Health benefits of Intermittent fasting

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What is intermittent fasting?
Intermittent fasting

Alternate day fasting
“Fast day” alternated with “Feast day”
Intermittent fasting

Alternate day fasting
“Fast day” alternated with “Feast day”

Fasting 1-2 days/week e.g. 5:2 diet
Intermittent fasting

- Alternate day fasting
  "Fast day" alternated with "Feast day"

- Time restricted feeding
  Eating within 4-12 h window/day

- Fasting 1-2 days/week
  e.g. 5:2 diet
Time restricted feeding (TRF)

Eating within an 8-h window
10am-6pm

Eating within an 6-h window
12pm-6pm
Lots of TRF books, but few human trials!
Time restricted feeding effective for weight loss in individuals with obesity?
Experimental design – 8h TRF study

12-WEEK STUDY

TRF n = 23
Eating 10am-6pm, fasting 6pm-10am

Control n = 23
Usual diet, no timing restrictions

Baseline
Body weight
Adherence/Diet
Metabolic disease risk

Week 12
Body weight
Adherence/Diet
Metabolic disease risk

Gabel et al. 2018. Nutr Healthy Aging
TRF = No calorie monitoring necessary!

Just watch the clock
## Log - Adherence and timing of food intake

<table>
<thead>
<tr>
<th>Day</th>
<th>Date</th>
<th>Start eating Time</th>
<th>Stop eating Time</th>
<th>To be completed by dietician (leave blank)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Adherent</td>
</tr>
<tr>
<td>Monday</td>
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<td>Saturday</td>
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</tr>
<tr>
<td>Sunday</td>
<td></td>
<td></td>
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<td>□</td>
</tr>
</tbody>
</table>
7-d food record used to assess energy intake
Adherence to the 8h feeding window

All values reported as mean ± SEM. TRF group was compliant with the prescribed eating window on 5.6 ± 0.3 d/week, and this level of adherence did not change over the course of the trial.

Gabel et al. 2018. Nutr Healthy Aging
Weight loss by 8h TRF

All values reported as mean ± SEM. Data were included for 46 participants; means were estimated using an intention-to-treat analysis using last observation carried forward. Body weight decreased in the time restricted feeding group relative to controls over 12 weeks (P < 0.001).

Gabel et al. 2018. Nutr Healthy Aging
### Unintentional calorie restriction - 8h TRF

8h reduced energy intake by ~350 kcal/d

<table>
<thead>
<tr>
<th></th>
<th>Time restricted feeding (n = 23)</th>
<th>Control (n = 23)</th>
<th>P-value Time × group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Week 12</td>
<td>Baseline</td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td>1676 ± 114</td>
<td>1335 ± 162</td>
<td>1645 ± 113</td>
</tr>
<tr>
<td>Protein (%)</td>
<td>16 ± 1</td>
<td>17 ± 1</td>
<td>17 ± 1</td>
</tr>
<tr>
<td>Carbohydrates (%)</td>
<td>47 ± 2</td>
<td>46 ± 2</td>
<td>46 ± 2</td>
</tr>
<tr>
<td>Fat (%)</td>
<td>37 ± 1</td>
<td>37 ± 2</td>
<td>37 ± 1</td>
</tr>
<tr>
<td>Cholesterol (mg)</td>
<td>279 ± 24</td>
<td>214 ± 27</td>
<td>275 ± 27</td>
</tr>
<tr>
<td>Fiber (g)</td>
<td>16 ± 2</td>
<td>13 ± 1</td>
<td>14 ± 1</td>
</tr>
</tbody>
</table>

All values reported as mean ± SEM. Data were included for 46 participants; means were estimated using an intention-to-treat analysis using last observation carried forward.

Gabel et al. 2018. Nutr Healthy Aging
Changes in metabolic risk by 8h TRF

<table>
<thead>
<tr>
<th></th>
<th>Time restricted feeding (n = 23)</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Week 12</td>
<td>Baseline</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>128 ± 4</td>
<td>121 ± 3</td>
<td>123 ± 4</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>83 ± 2</td>
<td>82 ± 2</td>
<td>81 ± 2</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>69 ± 2</td>
<td>71 ± 2</td>
<td>73 ± 2</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>177 ± 7</td>
<td>178 ± 9</td>
<td>192 ± 7</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>108 ± 5</td>
<td>110 ± 7</td>
<td>114 ± 7</td>
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<tr>
<td>HDL cholesterol (mg/dl)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>48 ± 2</td>
<td>49 ± 2</td>
<td>61 ± 3</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>105 ± 11</td>
<td>93 ± 9</td>
<td>89 ± 7</td>
</tr>
<tr>
<td>Fasting glucose (mg/dl)</td>
<td></td>
<td></td>
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</tr>
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<td></td>
<td>79 ± 4</td>
<td>82 ± 2</td>
<td>87 ± 2</td>
</tr>
<tr>
<td>Fasting insulin (uIU/ml)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>8.3 ± 1.0</td>
<td>5.7 ± 0.7</td>
<td>9.2 ± 1.4</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>1.6 ± 0.2</td>
<td>1.0 ± 0.2</td>
<td>2.0 ± 0.3</td>
</tr>
</tbody>
</table>
## Changes in metabolic risk by 8h TRF

<table>
<thead>
<tr>
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<td>2.0 ± 0.3</td>
</tr>
</tbody>
</table>
Is time restricted feeding (TRF) safe?
## Self-reported adverse events during 8h TRF

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Baseline (%)</th>
<th>Wk 1 (%)</th>
<th>Wk 12 (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>1.00</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0</td>
<td>0</td>
<td>12</td>
<td>1.00</td>
</tr>
<tr>
<td>Constipation</td>
<td>17</td>
<td>29</td>
<td>24</td>
<td>1.00</td>
</tr>
<tr>
<td>Bad Breath</td>
<td>18</td>
<td>14</td>
<td>12</td>
<td>0.50</td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>32</td>
<td>14</td>
<td>12</td>
<td>0.13</td>
</tr>
<tr>
<td><strong>Neurological</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>9</td>
<td>0</td>
<td>18</td>
<td>1.00</td>
</tr>
<tr>
<td>Weakness</td>
<td>14</td>
<td>0</td>
<td>6</td>
<td>0.50</td>
</tr>
<tr>
<td>Headache</td>
<td>32</td>
<td>24</td>
<td>24</td>
<td>0.50</td>
</tr>
<tr>
<td>Fatigue</td>
<td>14</td>
<td>10</td>
<td>12</td>
<td>1.00</td>
</tr>
<tr>
<td>Irritability</td>
<td>23</td>
<td>19</td>
<td>6</td>
<td>0.25</td>
</tr>
<tr>
<td>Unhappiness</td>
<td>14</td>
<td>14</td>
<td>0</td>
<td>1.00</td>
</tr>
</tbody>
</table>

**Note:** Values reported as mean percent occurrences at each time point (baseline: n = 23; week 1: n = 23; week 12: n = 17). Baseline values were measured 2 weeks before the start of the intervention (week 1). P value: McNemar’s test.

*Gabel et al. 2019. Appl Physiol Nutr Metab*
Eating disorder symptoms during 8h TRF

<table>
<thead>
<tr>
<th>Eating disorder symptoms</th>
<th>Baseline</th>
<th>Wk 1</th>
<th>Wk 12</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>32±1</td>
<td>32±1</td>
<td>32±1</td>
<td>0.90</td>
</tr>
<tr>
<td>Binge eating</td>
<td>28±2</td>
<td>27±1</td>
<td>27±1</td>
<td>0.79</td>
</tr>
<tr>
<td>Purgative behavior</td>
<td>13±1</td>
<td>11±1</td>
<td>12±1</td>
<td>0.23</td>
</tr>
<tr>
<td>Fear of fatness</td>
<td>41±2</td>
<td>39±2</td>
<td>41±2</td>
<td>0.89</td>
</tr>
<tr>
<td>Restrictive eating</td>
<td>28±2</td>
<td>27±2</td>
<td>29±2</td>
<td>0.68</td>
</tr>
<tr>
<td>Avoidance of forbidden foods</td>
<td>37±2</td>
<td>38±2</td>
<td>38±2</td>
<td>0.93</td>
</tr>
</tbody>
</table>

**Body image perception**

| Concerns about body size/shape           | 47±3     | 46±3    | 47±3    | 0.96   |

**Eating behaviors**

| Dietary restraint                        | 17±1     | 16±1    | 17±1    | 0.51   |
| Uncontrolled eating                      | 18±1     | 18±1    | 18±1    | 0.89   |
| Emotional eating                         | 7±1      | 7±1     | 6±1     | 0.96   |

*Note:* Values reported as means ± SEM (baseline: n = 23; week 1: n = 23; week 12: n = 17). Baseline values were measured 2 weeks before the start of the intervention (week 1). P value: ANOVA.
But won’t I be too hungry to sleep?
Sleep quality after 12 weeks of 8-h TRF

Pittsburgh Sleep Quality Index (PSQI) questionnaire. “All subjects” (n = 23).
“Good sleepers” (n = 13) PSQI total score equal to or below 5 at baseline
“Poor sleepers” PSQI total score greater than 5 at baseline (n = 10).
No significant changes between baseline, week 1, and week 12 in any group.
Summary of findings – 8h TRF

Body weight
- ~3% weight loss in 3 months
- Self-reported adherence was high (80%)
- Unintentional kcal restriction (~350 kcal/d)

Metabolic disease risk and safety
- Systolic blood pressure decreased
- No change plasma lipids/glucoregulatory
- TRF appears to be safe
Do shorter feeding windows (4h or 6h) produce greater weight loss?
Experimental design – 4h vs 6h TRF study

8-WEEK STUDY

4h TRF
- Eating 3pm-7pm, fasting 7pm-3pm

6h TRF
- Eating 1pm-7pm, fasting 7pm-1pm

Control
- Usual diet, No timing restrictions

Baseline
- Body weight
- Adherence
- Metabolic disease risk

Week 8
- Body weight
- Adherence
- Metabolic disease risk
Subject flow chart – 4h vs 6h TRF study

No dropouts due to issues with diet

Cienfuegos S et al. 2020. Cell Metabolism
Weight loss - 4h vs 6h TRF

4h and 6h produced similar reductions in body weight

All values reported as mean ± SEM. The 4-h TRF and 6-h TRF interventions produced nearly identical weight loss, relative to controls (P < 0.001).

Cienfuegos S et al. 2020. Cell Metabolism
Adherence to the eating window - 4h vs 6h TRF

4h and 6h had similar adherence to the eating window

Both groups adherent: 6.2 d/week

All values reported as mean ± SEM. 4 h and 6 h TRF were compliant with their prescribed eating windows on 6.2 ± 0.2 d/week, and this level of adherence did not change over the course of the trial.

Cienfuegos S et al. 2020. Cell Metabolism
Glucoregulatory factors - 4h vs 6h TRF

4h and 6h produced similar reductions in insulin and insulin resistance

All values reported as mean ± SEM. Fasting glucose was not affected by either 4-h or 6-h TRF. Fasting insulin and insulin resistance decreased similarly by 4-h TRF and 6-h TRF. *P < 0.05 relative to controls.

Cienfuegos S et al. 2020. Cell Metabolism
Blood pressure and lipids - 4h vs 6h TRF

4h and 6h have no effect on blood pressure or plasma lipids

Cienfuegos S et al. 2020. Cell Metabolism
Oxidative stress and inflammation - 4h vs 6h TRF

4h and 6h produce similar reductions oxidative stress

Both -35%

All values reported as mean ± SEM. 4-h and 6-h TRF produced similar decreases in 8-isoprostane (marker of oxidative stress to lipids). Inflammatory markers were not changed. *P < 0.05 vs controls.

Cienfuegos S et al. 2020. Cell Metabolism
Unintentional calorie restriction - 4h vs 6h TRF

4h and 6h produced similar reductions energy intake (~550 kcal/d)

All values reported as mean ± SEM. Comparable decreases in energy intake were observed in the 4h TRF group and 6-h TRF group, versus controls. *P < 0.05 relative to controls.
Summary of findings – 4h vs 6h TRF

Body weight (similar findings 4h vs 6h)
- ~3% weight loss in 2 months
- Self-reported adherence was high (90%)
- Unintentional kcal restriction (~550 kcal/d)

Metabolic risk reductions (similar 4h vs 6h)
- Insulin and insulin resistance
- Oxidative stress
- No effect on lipids/inflammation
Alternate day fasting
Alternate day fasting

Feast day
Day of ad libitum feeding

Fast day
25% energy intake (500-600 kcal)
Meal consumed at lunch or dinner
How much do people eat on the feast day?

How much do people eat on the feast day?

Feast day intake: 110% of needs
Inability to overeat on the feast day =
Inability to overeat on the feast day = Weight loss
Is fasting better for weight loss vs. daily calorie restriction?
Experimental design – ADF vs CR study

**ADF**
- Weight loss period (6 mo)
  - 500 kcal fast day
- Weight maintenance period (6 mo)
  - 1000 kcal fast day

**CR**
- Weight loss period (6 mo)
  - 25% restriction
- Weight maintenance period (6 mo)
  - Calories for maintenance

**CON**
- Weight loss period (6 mo)
  - Usual diet
- Weight maintenance period (6 mo)
  - Usual diet

**Baseline**
- BW, FM, FFM
- Metabolic disease risk

**Month 6**
- BW, FM, FFM
- Metabolic disease risk

**Month 12**
- BW, FM, FFM
- Metabolic disease risk
ADF and CR produced similar weight loss after 1 year

Data were included for 100 participants; means were estimated using an intention-to-treat analysis using a linear mixed model.

Trepanowski JF, 2017. JAMA IM.
ADF and CR produced similar weight loss after 1 year.

Data were included for 100 participants; means were estimated using an intention-to-treat analysis using a linear mixed model.

Trepanowski JF, 2017. JAMA IM.
Most weight loss occurred in first 3 months

Data were included for 100 participants; means were estimated using an intention-to-treat analysis using a linear mixed model.

Trepanowski JF, 2017. JAMA IM.
ADF and CR produced similar weight loss after 1 year

Data were included for 100 participants; means were estimated using an intention-to-treat analysis using a linear mixed model.

Trepanowski JF, 2017. JAMA IM.
But not everyone loses weight with fasting...

Alternate day fasting (ADF)

Low Weight Loss group (<5%)  High Weight Loss group (≥5%)

n = 20  n = 14

20% gained weight
38% lost 1-5%

42% lost 5-15%

Trepanowski JF, 2017. JAMA IM.
...Which is very similar to daily calorie restriction

Calorie restriction (CR)

Low Weight Loss group (<5%)  High Weight Loss group (≥5%)

- Weight loss at month 12 (%)
- n = 21  n = 14

- 20% gained weight
- 39% lost 1-5%
- 41% lost 5-18%

Trepanowski JF, 2017. JAMA IM.
12 months of ADF vs. CR in **healthy** adults with obesity

<table>
<thead>
<tr>
<th></th>
<th>ADF</th>
<th>CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight</td>
<td>↓ -5%</td>
<td>↓ -5%</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Heart rate</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Lipids</td>
<td>↓ TG</td>
<td>↓ LDL</td>
</tr>
<tr>
<td>Glucose</td>
<td>X</td>
<td>↓</td>
</tr>
<tr>
<td>Insulin</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

*Trepanowski JF, 2017. JAMA IM.*
BUT! ADF may be more effective than CR in subjects with obesity and insulin resistance
Weight loss was similar by ADF and CR in subjects with insulin resistance

ADF produced greater reductions in insulin resistance, versus CR, in subjects with insulin resistance.
Practical considerations
Who should not do intermittent fasting?

- Pregnant women
- People with binge eating disorders
- Shift workers
- Frequent snackers
Advice when starting intermittent fasting...

- First 10 days are rough
- Most common complaint: headaches
- Eventually you feel boost of energy on fast days
- Eat 50 g protein on fast day – keep hunger low
Which diet should I choose?

Alternate day fasting

- Faster weight loss
  - 10-15 pounds in 3 months

- Harder to follow
  - Need to count calories

Time restricted feeding

- Slower weight loss
  - 5-10 pounds in 3 months

- Easier to follow
  - Don’t need to count calories
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  • 09SDG2170077
  • 12PRE8350000

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