting includes tobacco abstinence, which in turn is associated with improved depressive symptoms.<sup>[38]</sup> It should be considered that the specific effects of Ramadan fasting on anxiety levels are distinct from those of other types of fasting and may involve changes in hormone levels. Ramadan fasting is accompanied with some covariates such as changes in mealtime, sleep-wake time, sleep duration, exposure to light, and exercise, which can affect some hormone levels such as Leptin and Ghrelin.<sup>[39,40]</sup> The effects of Ramadan fasting on mental health may be mediated by some psychoneuroendocrine mechanisms such as the release of growth hormone, which can help reduce stress and anxiety.<sup>[22,41]</sup> Furthermore, Ramadan fasting can affect the circadian rhythms of various biological variables.<sup>[23,42]</sup> So, comparing the effects of IF with Ramadan fasting on mental health needs high precision. However, there is no consistency on the association between Ramadan fasting and mood. For example, some researchers did not observe a significant change in the level of Ghrelin and Leptin, while others reported some significant changes in the levels of these hormones during Ramadan.<sup>[43]</sup> There is a need for better-structured studies with larger samples and more variables to elucidate these mechanisms that mediate the effect of Ramadan fasting on mental health.

By the way, both Ramadan fasting and time-restricted feeding have been found to have some positive psychological effects, including improved mental clarity, reduced stress, and enhanced mood. However, the specific psychological effects and mechanisms may differ between the two practices.<sup>[44]</sup>

### Conclusions

IF shows promise as a potential therapeutic approach for treatment of depression and anxiety, but the effects appear to be varied and the current evidence is preliminary. This systematic reviews will clarify the answer of some important questions like “If fasting interventions has any effectiveness on stress, anxiety and depression”? and “If there is any difference between the effects of Ramadan fasting and other types of fasting on mental health”? It is hoped that the results can provide a new treatment for the most

prevalent mental disorders. However, healthcare providers should be cautious in recommending IF as a treatment for mood disorders until further evidence is available. Larger, controlled studies in clinical populations are warranted to clarify the benefits and risks of fasting for mental health.

### Financial support and sponsorship

National Nutrition and Food Technology Research Institute has supported financially this project.

### Conflicts of interest

There are no conflicts of interest.

**Received:** 08 Oct 24 **Accepted:** 27 Nov 24

**Published:** 30 Jul 25

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