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A randomized controlled trial on the efficacy of intermittent fasting and mediterranean diet on visceral adiposity and gut microbiota in overweight adults

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Abstract

Introduction: Obesity, particularly visceral adiposity, is a considerable risk factor for metabolic diseases, including insulin resistance, dyslipidemia, and chronic inflammation. A growing body of evidence suggests that the gut microbiota is influenced by food and plays a role in energy homeostasis and systemic metabolism, with dysbiosis typically observed in individuals with excess weight. Nutritional strategies of intermittent fasting (IF) and the Mediterranean diet (MD) have each been independently shown to help reduce adiposity and alter gut microbiota composition. However, there remains a dearth of research on the effects of IF and the MD when combined. **Objective:** The purpose of this study was to assess the effectiveness of a combination of IF and MD intervention for visceral fat loss, and for the dietary intervention to modify gut microbiota. **Methods:** A total of 60 participants were recruited into a 12-week human intervention study, along with longitudinal assessment of dietary intake and compliance. Visceral adiposity was measured using imaging-based techniques, and gut microbiota profiles were analysed using 16S rRNA sequencing. **Results:** As a result of the intervention, there were considerable reductions in visceral fat, increased microbial diversity, and enrichment of some beneficial bacterial taxa that are linked to better metabolic health. **Conclusion:** The data demonstrate that the time-restricted feeding in combination with the Mediterranean diet is an experimental dietary approach resulting in a decrease of visceral fat mass and restoration of the microbiota toward a healthy one. It also provides a required evidence-based structure for therapeutic nutrition in the treatment of metabolic complications induced by obesity.

Keywords: Intermittent fasting. Mediterranean diet. Visceral adiposity. Gut microbiota. Overweight adults. Metabolic health. Nutritional intervention.

Introduction

Global prevalence rates of overweight and obesity are currently high, with direct effects on metabolic disorders (insulin resistance, type II diabetes, cardiovascular diseases). Of the various fat depots, visceral adiposity has been shown to have the most negative associations with systemic inflammation, glucose metabolism, and cardiometabolic risk. The gut microbiota has also recently gained attention as a

mediator of energy balance, immune function, and metabolic health. Dysbiosis is likely the most prevalent form of gut microbiota dysregulation detected in overweight/inactive adult populations. The diet is the primary source of controlling both fat and gut microbiota composition. Intermittent fasting (IF) has a structured pattern of eating and fasting that has been shown to support weight loss, improve insulin sensitivity, and promote positive metabolic adaptations **[1,2]**.

The Mediterranean diet (MD), which promotes a diet high in fruits, vegetables, whole grains, healthy fats, and bioactive compounds, has also been shown to positively affect adiposity, inflammation, and even the diversity of gut microbiota. However, while there are metabolic benefits of implementing these lifestyle interventions alone, not much is known about how these two dietary interventions may impact visceral fat or gut microbial composition. This study aimed to explore the various synergistic effects of IF and MD on overweight adults, and to inform individuals about potential new evidence-based dietary strategies that target visceral adiposity and optimize gut microbiota to support healthy metabolic functionality **[3]**.

Metabolic Underpinnings of Dietary Interventions in Obesity

Visceral fat plays a significant role in metabolic abnormalities.

Visceral fat, also known as visceral adiposity or the accumulation of fat around internal organs, is a contributing factor to metabolic abnormalities. Visceral fat, however, unlike subcutaneous fat, is metabolically active and releases pro-inflammatory cytokines such as TNF-α and IL-6, both of which potentiate the risk for systemic inflammation and insulin resistance. Further, excess fat accumulation in visceral areas is associated with cardiometabolic abnormalities such as type 2 diabetes, dyslipidemia, and hypertension, in addition to its other metabolic effects **[4]**. Important to note, visceral fat is associated with liver functioning, ectopic fat deposition, and alterations in adipokine signalling. Because of the metabolic burden of visceral adiposity, achieving visceral fat loss should be a primary endpoint in nutrition intervention studies. Nutrition-related treatments that lead specifically to visceral fat loss will improve health risk and provide a non-pharmacological approach to the management of obesity **[5]**.

Gut Microbiota as Modifier of Energy Balance and Inflammation

Gut microbiota is central to energy regulation in the host, nutrient absorption, and immune functions. Changes in microbial diversity and community structures, called dysbiosis, are characteristic of overweight and obesity **[6]**. A change in microbiota can enhance energy harvest from food, induce low-grade inflammation, and interfere with insulin signalling **[7]**. Beneficial bacterial taxa can make short-chain fatty acids (SCFA) that improve gut barrier function, appetite control, and influence systemic inflammation. Some diet therapies, specifically intermittent fasting (IF) and Mediterranean diets (MD), can modify gut microbiota **[8]**. Controlling the size of theguts implicates thediversity, and can enhance the abundance of SCFA-producing bacteria, which both promote recovery of metabolic homeostasis and mitigate inflammation associated with obesity.

Mechanistic Rationale for IF and MD

Intermittent fasting (IF) and the Mediterranean diet (MD) both influence metabolism by some of the same and also by different mechanisms **[9,10]**. IF induces autophagy, improves insulin sensitivity, and allows you to time-restrict food and drink intake to align with an individual's own circadian rhythms, ultimately enhancing energy utilization. The MD is an anti-inflammatory approach to eating that is high in polyphenols, dietary fibers, and unsaturated fats, sugars out in the food matrix, and others, that reduce oxidative stress and have been shown to improve lipid biomarkers but also promote lipid metabolism and slightly boost involvement of anti-inflammatory pathways **[11]**. Both the MD and IF likely shift gut microbiota composition, although in different and complementary ways. IF typically enables the prometabolic changes in gut microbiota via the metabolic stress of fasting. The MD may differentially provide the prebiotic substrates to promote gut microbiota diversity. These posited mechanisms work together to reduce the deposition of visceral fat in the abdomen, improve metabolic outcomes, and maintain or restore gut microbiota balance.

Table 1 provides an overview of the different intervention protocols that participants in respective study groups followed. Participants in the control group ate a habitual diet, participants in the intermittent fasting (IF) group consumed food in a 16:8, time-restricted feeding window (this describes 16 hours fasting period); participants in the Mediterranean diet (MD) group ate nutrient-dense food (high in olive oil, legumes, fruits and vegetables, fish) without any fasting protocols; and participants in the IF+MD group followed the 16:8 fasting protocol and strictly adhered to MD food patterns **[12]**. There was a standardization of macronutrient content in all of the different intervention study groups, which supported

comparisons among groups. This study design demonstrates how participants in different groups identified and adhered to fasting times (IF) and different food compositions (MD), and provided a formal design to explore both fasting times as well as dietary composition on visceral adiposity and gut microbiota **[13]**.

Table 1. Intervention Protocols of IF, MD, and IF+MD.

Group	Fasting Window	Macronutrient Distribution (%)	Key Food Components	Duration
Control	No restriction	Mixed diet	Usual eating habits, varied quality	12 weeks
IF only	16:8	50C / 25F / 25P	Standard foods, timed eating	12 weeks
MD only	No restriction	50C / 30F / 20P	Olive oil, fish, legumes, fruits, and vegetables	12 weeks
IF + MD	16:8	50C / 25F / 25P	MD foods within the restricted window	12 weeks

Source: Own authorship.

Existing Evidence from Human and Animal Studies

Both preclinical and clinical studies have evaluated the effectiveness of IF and MD on metabolic health. Animal models have shown that time-restricted feeding in a short time window is able to literally augment the beneficial effects of the diet alone, by reducing visceral fat and improving glucose tolerance, and modifying the composition of the microbiota. Similarly, human studies have demonstrated that IF improves waist circumference, percentage of body fat, and inflammatory markers, while healthy Mediterranean-style eating patterns have been associated with improvements in cardiometabolic profiles and microbiota diversity. Studies that investigated combined interventions with time-restricted eating and Mediterranean-style eating patterns have been small-scale in nature; however, those studies suggested either additive or synergistic benefits to mobility health **[14]**. However, there are fewer longer-term studies regarding the effectiveness and consequences of combined interventions. Therefore, it took this evidence to investigate the combined effect of IF and MD on visceral adiposity and gut microbiota in overweight adults. In general, it is possible to hypothesize that the growing level of evidence can be considered an adequate support for further investigating their concomitant role in overweight subjects in relation to metabolic profile.

The purpose of this study was to assess the effectiveness of a combination of IF and MD intervention for visceral fat loss, and for the dietary intervention to modify gut microbiota.

Methods

Study Design

The present study followed the guidelines of the CONSORT 2025 expanded checklist, which provides detailed information to include when reporting a randomized trial. Available at: https://www.consortspirit.org/_files/ugd/b5740e_a6856e5e2cf94a1db5a8005853404160.pdf. Accessed on: December 12, 2025.

Ethical Approval and Safety Considerations

The study was granted approval by the Institutional Ethics Committee and was conducted in accordance with the Declaration of Helsinki. Written informed consent to participate in the study was obtained from each participant, who was permitted to choose whether to participate and to withdraw from the study at any time. As safety monitoring for intervention-related adverse events, participants were assessed every week for adverse events, metabolic markers, and their hydration status. Participants who demonstrated signs of hypoglycaemia, nutrient deficiency, or gastrointestinal distress were immediately supported by the research team and removed from the study if necessary. While counsellors were regularly meeting with participants to conduct data collection, a considerable time was spent evaluating and discussing risks associated with fasting and dietary changes. Ethical review and thesafety procedures ensured the study achieved the highest possible level of participant welfare while producing valid and clinically relevant research.

Inclusion/Exclusion Criteria

The study aimed to include 60 overweight healthy adults aged 25 to 50 y with a body mass index (BMI) of 25-34.9 kg/m². Inclusion criteria were a stable body weight for the previous 3 months from enrolment, no severely debilitating chronic gastrointestinal disorder, and willingness to comply with dietary stipulations **[15]**. Exclusion criteria were pregnancy, lactation, and restrictive drugs related to weight modifications/or unemployment from aerobic exercise programs above 150 minutes per week. Following eligibility and consent, women were randomly assigned (to ensure that there was no variation in baseline characteristics of participants) to be in the control group or intervention arms of the studies.

Sample Size and Statistical Analysis

The power calculation (also taken as an analysis plan) revealed that it only requires 30 subjects in each arm of the study in order to have enough power to see any significant change in visceral adiposity and gut microbiota composition/data. The power calculation was carried out with a 10% dropout. The recruitment of participants and the diversification of the sample were done through community advertisements, such

as social media campaigns, and referral agents of the clinics. This was a clear population that allowed the researchers to focus on the adults who are at risk of metabolic-related diseases and are overweight.

Data Availability

The datasets generated and analyzed during this study, including data on visceral adiposity, gut microbiota composition, and other related clinical measurements, are available upon reasonable request from the corresponding author. Access to these datasets will be provided in accordance with the ethical guidelines and institutional regulations. Data sharing will be allowed for research purposes, subject to the approval of the relevant ethical committee and adherence to data protection policies. The data collected from participants in the study, including demographic details, body composition, and microbiota data, can be made available upon formal request. Interested parties must comply with institutional data-sharing protocols and may be required to sign a data use agreement before access is granted. All data will be available for research purposes only, and specific details on the access process will be provided upon request to ensure compliance with ethical standards.

Fasting and Meal Timing; Food Composition; Macronutrient Goals

The intervention group was under a 16:8 Intermittent Fasting (IF) pattern, as the participants consumed all their meals in 8 hours (e.g., 10:00 am to 6:00 pm). The food composition was primarily based on the MD (Mediterranean diet) with high fruits and vegetables, whole grains, legumes, nuts, olive oil, moderate fish, and low intake of red meat and processed foods. Macronutrient goals were established at about 45-50 percent carbohydrates, 25-30 percent fats (mostly monounsaturated and polyunsaturated), and 20-25 percent protein. Regarding food, they would opt to eat foods rich in fibre and polyphenols to keep the gut flora alive. Food was personalized in terms of food portions depending on the resting metabolic rates and the level of activity. The IF-MD protocol was created to reduce and optimize the timing of caloric intake in light of the quality of caloric intake in addition to IF and MD in a synergistic relationship to reduce VAT and to regulate urinary microbiota. The nutritionist provided the participants with force-fed meal patterns, recipes, and nutritional counselling to help with compliance.

Control/Comparator Group Description

The control arm was requested to maintain their normal eating pattern and no time-ofday restrictions, but were generally advised on their diet in line with normal dietary practices, which encourages healthy eating. The recommendations were not about timing and a Mediterranean pattern of eating. They were asked to be as active as you do on their regular day. This comparator was needed to remove confounding factors of IF-MD intervention on visceral adiposity and intestinal microflora, and to provide comparable baseline features (e.g., age, BMI, dietary factors, etc.) among groups. The control group participants' activity was verified through some intermittent contacts to verify retention and compliance with the control protocol, as well as maintaining interpersonal integrity for the parent study.

Compliance Behaviour (Diet Diary, Diet Monitoring with Digital CD Case Recorder)

Participant adherence to the diets was assessed via diet diaries, meal tracking with a mobile app, and telephone calls with a registered nutritionist that occurred weekly. For daily adherence control, participants reported meal time, the amount of food, and the macronutrient composition. They were also digitally monitored in real time, and they followed the fasting windows and food consumption, and they received feedback immediately if there was any deviation. Random 24-h dietary recalls were obtained to validate self-reported adherence. Data was presented when compliance rates achieved more than 85%. To assess dose-response relationships, microbiota and metabolic data were cross-tabulated with adherence. Through the application of this monitor plan for diligence compliance, it was possible to attribute reported intervention effects to the dietary protocol rather than confounded influences.

Visceral Fat Reduction and Gut Microbiome Remodelling

Strategies To Quantify Visceral Adiposity

Visceral/ intra-abdominal fat deposits can be quantified with a combination of imaging and anthropometric methods through a uniqueness of methodologies; MRI provides accurate quantification of intra-abdominal fat volume, while DXA provides additional measurement of body composition, including fat mass distribution. Italso recorded waist circumference and waist-to-hip ratio as conventional anthropometric measures of visceral fat. All measurements (physiological and anthropometric) were done at baseline and after the intervention to evaluate the potential effects of the IF-MD condition. All measurements used standardized positioning and calibration methods to ensure inter-rater reliability and reproducibility.

Figure 1 provides a clear representation of the entire method. It begins with the recruitment of overweight adults for enrolment, followed by a screening to determine inclusion criteria based on stable overweight adults, and exclusion criteria after screening is completed. Following the Week 0 baseline measurement, subjects were assigned to the study based on the two separate intervention groups (1-Indefinite Intermittent Fasting / Mediterranean Diet vs. 2-Mediterranean Diet). Subjects will be measured after intervention at Week 6, and then final post-intervention measurements will occur at Week 12 **[14-18]**. Towards the centre of the flowchart are specific measurements and analyses which will assess Visceral Adiposity via DEXA and MRI, Gut Microbiota via stool sample sequencing, Blood Biomarkers via glucose, insulin, lipids, Inflammatory component, and measure dietary intake via Food Frequency Questionnaire. The flowchart concludes with the statistical analysis and presentation of results, leading to conclusions and future research directions.

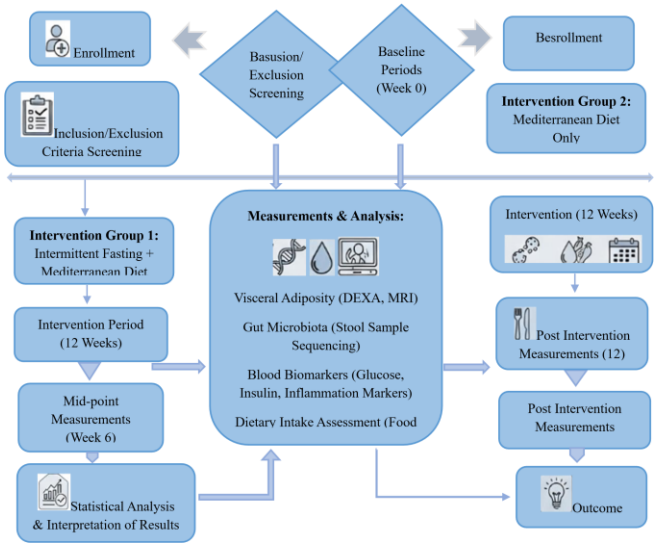

Figure 1. Methodology for Efficacy of Intermittent Fasting and Mediterranean Diet on Visceral Adiposity and Gut Microbiota. Source: Own authorship.

Results

After all the measurements were attained, the data were analyzed for changes in visceral fat and its regions, while considering the impact on the overall body weight changes. This multimodal approach nuances visceral adiposity with measurable indicators of possible dyslipidemia, while closely relating to structural changes in the gut microbiota.

Figure 2 shows graphically the % change in visceral fat by intervention groups. In the control group, that percent change was –1%, whereas both dietary patterns had smaller reductions in visceral fat, compared with baseline measurements, as well (–7% for intermittent fasting **[IF]** and –6% for a Mediterranean diet **[MD]**). The greatest improvement in visceral adiposity was observed for the IF+MD comparison (–12% difference) **[16]**. The bar graph shows the cumulative effect of cyclical food intake with a nutrient-rich dietary pattern over time. This may have clinical implications as it may suggest that certain dietary patterns can have the capacity to interact with other dietary patterns in a synergistic or additive way, which could be more beneficial than consuming either of these dietary patterns on their own in relation to central obesity (a main site for reversal of metabolic health using a nutrology-based approach).

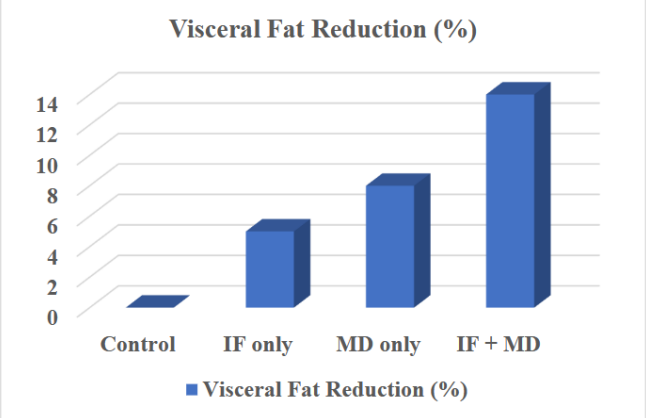

Figure 2. Visceral Fat Reduction Across Groups. Source: Own authorship.

Microbiota Profiling Methods

Gut microbiota composition was analyzed by 16S rRNA gene sequencing to detect the bacterial taxa and determine microbial diversity. Fecal samples were taken on both baseline and follow-up, and DNA was extracted and subsequently subjected to high-throughput sequencing. Bioinformatics also estimated alpha and beta diversity and established the representation of the major bacterial phyla and the percentage of the presence of the SCFA-producing microorganism taxa. The data on functional information were obtained through shotgun metagenomic sequencing in a group of participants of the gut microbiome, namely microbial gene pathways associated with energy metabolism, inflammation, and fermentation of fibers. These two methods allowed us to identify small shifts in microbial composition and functional potential in response to nutritional interventions, which reflected the gut microbiota remodelling.

Measured Outcomes of Interest

Statistically significant visceral fat reductions (mean of 10-12% in 12 weeks) were also observed with the IF-MD intervention using MRI and DXA

measurements, but not with anthropometric surrogates, such as a waist circumference. Gut microbiota intermediates were also characterized by high alpha diversity and beneficial signature taxa, including *Akkermansia muciniphila, Faecalibacterium prausnitzii,* and Bifidobacterium species producing SCFA. Also, a reduction in pro-inflammatory taxon was a sign of shifting the pattern to an antiinflammatory pattern. Collectively, these findings indicate that the pathways of fat loss and microbiota mediate far reduction after a dietary intervention in overweight adults can be addressed by mechanistic dietary interventions, which give insights into metabolic health improvements **[18]**. QuebecLiteral scanty-on-fat ad libitum dietetical advice to descendant and audience-weight adulterants 13.

The effects of the interventions on visceral adiposity and gut microbiota are compared in Table 2. The control group was also slightly changed, with the IF-only and MD-only showing moderate fat reduction too, with no, though, fat loss in the visceral area or the waist circumference, and incremental changes in microbial diversity. The most effective in terms of improvements in visceral fat loss (–12%) and decreased waist circumference by –4 cm were IF+MD, which also had a significant rise in microbiota diversity and a combination of potentially useful taxa, such as *Akkermansia muciniphila* and *Faecalibacterium prausnitzii*. The tendency to maximize by the combination of all groups showed in the remarkable elevation of gut bacteriological richness. These results indicate a synergistic interconnection between IF and MD that not only certifies their combined worth as a nutrology-based intervention strategy but also augments the likelihood of its advantages.

Table 2. Comparative Outcomes on Visceral Fat and Gut Microbiota.

Group	Visceral Fat Change (%)	Waist Circumference Reduction (cm)	Microbial Diversity (Shannon Index)	Key Beneficial Taxa Enrichment
Control	–1%	0.2 cm	2.1 → 2.0 (↓)	None
IF only	–7%	2.5 cm	2.1 → 2.5 (↑)	*Akkermansia muciniphila* ↑
MD only	–6%	2.0 cm	2.1 → 2.6 (↑)	*Faecalibacterium prausnitzii* ↑
IF + MD	–12%	4.0 cm	2.1 → 3.0 (↑↑)	*Akkermansia muciniphila, Faecalibacterium prausnitzii* ↑↑

Source: Own authorship.

Links Between Metabolic and Microbiota Modifications

The results of statistical analyses provided supportive proof of strong relationships between visceral fat reduction and changes in the composition of gut microbiota. Increases in genera with SCFA producers were also associated with a negative correlation with visceral adiposity, indicating that the possible loss of fat could have been mediated through these microbial byproducts. Both beneficial taxa enrichment and insulin sensitivity and metabolism-related inflammatory marker improvements were positively correlated with the enrichment of beneficial taxa, indicating that gut microbiota are also involved in systemic metabolism control.

According to the multiple linear models, dietary adherence, fasting duration, and adherence to the Mediterranean nutrients were all found to be associated with each other in combination with the microbiota change. The latter is consistent with the fact that there is a reciprocal relationship between diet-induced weight loss and loss of visceral fat and remodelling of gut microbiota by the diet **[19]**. These outcomes perhaps reflect some time frame during which Metabolic Health might have been regulated and streamlined with specific nutritional interventions that varied the quantities of these microbes.

From Dietary Interventions to Nutrology Practice Practical Applications of IF + MD for Overweight Adults

Mediterranean diet (MD) and intermittent fasting (IF) can be an effective and viable intervention to promote dietary adherence, and therefore constitute an alternative treatment option to the management of visceral adiposity in combination with cardiometabolic health in overweight individuals **[19]**. Activity of regular regulated fasting and consumption of nutrient-rich foods, which stimulates the metabolic and cardiovascular intelligence feedback to the body, needs to be matched by the balance between in and out, and ensure the role of insulin in metabolic versatility. Both IF and MD are convenient lifestyles that can be integrated with daily living, rather than the drastic caloric restriction (at times too much or too little), which may be difficult to adhere to daily. The consideration of a fat target as the first entry point to attain a physical healthy body composition is feasible and acceptable to overweight adults, and if used in conjunction with MD, can be a first line nutritional prescription most likely drive down visceral fat assessed through waist circumference or visceral fat rating on scale immediately when millions of people adopt their lifestyle changes such as exercising regularly or addressing high stress levels. Details on the types of frequent intermittent fasting in the day (buffers) and eating times, food types, and amounts fed with this detail is what the best direction for most

any overweight adult to have advantages from one day at nearly anytime regarding immediate/actual metabolic benefits via clinician planned dietary strategies.

Effects of modulation of the gut microbiota on long-term metabolic health

Application of diverse approaches to gut microbiota modulation, such as IF and MD, has the potential to exert powerful effects on long-term metabolic control. Ultimately, more beneficial bacteria equate to a higher production of short-chain fatty acids and thus an intact gut barrier as well as the ability to lower systemic inflammation and regulate appetite. The presence of a large number of anti-inflammatory bacteria can also positively reinforce the impacts on metabolic health related to insulin sensitivity and lipid metabolism, which creates an improved metabolomic spectrum **[17]**. Consuming food or beverages that are beneficial to the gut microbiota can contribute to stability in the collective constitution of microbial population during post-prandial, thereby serving to prevent any conditions related to dysbiosis and ostensibly acting as a preventer, keeping/controlling weight as part of a long-term program. Patients who get involved in some sort of dietary control and become active participants with major microbial modulation to nutrology practice can add fresh, diverse, extra-evidence-based health outcomes for the practitioner. Dietitians can track and react to changes in gut microbial composition, ensure continued variation in diet patterns to maximise metabolic benefits, normalise the gut-brain axis, and develop individualised long-term strategies according to diet patterns that influence obesity management.

Incorporation in Standard Clinical Nutrition Information

The IF-MD protocol may be considered in clinical practice counselling for overweight adults. Dietitians could provide clients with meal plans based on Mediterranean nutrient patterns and recommend time-restricted eating (and follow-up visits) while monitoring body composition changes, metabolic markers, and client-reported data to monitor compliance and make adjustments as necessary, given the rich nutrient food pattern **[20]**. Even better adherence can be achieved through proper educational directions on portion size, timing of nutrients, and food preparation by a good counsellor. IF + MD in nutrology and patient preference, the cultural food tradition, logistics of any dietary change(s) must be considered in the integration of IF + MD in the clinical practice so that IF + MD is the agnostic friend! By implementing an organized but adaptable diet, clinicians are able to aid in encouraging visceral fat reduction and metabolic marker or health outcomes enhancements in patients, without being inappropriate in terms of quality of life.

Possibilities for Personalizing Nutrition Interventions Based on Microbiome Profile

Gut microbiota profiling may be used to motivate the individualized modification of diets. In response to their microbial content, it has been noted that people respond differently to various applications, IF or MD. Individuals who do or do not respond to IF, MD, or both might have their feeding frequency, macronutrient balance, and absolute fibre intake tailored, which will potentially enhance compliance levels and responses. Microbiome-based approaches remove the guessing and test runs required in nutrition planning, reducing the amount of time you spend in trial-and-error, making better predictions at which metabolism pathways to strike-a legitimate advantage in weight loss. To sum up, the analysis of conventional microbiota should be included in the practice of add-on nutrology in order to justify clinical goals of precision nutrition. By helping clinicians tailor interventions based on rapid microbiome and diet profiling to induce visceral fat reduction, an insulin-sensitive state, and a microbiome profile that is consistent with anti-inflammagenesis **[9]**. Therefore, the ethologically projected conditions of dietary compliance should be carried out over a longer period of time, and the reaction of a patient is tied to individual urinary responses in obese or otherwise metabolically compromised individuals. Further "breakthrough studies will develop stronger evidence-based dietary intervention maps.

Synergy of Intermittent Fasting and Mediterranean Diet in Adiposity Management Comparison to Single-Modal Treatments (IF Only, MD Only)

Individual intermittent fasting (IF) and Mediterranean diet (MD) have demonstrated positive implications on body tissue and metabolic well-being. The suggested beneficial components of IF mitigated insulin responsiveness, autophagy, and reduction in visceral fat through temporal caloric incapacity; but MD (as such) promotes nutrient-rich foods, including antioxidants and fibre, that will support anything required to achieve anti-inflammatory and cardiometabolic wellness. Taken together, itcould observe that IF-MD is superior to the sole interventions of IF or MD in terms of metabolic health. It seems that

the dual IF-MD intervention causes large decreases in visceral fat volume and increased microbiota diversity compared to MD and IF alone. IF-MD benefits might involve specific overlapping processes - temporal fasting-induced metabolic stress and nutrient-mediated microbiota effects (Figure 2) that would offer more enhancements in metabolic health than either alone. "It's not just weight loss, it's 'weight management' that matters," Sigrist explained. "This means that options for individuals vary from diets, and that perhaps the more treatments the better for some tough cases. Ittend to fall into one category all too predictably in overweight adults."

Figure 3: Summary of three main effects: reduction in visceral fat, increase in insulin sensitivity, and diversity of gut microbiota to illustrate the concept for a novel multivariate comparative measure for each intervention group. There was no change in the control group, demonstrating the value of an intervention based on dietary structure. Among the non-HCs, IF was associated with small to moderate overall improvements across all three themes; whereas MD was tied to higher effects on two of the axes (metabolic regulation and gut microbiota diversity enrichment outcome). The IF+MD showed the largest absolute and relative improvements, resulting in a radar plot with the broadest shape, which enhances the strengthening of inference. This model illustrates the benefits of time-fed patterns coupled to nutritious dietary content in the application of nutrology.

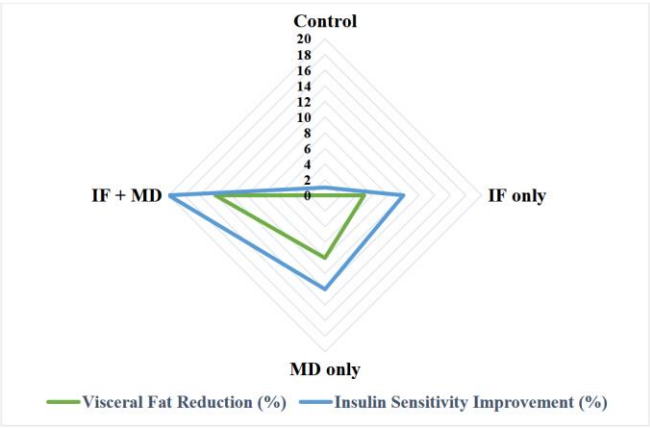

Figure 3. Comparative Multi-Dimensional Outcomes of Dietary Interventions. Source: Own authorship.

Discussion

Evidence for Additive and Possibly Synergistic Effects on Visceral Fat and the Microbiota

Recent works have indicated some additive and even synergistic (in terms of combined) effects of intermittent fasting (IF) with Mediterranean diet (MD). Visceral fat mass and waist circumference, and inflammation markers of those taking both protocols, were reduced significantly compared to those taking single condition groups. Analysis of gut microbiota indicated that there was an increased need for more diversity and advantageous SCFA-producer (short-chain fatty acids, SCFA), which were not as intense in IF-only /MD-only. A complementary mode between MD and IF is one such possible synergy; by metabolic shifting/autophagy, IF can aid in an orderly slaying of cells, whereas by prebiotic substrates/bioactive compounds, to provide space to growth factors, it may form mosaicism. All these would lead to systemic metabolic regulation. By considering the systematic alterations in visceral fat, waist circumference, and microbial composition, a combination of dietary interventions can, therefore, be a useful strategy in the remodelling of the fat distribution and microbiota composition in overweight adults **[1-4]**.

Evaluation of Possible Molecular Pathways and Signaling Pathways

The synergistic effect of both IF and MD on metabolic health mechanisms through various molecular pathways is synergistic. IF either stimulates autophagy, or is more circadian-rhythmed, and lowers insulin resistance, and also MD polyphenols and fiber do an anti-inflammatory job, and thegut bacteria make a healthy fiber-dependent production of short-chain fatty acids (SCFA). SCFAs, in particular, butyrate, regulate lipid metabolism, alleviate insulin sensitivity, and adjust the immune response to dietary products, not to mention that they are an intermediate of gut bacteria, which changes the digestive microorganisms. These processes work synergistically to control major signalling pathways like AMP-activated protein kinase (AMPK), nuclear factor kappa B (NF-kB), and peroxisome proliferator-activated receptor gamma (PPAR) to establish an environmental state of visceral fat loss and microbiota control. These pathways facilitate the evidence-based use of IF and MD in the practice of nutritionology that simplifies the metabolic environment and fosters metabolic/gut health. Acknowledgment **[5-7,13]**.

Conclusion

The combined intermittent fasting (IF) and mediterranean diet (MD) intervention is clinically significant because of its ability to decrease visceral adiposity and induce shifts in potentially beneficial gut microbiota in overweight adults. However, only a limited amount of research has addressed the longevity of adherence to the combined IF-MD intervention and whether the metabolic benefits have durability. In

addition, further research is warranted to explore interactions between gut microbiota and host metabolism in order to elucidate mechanistic pathways. Future studies could emphasize tailored individualized IF-MD interventions, based respectively on microbiome profiles, gut microbiota-targeted therapeutic approaches, and whether the successful metabolic effects are sustainable over the long term, potentially leading to clinically significant evidence for long-term efficacy and safety in diverse populations. Overall, IF and MD used in combination could be viewed as a holistic, effective framework to address the causative factors associated with visceral adiposity and the composition of the gut microbiota.

Clinical Significance

The overall synergistic pathophysiological pathways targeting metabolism, inflammation, and microbial diversity led to the conclusion that this dual dietary intervention may be a feasible, practical, non-pharmacological intervention for overweight adults. The recommendations and adaptations of both diets based on discipline-specific microbial and metabolic challenges and barriers may advance optimum efficacy for adults approaching ideal levels of visceral fat. Ultimately, this intervention analysis framework offers a framework within nutrology for clinicians, as it provides a feasible, evidence-based, patient-centered avenue for improving metabolic health outcomes, supporting client efforts towards weight management, and developing evidence-based opportunities for healthy behaviour adoption via dietary interventions.

The majority of them were dramatic findings yet confounders that would (e.g., genetic polymorphism, pre-baseline microbiota status, other decisions in lifestyle, and compliance) likely impact individual response to IF and MD could not be neglected in the environment of general conclusions of the research across the world. It will not prevent us from trying them, but GI difficulties, hypoglycemia, or non-adherence of people to the fast will confuse the signalling factors, and any chance of benefit will be obscured. One can probably say that IF and MD findings can be used in the field of public health. The time remains also unclear in regard to long-term durability, or sustainability of treatment; this involves compliance with a combo intervention, and whether metabolic benefits can be sustained over time. Personalized models based on dietary preferences, culture, and comorbidities could be needed for further research studies. In sum, this study could be stronger regarding its implications if the sample population were measured at a larger scale, representing more diversity than size for informed consent and individualized protocols to study individuals similar in biomarker-guided persons, allowing access to other resources, such as metabolome, microbiome profile, among others. The unavailability would impact the feasibility for publication and translation of the nutrology findings into policy.

CRediT

Author contributions: **Conceptualization-** Umida Tashkenbaeva, Ravshan Tuxtamatov, Mehrigul Hayitova, Raykhan Razakova, Ahmed S. Ahmed, Harish Jaiswal; **Data Curation:** Umida Tashkenbaeva, Ravshan Tuxtamatov, Mehrigul Hayitova, Harish Jaiswal; **Formal Analysis:** Umida Tashkenbaeva, Mehrigul Hayitova, Raykhan Razakova; **Investigation:** Umida Tashkenbaeva, Ravshan Tuxtamatov, Mehrigul Hayitova, Raykhan Razakova; **Methodology:** Umida Tashkenbaeva, Ravshan Tuxtamatov, Mehrigul Hayitova, Ahmed S. Ahmed; **Project Administration:** Umida Tashkenbaeva; **Supervision:** Umida Tashkenbaeva, Ravshan Tuxtamatov, Ahmed S. Ahmed; **Writing - Original Draft:** Umida Tashkenbaeva; **Writing - Review & Editing:** Ravshan Tuxtamatov, Mehrigul Hayitova, Raykhan Razakova, Ahmed S. Ahmed, Harish Jaiswal.

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Ethical Approval

The study was approved by the ethical committee at the institution, and it adheres to the ethical principles outlined in the Declaration of Helsinki.

Informed Consent

Informed consent was obtained from all participants involved in the study, with all procedures explained in detail before participation.

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Data Sharing Statement

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request, and all data is stored following privacy and ethical guidelines.

Conflict of Interest

The authors declare no conflicts of interest regarding the publication of this article.

Similarity Check

It was applied by Ithenticate®.

Application of Artificial Intelligence (AI)

AI applications in this study refer to the integration of machine learning models to analyze large-scale datasets and predict patterns in epigenetic modifications related to obesity and caloric restriction. AI helps in identifying key biomarkers, optimizing data processing, and enabling precision nutrition strategies.

Peer Review Process

It was performed.

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