

# THE EFFECTS OF INTERMITTENT FASTING ON CARDIOVASCULAR HEALTH OF PREDIABETES AND TYPE 2 DIABETES MELLITUS PATIENTS: A SYSTEMATIC REVIEW

Muhammad Naif Hafizin Afdzal Rasif<sup>a</sup>, Amirah Farhana Nazri<sup>a</sup>, May Khin Soe<sup>a,b</sup>

<sup>a</sup>Kulliyyah of Pharmacy, International Islamic University Malaysia (IIUM)

<sup>b</sup>Department of Basic Medical Sciences, Kulliyyah of Pharmacy, International Islamic University Malaysia (IIUM)

## INTRODUCTION AND AIM OF THE STUDY

### INTRODUCTION

- Diabetes mellitus is one of the chronic diseases that has high prevalence worldwide.
- In 2021, there are 537 million (10.5%) adults living with diabetes worldwide and this number is predicted to increase to 643 million by 2030<sup>1</sup>.
- IDF in their most recent research reported that 352 million adults between the ages of 20 and 79 may have prediabetes<sup>1</sup>.
- It is well established that patients with prediabetes and T2DM will commonly have a 2-3-fold increased risk of developing cardiovascular diseases<sup>2</sup>.
- Intermittent fasting (IF) is one of the common approaches that is being practiced to reduce the daily calorie intake and as a form of dietary intervention to prevent and manage prediabetes and T2DM and their associated complications<sup>3</sup>.
- There are many reported benefits of IF but there are no studies found that discuss specifically regarding the benefits of IF on cardiovascular system T2DM patients.

### AIM OF THE STUDY

This study aims to investigate the effects of IF on cardiovascular health of prediabetes and T2DM patients by systemically review published articles and research.

## METHODOLOGY

### PROTOCOL AND REGISTRATION

This systematic review followed the statement of PRISMA and was registered at PROSPERO with the number CRD42022378349

### SEARCH STRATEGY

**Databases**  
Scopus, PubMed, Cochrane library, Google scholar, snowball technique

**Keywords**  
"Effects", "T2DM", "Intermittent fasting", "prediabetes", "cardiovascular health"

**Boolean operators**  
AND: connect between main domains.  
OR: connect between subdomains within the same domain

**Mendeley**  
To keep all retrieved articles and duplicates removal

### ELIGIBILITY CRITERIA

Table 1: Eligibility criteria for articles search

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> <li>≥ 18 years</li> <li>Has prediabetes or diagnosed with T2DM</li> <li>RCT, cohort studies, case reports, case series, quasi-experimental study</li> <li>Articles published in English between 2000 - 2022</li> <li>Studies that reported the targeted primary and secondary outcomes.</li> </ul>	<ul style="list-style-type: none"> <li>Animal studies</li> <li>Review articles and study protocols</li> <li>Studies that did not report the targeted primary and secondary outcomes</li> <li>Patients who are T1DM, pregnant/breastfeed, smokers, active athletes, have CKD stage 4&amp;5, and have history of psychiatric or eating disorders</li> </ul>

### DATA EXTRACTION

Authors, publication year, study region, study design, total number of participants recruited, study intervention or type of IF being implemented, duration of the study and the results of targeted primary outcomes and second outcomes.

### RISK OF BIAS IN INDIVIDUAL STUDIES

- Independently assessed by two authors by using the Joanna Briggs Institute critical appraisal checklist. Disagreements were dissolved by discussion.
- <50% - high risk of bias; 50%-70% - moderate risk of bias; >70% - low risk of bias
- Results were visualized as traffic light plots, generated by using robvis tool.

## CONCLUSION

- IF is beneficial for cardiovascular health of prediabetes and T2DM patients.
- Studies included in this systematic review showed that IF helps to improve the blood pressure readings, lipid levels and glycemic parameters for the participants intervened with the IF regimen, with respect to the baseline levels/readings or the control group.
- These benefits are mainly achieved due to reduction in insulin resistance and blood glucose levels at the end of intervention.
- RCTs are needed to confirm the benefits of IF focusing on cardiovascular health specifically for prediabetes and T2DM patients as it has a high potential to be used as one of the interventions in managing and preventing prediabetes and T2DM and their associated complications.

## RESULTS/FINDINGS

### STUDIES SELECTION

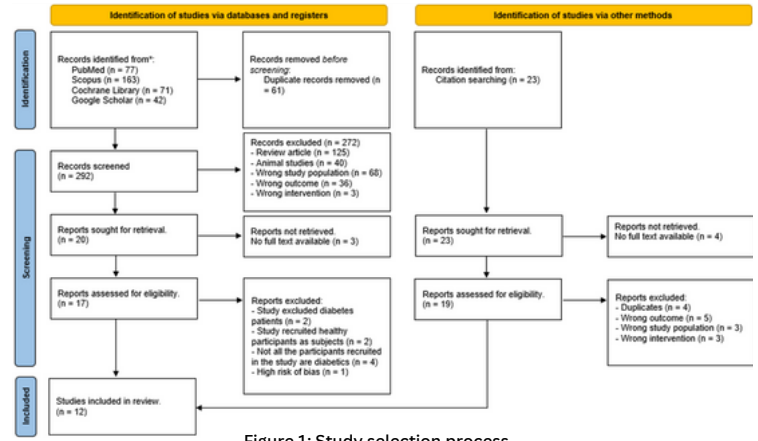


Figure 1: Study selection process

### RISK OF BIAS IN INDIVIDUAL STUDIES

Study	Risk of bias for all included studies													Overall
	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	
Tang et al., 2020	Green	Yellow	Green	Red	Red	Red	Green	Green	Green	Green	Green	Green	Green	Yellow
Hua et al., 2022	Green	Green	Green	Red	Red	Red	Green	Green	Green	Green	Green	Green	Green	Green
Che et al., 2021	Green	Green	Green	Red	Red	Red	Green	Green	Green	Green	Green	Green	Green	Green
Carter et al., 2018	Green	Yellow	Green	Red	Red	Red	Green	Green	Green	Green	Green	Green	Green	Yellow
Sutton et al., 2018	Green	Green	Green	Red	Red	Red	Green	Green	Green	Green	Green	Green	Green	Yellow
Conley et al., 2018	Green	Green	Green	Red	Red	Red	Green	Green	Green	Green	Green	Green	Green	Yellow
Abdullah et al., 2020	Green	Green	Green	Red	Red	Red	Green	Green	Green	Green	Green	Green	Green	Green
Li et al., 2017	Yellow	Green	Green	Red	Red	Red	Green	Green	Green	Green	Green	Green	Green	Yellow
Al Saada et al., 2010	Green	Green	Green	Red	Red	Red	Green	Green	Green	Green	Green	Green	Green	Yellow
Kovl et al., 2020	Green	Green	Green	Red	Red	Red	Green	Green	Green	Green	Green	Green	Green	Yellow
Amason et al., 2017	Green	Green	Green	Red	Red	Red	Green	Green	Green	Green	Green	Green	Green	Yellow
Parr et al., 2020	Green	Green	Green	Red	Red	Red	Green	Green	Green	Green	Green	Green	Green	Green

Figure 2: Risk of bias in individual studies (6 articles had low risk, 6 moderate risk of bias)

### OUTCOMES OF THE STUDIES

Table 2: Targeted primary outcomes from the included studies

Outcome	Findings
SBP & DBP	<ul style="list-style-type: none"> <li>7 out of 12 studies recorded the effects of IF on SBP and DBP of the participants.</li> <li>3 studies<sup>4, 5, 6</sup> recorded significant reductions (<math>p &lt; 0.05</math>) in both SBP and DBP readings after the intervention.</li> <li>3 studies recorded reductions in both SBP and DBP but not statistically significant when compared to the baseline readings or control groups.</li> <li>1 study recorded no improvement for both SBP and DBP for the recruited participants with respect to the baseline readings.</li> </ul>
Primary outcomes	<ul style="list-style-type: none"> <li>10 out of 12 studies reported the effects of IF on lipid profiles of the participants.</li> <li>3 studies recorded significant improvement (<math>p &lt; 0.05</math>) for all of the lipid profiles which include TG, TC, LDL-c and HDL-c at the end of interventions.</li> <li>1 study reported significant improvement (<math>p &lt; 0.05</math>) for all of the lipid profiles except for HDL-c.</li> <li>2 studies recorded no significant improvement in lipid profiles at the end of intervention.</li> <li>There was also one study that reported significant improvement (<math>p &lt; 0.05</math>) in TC and TG at the end of intervention. That circulating TG might increase due to a longer fasting period (18 hours) prior testing and most likely reflects triglyceride re-esterification following lipolysis, as well as hepatic and intramuscular triglyceride storage.</li> </ul>
Lipid profiles	

### REFERENCES:

- IDF Diabetes Atlas 10th Edition. (n.d.). Retrieved October 19, 2022, from <https://diabetesatlas.org/>
- Ministry of Health Malaysia. Clinical Practice Guideline Management of T2DM (2020).
- Annason, Terra G., Matthew W. Bowen, and Kerry D. Mansell. 2017. 'Effects of Intermittent Fasting on Health Markers in Those with Type 2 Diabetes: A Pilot Study'. World Journal of Diabetes 8(4):154.
- Sutton, E. F., R. Beyl, K. S. Early, W. T. Cefalu, E. Ravussin, and C. M. Peterson. 2018. 'Early Time-Restricted Feeding Improves Insulin Sensitivity, Blood Pressure, and Oxidative Stress Even without Weight Loss in Men with Prediabetes'. 27(6).
- Tang, Fang, and Xuan Lin. 2020. 'Effects of Fasting-Mimicking Diet and Specific Meal Replacement Foods on Blood Glucose Control in Patients with Type 2 Diabetes: A Randomized Controlled Trial'. Oxid Med Cell Longev 2020:6615295.
- Li, C., B. Sadraie, N. Steckhan, C. Kessler, R. Stange, M. Jellter, and A. Michalsen. 2017. 'Effects of A One-Week Fasting Therapy in Patients with Type-2 Diabetes Mellitus and Metabolic Syndrome - A Randomized Controlled Exploratory Study'. (9).
- Abdullah, K., M. Al-Habibi, and E. Al-Eryani. 2020. 'Ramadan Intermittent Fasting Affects Adipokines and Leptin/Adiponectin Ratio in Type 2 Diabetes Mellitus and Their First-Degree Relatives'. BioMed Research International 2020.
- Annason, Terra G., Matthew W. Bowen, and Kerry D. Mansell. 2017c. 'Effects of Intermittent Fasting on Health Markers in Those with Type 2 Diabetes: A Pilot Study'. World Journal of Diabetes 8(4):154.