Intermittent Fasting: A Novel Approach to Reduce the Risk of Cardiometabolic Disease or Just Another Diet Fad

Webinar Questions Answered by Kristin Hoddy, PhD, RD

- What do you think about intermittent fasting vs. intuitive or mindful eating?
  The two approaches have not been considered formally in a head-to-head comparison or combined study. From my personal experience and anecdote from participants, people seem to become more in touch with appetite cues. For this reason, I believe the two approaches have the potential to be combined. Additionally, if someone practices mindful eating prior to engaging in intermittent fasting, they may have more insight into an appropriate regimen for their lifestyle and/or preferences.

- Can you please provide fast day tips?
  Please see fast day tips slide.

- On perhaps a different note, do you know anything about positive/negative effects of IF with IBS?
  I am not aware of research in this specific patient type. Presently, I would consider similar contraindications as calorie restriction for IF approaches that have a calorie restriction component.

- How was the 25% of the participants' needs determined? Average daily needs? Were these individuals doing any type of physical activity or were they asked to refrain from activity during the study?
  For my research, 25% was based on previous studies. This calorie allotment allows for a full meal to be served and is similar to the daily calorie allotment given during very low calorie diets (VLCD).

- Any comparisons to fasting mimicking diets (FMD) with reduced intake 5 consecutive days per month?
  To my knowledge FMD have not been compared to IF regimens, nor have intermittent fasting regimens been compared to one another in a randomized clinical trial. Here is the closest study in humans that I could find https://www.mdpi.com/2072-6643/13/5/1523/htm. If was published after the creation of the webinar.

- Please tell about the changes in appetite?
  Discussed in appetite slide.

- Can you explain the Homeostatic Model Assessment for Insulin Resistance test?
  Here is a standard formula to calculate HOMA fasting insulin (microU/L) x fasting glucose (nmol/L)/22.5. Overall, the higher the number the more insulin resistant someone is. Here is one of the original papers on the topic: https://pubmed.ncbi.nlm.nih.gov/3899825/

- Is any information available that talks about what happened when people went off of IF in these studies? What happened with weight and other markers?
  This was discussed during presentation and Q&A.

- Are people who use IF able to meet DRI needs?
  We have not observed nutritional deficits with IF, but this is not readily assessed. Standard recommendations for calorie restriction should be practiced. Based on the individual nutritional

assessments, a multi-vitamin may be recommended. There is unlikely an issue with meeting DRIs during time restricted eating.

- For maintenance of weight following IF for weight loss is the person typically expected/recommended to continue intermittent fasting a few days per week?
  If maintenance of weight loss is the goal, then some degree of energy restriction from their initial intake will be required to achieve energy balance at a new lower body weight.

- Have you seen any effects of intermittent fasting and women's menstrual cycles? This outcome isn't readily reported. Anecdotally, none of my participants reported this.

- How does the hepatic production of blood sugar impact blood sugar when there is more than a 5-6 hour fast? The idea that at the eating window in TRE should be ≤10 hours is based on an intersection of decreasing glycogenolysis due to depletion and increasing gluconeogenesis and free fatty acid oxidation that occurs right around 16 hours of fasting.

- I've seen some research that intermittent fasting can cause more muscle loss than other calorie restricted diets. Is this typical and why does this happen?
  This has not been established in the human literature. Some studies show lean mass retention others don't. This depends on the IF approach and measurement methods. The most rigorous studies will utilize DXA to assess body composition. Presently, there is not agreement in the literature even among studies just relying on DXA. When studies are considered collectively, there does not seem to be a difference in body composition between the two approaches.

- I wonder about overeating at the next meal or the body thinking it's "starving" and storing fat better. Is there research on that?
  We have not observed a next-day response with over-eating. See energy in take slide with data from Trepanowsk et al 2017. Alterations in body composition suggest that changes in fat mass are similar between IF and CR. Additionally, increased metabolic flexibility with time restricted eating suggest that people may be able to tap into their fat stores better during TRE vs free eating.

- What was the calorie intake in the TRE studies?
  It depends on the person and the study. Most TRE studies have not required energy restriction and either recommend or physically feed participants the required amount of calories to maintain body weight. In studies with poor dietary control, like when participants live at home and eat whatever they want, there appears to be an energy deficit resulting in about 2-3% weight loss.

- For a patient on tube feeding with uncontrolled BS would it be recommended to implement intermittent (whether it would be 6, 8 or 12 hours)?
  This has not been evaluated. Until it has, I highly recommend the ASPEN guidelines for tube feeding practices. If you are interested in this type of work, I would consider following work by Dr. Hassan S. Dashti (https://connects.catalyst.harvard.edu/Profiles/display/Person/147683) as he recently received a grant to look at meal timing practices in ICU patients.

- I have patients that don't eat all day due to work schedules -like truck drivers -and only eat at night. They are not following intermittent fasting. They often are overweight. How is intermittent fasting different than people who don't eat all day and eat one meal/day.

Night shift and irregular working hours increase risk for chronic diseases, like obesity. Although, it is hard to say how IF would be different for this cohort. Some research suggests that smaller meals or fasting during the nighttime may be beneficial. Here is a resource to look into further: https://pubmed.ncbi.nlm.nih.gov/28635334/

- If someone drinks essential amino acids during the fasting time, do the EAA's "break the fast?" This has not been established. Likely, anything that is consumed other than water, like caffeine, could break the fast. Some work is being done in the fast-mimicking-diet space on this. It looks like some food choices may be able to extend a fast, but the health effects of this have not been determined. If the goal is to have extended fasting through using TRE, a water fast is ideal. Also keep in mind that the benefits from regimens like alternate day modified fasting and 5:2 are likely driven by the caloric deficit.

- Does exercise impact weight loss results with either CR or IMF?
  Similar to other energy restriction approaches, exercise appears to be complementary.

- In the study showing differences in early or late feeding window glucose levels, were sleeping schedules the same in both groups?
  Inpatient studies typically keep bed and wake times standard. TRE may have an effect on sleep, but this has not been determined.

- Could you speak about the safety of exercise, particularly on fast days? Specifically timing of exercise and eating?
  In our studies we did not observe issues with fast day exercise over the course of the intervention. Exercise and fasting tolerance will likely be dependent on the intensity and type of exercise along with the individual's exercise tolerance. To be conservative, I would recommend exercising on feed days in the case of alternate day fasting, alternate day modified fasting, and 5:2 until the individual knows how their body responds. Anecdotally, 2 weeks is a common adjustment period. If performance is the goal for a particular exercise intervention, like in the case of athletes, I would not recommend intermittent fasting.

- I have seen reports that time restricted IF less than 18 hours was not effective for metabolic benefits. If a client wanted to do a time restricted IF 1x per week, would you recommend an 18-24 hour fast?
  I do not endorse 24-hour fasts. If choosing TRE, this should really be across several days with a couple "free-day's" to help with compliance.

- Can you explain the significance of the less than 10 hour feeding window? Please see item 13.

- How does IF effect microbiome? I have heard many claims regarding this and immunity
  This has not been confirmed in humans. Even in animals, this is not well established.

- How do you factor in risk for causing or triggering an eating disorder with IF?
  Disordered eating symptoms and body image have been assessed as exploratory outcomes in the intermittent fasting literature, and there does not appear to be associated harm or risks. Existing studies often list a history of eating disorders as an exclusion to study participation. As such, there are no recommendations for this particular patient type. In practice, any restrictive behavior could be triggering based on the patient's history.

- For timed fasting, is it you would eat for 6 hours and fast 18?

Yes, typically and eating opportunity of ≤10 hours is used in research.

- Why should it be avoided in patients with recent ischemic events?
  To my knowledge, IF has not been evaluated in this patient type.

- Do you promote utilization of any other dietary choices in intermittent fasting such as keto restrictions, low carb. restrictions, vegan choices within the intermittent fasting module?
  These variations have not been rigorously tested. Intermittent fasting is supposed to be a simplified version of calorie restriction. As with any restrictive diet, we need to be mindful about not being too restrictive.

- Is intermittent fasting contraindicated for those with reactive hypoglycemia?
  This has not been studied. Additionally, there are several different intermittent fasting regimens that they may respond differently to.

- It seems like there is less RCT data on time-restricted eating, which seems to be really growing in popularity amongst the regular population. Are there any contraindications for the general population utilizing TRE? Wondering if any conditions (aside from poorly controlled DM and eating disorders) would be a red flag?
  I would identify those as the primary red flags, but any condition that has a large dietary component should be evaluated for potential risk.

- Do you have thoughts regarding Dr Panda's recent study last year that showed that melatonin production increased 2 hours before normal sleep time? He found melatonin receptors on the pancreatic beta cells received the melatonin and started shutting down insulin production.
  I'm not familiar with this particular study, but this review nicely summarizes this research area: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7349733/ (Figure 1 in particular). There is an expected rise in melatonin prior to bedtime. While this is physiologically appropriate, there are potential consequences when you pair food consumption with high levels of melatonin.

- I've had many postmenopausal women that do not see results with IF and some experience worsening hormonal symptoms. Any research regarding this or a high-stress population & which IF protocol would be best?
  There is not a lot of research on this. One secondary analysis did not show a difference in weight loss. https://pubmed.ncbi.nlm.nih.gov/33358713/ To really address your question, there would need to be a study in postmenopausal women where symptoms were assessed, and specific tests were performed to specifically consider this special population.

- How often would you recommend people who are IF check in with RD?
  In our experimental studies, participants have a weekly check-in. There are not standard recommendations visit frequency with an RD or other healthcare providers. While support from a trusted professional could promote success, intermittent fasting does not require supervision from a health care professional for low-risk individuals.

- What about the thinking that breakfast is the most important meal of the day vs. late-day intermittent fasting?
  Breakfast is actually a rather subjective term and has timing, quantity, and quality components. For example, breakfast may have a different meaning to different people or groups and there is debate

over the actual definition of breakfast. Breakfast is also traditionally smaller and may be comprised of higher quality foods compared to other standard meals. Lastly, research surrounding optimal meal timing is of growing interest in nutrition research. While there are not exact recommendations, it appears that energy intake that is not too early or too late in the day is optimal.

- Your slides state that intermittent fasting mimics the fast-feed cycle of the Late-Paleolithic Era human. Please provide the evidence you have of humans following this diet during that era of time.
  This statement was strictly theoretical for why there may be benefits for intermittent fasting in modern humans. Physiologically, it is well established that the human body is suited to handle fasting. The ability to survive as fast would have been important species survival during limited food availability. Additionally, animal research has demonstrated optimal life and health-span with some degree of calorie restriction. Here is a nice review that summarizes this: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4057799/