

## Intermittent fasting for the prevention of cardiovascular disease.

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Cardiovascular disease (CVD) is the leading cause of death worldwide. Lifestyle changes are at the forefront of preventing the disease. This includes advice such as increasing physical activity and having a healthy balanced diet to reduce risk factors. Intermittent fasting (IF) is a popular dietary plan involving restricting caloric intake to certain days in the week such as alternate day fasting and periodic fasting, and restricting intake to a number of hours in a given day, otherwise known as time-restricted feeding. IF is being researched for its benefits and many randomised controlled trials have looked at its benefits in preventing CVD.

### Objectives

To determine the role of IF in preventing and reducing the risk of CVD in people with or without prior documented CVD.

### Search methods

We conducted our search on 12 December 2019; we searched CENTRAL, MEDLINE and Embase. We also searched three trials registers and searched the reference lists of included papers. Systematic reviews were also viewed for additional studies. There was no language restriction applied.

### Selection criteria

We included randomised controlled trials comparing IF to ad libitum feeding (eating at any time with no specific caloric restriction) or continuous energy restriction (CER). Participants had to be over the age of 18 and included those with and without cardiometabolic risk factors. Intermittent fasting was categorised into alternate-day fasting, modified alternate-day fasting, periodic fasting and time-restricted feeding.

### Data collection and analysis

Five review authors independently selected studies for inclusion and extraction. Primary outcomes included all-cause mortality, cardiovascular mortality, stroke, myocardial infarction, and heart failure. Secondary outcomes include the absolute change in body weight, and glucose. Furthermore, side effects such as headaches and changes to the quality of life were also noted. For continuous data, pooled mean differences (MD) (with 95% confidence intervals (CIs)) were calculated. We contacted trial authors to obtain missing data. We used GRADE to assess the certainty of the evidence.

### Main results

Our search yielded 39,165 records after the removal of duplicates. From this, 26 studies met our criteria, and 18 were included in the pooled analysis. The 18 studies included 1125 participants and observed outcomes ranging from four weeks to six months. Of quantitatively analysed data, seven studies compared IF with ad libitum feeding, eight studies compared IF with CER, and three studies compared IF with both ad libitum feeding and CER. Outcomes were reported at short term ( $\leq 3$  months) and medium term ( $> 3$  months to 12 months) follow-up.

None of the included studies reported on all-cause mortality, cardiovascular mortality, stroke, myocardial infarction or heart failure.

Body weight was reduced with IF compared to ad libitum feeding in the short term (MD -2.88 kg, 95% CI -3.96 to -1.80; 224 participants; 7 studies; low-certainty evidence). We are uncertain of the effect of IF when compared to CER in the short term (MD -0.88 kg, 95% CI -1.76 to 0.00; 719 participants; 10 studies; very low-certainty evidence) and there may be no effect in the medium term (MD -0.56 kg, 95% CI -1.68 to 0.56; 279 participants; 4 studies; low-certainty evidence).

We are uncertain about the effect of IF on glucose when compared to ad libitum feeding in the short term (MD -0.03 mmol/L, 95% CI -0.26 to 0.19; 95 participants; 3 studies; very-low-certainty of evidence) and when compared to CER in the short term: MD -0.02 mmol/L, 95% CI -0.16 to 0.12; 582 participants; 9 studies; very low-certainty; medium term: MD 0.01, 95% CI -0.10 to 0.11; 279 participants; 4 studies; low-certainty evidence).

The changes in body weight and glucose were not deemed to be clinically significant.

Four studies reported data on side effects, with some participants complaining of mild headaches. One study reported on the quality of life using the RAND SF-36 score. There was a modest increase in the physical component summary score.

### Authors' conclusions

We are uncertain about the effects of intermittent fasting on clinical events such as mortality, myocardial infarction and heart failure due to lack of data for these outcomes. The individual meta-analyses show that intermittent fasting may be effective in reducing weight when compared to ad libitum feeding and may be as effective as continuous energy restriction. Despite this, these changes appear to be clinically insignificant at short-term follow-up. The quality of the available evidence is low to very low which means that many areas of uncertainty remain. Further research is needed to understand which patient groups would and would not benefit from intermittent fasting (e.g. patients with diabetes or eating disorders) as well as the effect on longer-term outcomes such as all-cause mortality and myocardial infarction.

### Biography

Mohamed Allaf is a medical doctor in London, United Kingdom. He recently completed his medical degree at Imperial College London. He has a particular interest in cardiovascular disease

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