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**WOX7001 RESEARCH METHODOLOGY
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< Weather Time-restricted Eating is Suitable for All Ages >

**INDIVIDUAL ASSIGNMENT 2
LITERATURE REVIEW**

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Introduction

With the improvement of people's quality of life, the obesity problem has become a serious trend year by year. By 2021, about 40% of the U.S. population is already obese. Obesity is often accompanied by physical abnormalities such as increased blood pressure (BP), impaired glucose tolerance, and dyslipidaemia. (World Population Review, 2022) In medical terms, these chronic diseases can be thought of as the same type of disease known as Metabolic Syndrome (MeTS). Poor Eating Habits (PEH) are now linked to increase the risk of MeTS diseases. PEH includes under- or over-eating, not having enough of the healthy foods people needed every day, or consuming too many types of foods and drinks, which are low in fibre or high in fat, salt or sugar. (SA Health, n.d., 2022) Such as irregular diets, high-calorie Western-style meals, sedentary lifestyles, and chronic insomnia and so on. (Croese et al., 2021a)

In the past, people have to take medication to prevent and alleviate some of the diseases caused by MeTS. Drug therapy is often accompanied by increased renal burden which may shorten people's life. Extensive evidences and literature researches proposed that MeTS is also closely related to people's circadian clock (CC). (Phillips et al., 2021a) Therefore, some medical experts proposed a method to reduce the effects of PEH and CC. They suggested people can adjust the body's metabolism by adjusting the meal time. By adjusting meal times, people can delay and reduce their risk of suffering MeTS. They call the method Time-restricted feeding (TRF) or Time restricted eating (TRE) .

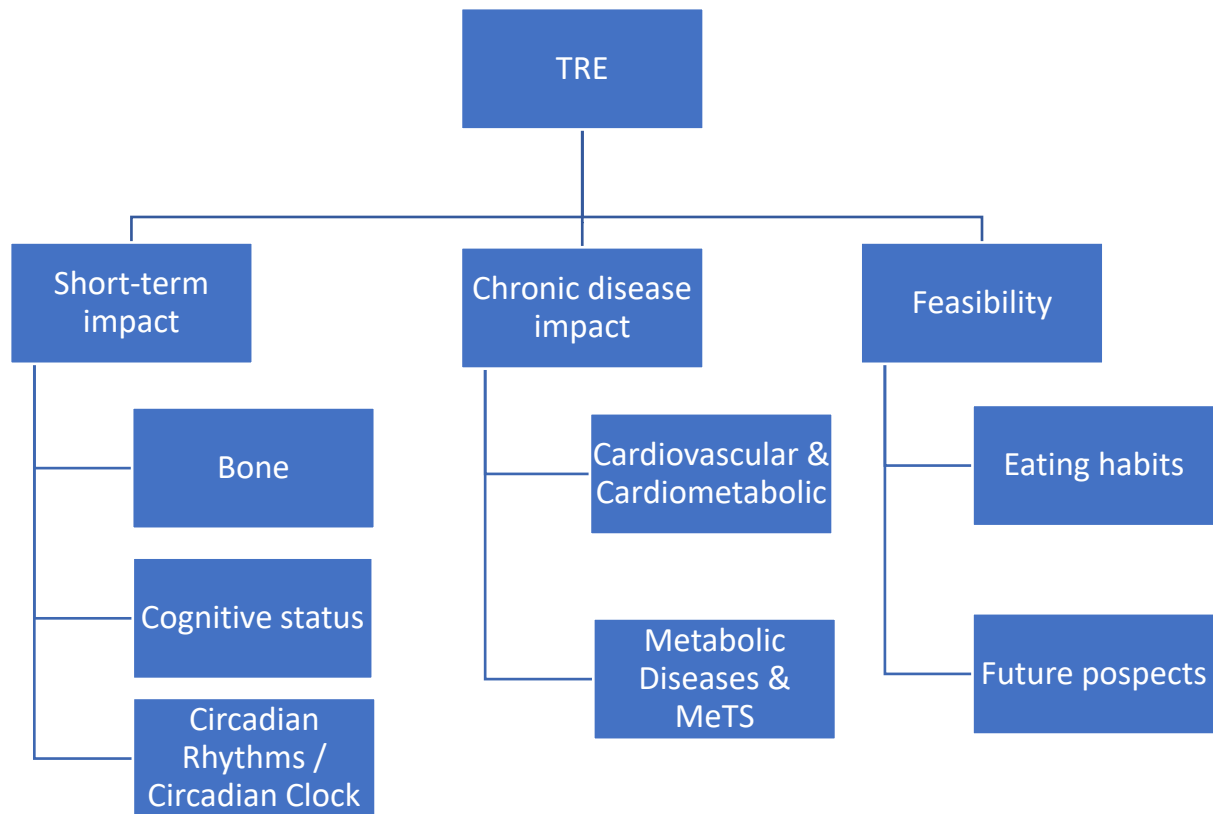
TRF/TRE has become a very popular method for improving the people's metabolism in recent years. It refers to a method that restore circadian rhythm and improve metabolic mechanisms by shortening the time people eat each day and do not limit the foods type people eat. That is, extending the daily fasting time. (Światkiewicz, Woźniak, et al., 2021a) For example, the original participants had breakfast at 6 am and dinner at 6 pm. Through the improvement of TRE method, breakfast time will be delayed by 2 hours and dinner time will be advanced by 2 hours. Which means the participant's eating time in a day was 12 hours in past, and for TRE window time it decreases to 8 hours. **TRE "Window"** defined as the time interval during a day in which 95% of all calorie-containing ingestion events occur. (Wilkinson et al., 2020a) The eating time will be increased from 12 hours to 16 hours. The participant then had 16 hours of metabolic dormancy in their daily life.

The foods people eat are affected by circadian rhythms in people's bodies. Eating late at night or early in the morning can disrupt sleep cycles. (BBC News, 2021) For example, every night people's body is trying to make the sleep hormone melatonin. The sleep hormone melatonin will stop the body from releasing insulin, and if people eat without the help of insulin, the fat and sugar may stay in people's blood for a long time. So, it will increase the risk of diabetes and cardiovascular disease.

In fact, clinical trials have shown that TRE has a significant ameliorating effect on MeTS diseases. However, some experts have raised some controversies that TRE may face. Firstly, most of the current TRE clinical trial subjects are adults aged 18-60 and their body already faced MeTS diseases issues. This makes some of the effects of TRE on the prevention of MeTS a theoretical inference and difficult to prove. Secondly, underage children are in the period of growth and development, and they need supplemental nutrition to promote growth and development. If TRE is used to control underage children, will it affect their ongoing development? Also, will the use of TRE cause the elderly people to suffer orthopaedic diseases such as calcium deficiency?(Lobene et al., 2021a) In the end, physical fitness varies from person to person which may be greatly affected by age. Therefore, people of different ages need to participate in different TRE Window management methods. (Schuppelius et al., 2021a)For example, does the child TRE Window need to be extended longer? Does the TRE Window need to be shortened year by year as people age?

Literature review Taxonomy

Thematic method approach



Comparison table

ID & link	Author Name	Participant and age	Research Method	Mainly research issues	Issues may face in the future (limitation)
Short-term disease impact					
1	Stabouli et al. 2021	Children and Adolescents	Quantitative research	Eating Disorders (ED) affect the obesity in Children and Adolescents.	Mental health may affect obesity and ED.
2	Lobene et al. 2021	20 adults (Age 18-65)	Quantitative research	The effect of TRE on Bone .	The trail does not include elder people and children. Smoking and alcohol may affect TRE results.
3	Currenti et al. 2021	50 women 48 men (mean age 65)	Quantitative research	TRF affect Cognitive Status in older Italian adults.	Trail too little about TRF and cognitive Status. Need more trails on the effect of Cognitive status, regional brain volumes, neural network activity, and cerebrospinal fluid.
4	Mattson et al. 2017	/	Qualitative research	Effects of intermittent fasting on health and disease .	IF may improve health and prevent fighting aging diseases.
5	Chawla et al. 2021	17 women 40 men (Age 38±11.2)	Quantitative research	TRE effects on Cortisol and Melatonin Secretion (Factors of Circadian Rhythms) .	Pregnancy, pathology, and exercise status may affect TRE results. Ramadan effects.
6	Manoogian & Panda 2017	Animals (Mice & Drosophila) and humans	Quantitative research	Relationship among Circadian Rhythms , TRF and Aging characteristics.	Feeding/fasting patterns may improve health.
7	Jamshed et al. 2019	18 Adults (Age 20-45)	Quantitative research	eTRF improve the glucose level, Circadian Clock , Aging and Autophagy.	Sample size too small. Trial period is too short. Inconsistencies in data measurement time might lead to some errors.
Chronic disease impact					

8	Christensen & Kirkham 2021	Ladies (age >18)	Quantitative research	TRE can prevent Breast Cancer and Cardiovascular Disease .	TRE trial period is too short. TRE barriers. Currently no trial in cancer or cardiovascular disease.
9	Gabel et al. 2021	/	Qualitative research	Effect of TRE in Cardiovascular Health .	TRE trial period is too short. Sample size is too small. Comparison of TRE and traditional dieting method. Cross-over method not a good method. No trial study on maintains weight loss.
10	Świątkiewicz, Mila-Kierzenkowska, et al. 2021	30 (Before) N (After)	Quantitative research	TRE reduces Cardiometabolic risk .	Sample size too small. Age limit.
11	Peters et al. 2021	30 overweight ladies (Age 18-70)	Quantitative research	eTRE VS ITRE on Cardiometabolic Health .	Different age, gender, and chronotypes and subjects with diabetes, metabolic syndrome.
12	Park et al. 2021	34 adults (Age 18-28)	Quantitative research	TRE effects on Body Composition and Cardiometabolic .	Sample size too small Single-arm study with no comparison. Does not collect the data before TRE intervention.
13	Garcidueñas-Fimbres et al. 2021	Children and adults	Quantitative research	Effect of eating speed, eating frequency, and food quality to the risk of MeTS .	Trial period is too short.
14	Charlot et al. 2021	/	Qualitative research	Effects of eTRF on Metabolic Diseases .	May lead to isolation, loneliness or depression. Lack of protocol standardization. Season change may affect the result.
15	Wilkinson et al. 2020	35 adults and mice (Age 59±11.14)	Quantitative research	TRE & TRF can reduce the risk of MeTS .	TRE & TRF may conflict with cardiovascular drugs, lipid-lowering drugs, antihypertensive drugs, and antidiabetic drugs.
16	Schuppelius et al.	People (Age 18-	Quantitative research	Effect of TRE in Metabolic Disturbances .	Changes in nutrient and calorie intake during TRE.

	2021	70)			<p>Comparison of eTRE and ITRE.</p> <p>Differences in the time setting of different eating windows.</p> <p>Based on long-term, large-participant trials.</p>
17	Manoogi an et al. 2022	/	Qualitative research	Effect of TRE in prevent manage Metabolic Diseases .	<p>Success of TRE relate to self-monitoring, education, and compliance.</p> <p>TRE challenges and barriers.</p>
Future Feasibility of TRE					
18	Phillips et al. 2021	213 adults (mean age 40.1)	Quantitative research	The effect of TRE and Standard Eating.	<p>Data lost by mobile apps.</p> <p>Drugs interference.</p>
19	Światkiewicz, et al. 2021	Adults (Age 18-70)	Quantitative research	The future of TRE and MeTS.	<p>Sample size too small.</p> <p>Some trail results may not suitable for MeTS participant.</p> <p>The trail periods too short.</p> <p>TRE time setting may have different results.</p> <p>Need standard window time setting.</p>
20	Croese et al. 2021	17 women and 3 men (Age 45.5±12.1)	Quantitative research	The effect or TRE on the life quality of obesity people.	<p>Sample size too small.</p> <p>Weight loss may affect mental health.</p> <p>Mental health help to promote TRE to the world.</p>

Constructive reviews

Time-restricted eating (TRF) and time-restricted eating (TRE) have been studied for a long time. In the past, the sample of trial was mice or animal, so TRF was used to name the method. Since scientist found that the method is safe to human, they used TRE instead of TRF when the sample of trial is people. Twenty of these articles were selected for this review and they can be classified according to short-term impact, impact of chronic disease, and feasibility.

Short-term disease impact

After TRE intervention in children and adolescents by Stabouli and his group, it was confirmed that TRE could control and prevent eating disorders and obesity in this population. They found that the prevalence of eating disorders was very high among the obese child subjects. Most of them suffered from bulimia nervosa and binge eating disorder. The treatment options for both conditions are varied. From milder nutritional management, psychotherapy, to extreme medication and surgery. Among these methods, the former has high economic pressure on patients and is not suitable for promotion. The latter may have the hidden danger of disease rebound. Therefore, these methods are not suitable for large-scale promotion. In contrast, tailor-made TRE intervention strategies for patients are more economic, health and security. (Stabouli et al., 2021)

Lobene and his group investigated the effects of 12-week TRE on bone mineral density and bone turnover in obese adults aged 18-65 years. Their experiments used an 8-hour TRE window and non-TRE as usual to compare bone parameters. The results suggested that a short-term TRE intervention with an 8-hour eating window did not adversely affect obese adults. However, they believe that clinical changes in BMD assessed by the official authoritative channel DXA require at least 1-2 years to be based data. Also, the target population their study cited could not show whether TRE blocks bone development in children and if TRE causes osteoporosis in the elderly. In addition, the menopausal status of older women also has an impact on bone status. Due to the small sample of older women in their study, the recommendation requires further clinical data. Finally, they propose that exercise can attenuate bone loss in humans caused by changes in diet quality. Their TRE clinical data did not exclude external interference from these two factors. Therefore, they thought that further studies were needed to corroborate the long-term (1-2 years) effect of TRE on bone loss. (Lobene et al., 2021)

Currenti and his group did research on the effects of TRF on the brain health of people over the age of 50, such as Alzheimer's disease. They calculated the average daily time window based on the dietary characteristics and frequency of more than 800 elderly Italians. After ruling out some potential additional factors affecting them, it was found that the probability of cognitive impairment in the elderly who adhered to TRF was greatly reduced. However, they believe that TRF has the following two limitations. Firstly, TRF affected the eating habits of the elderly with cognitive impairment. Some populations with lower education levels might have difficulty in properly implementing TRF due to lack of health awareness, thereby affecting the accuracy of the experiment. In addition, the effects of TRF on regional brain volume, cerebrospinal fluid, and neural network activity still required extensive human experiments to demonstrate. (Currenti et al., 2021)

Mattson and his group made some qualitative research on the effects of intermittent fasting (IF) of people. Firstly, for sedentary people, overeating during the open TRF window may cause metabolic diseases. Secondly, the populations of IF may face issues with little capacity intake for longer periods of time. However, IF may have positive effects on diabetes, cardiovascular disease, cancer, Alzheimer's disease, Parkinson's disease and stroke. In addition, IF, PF, TRF have been shown to be effective in weight loss. It improves mitochondrial health, DNA repair, autophagy, metabolism while improving health indicators. Finally, they proposed that IF might have efficacy in improving general health and fighting aging diseases. (Mattson et al., 2017)

Chawla and his group investigated the negative effects of traditional TRE patterns and Ramadan fasting (RF) patterns on two circadian parameters (cortisol and melatonin). The results showed that the RF pattern cortisol circadian rhythm was weakened, and melatonin was also less. This means that the target population will get worse sleep time and sleep quality. However, there are few papers in TRE research that study the effects of these two parameters on the human body. In addition, they suggest that TRE may have effects on women with PCOS and pregnant women, so for the female experimental population, pregnancy-related, pathological and physiological effects should be considered. Third, since light, energy consumption, and sleep time all affect the accuracy of serum parameters, they feel that these factors need to be taken into account in evaluating TRE performance. Finally, they concluded that a TRE regimen that skipped breakfast would have a different effect on circadian rhythms than a TRE regimen that skipped dinner. (Chawla et al., 2021)

Manoogian and his group published a study examining the relationship among circadian rhythms, TRF and aging characteristics. They advocated improving physical health by adjusting circadian rhythms to coordinate cells, tissues, and behaviour. These impacts diminish with human age grows. TRF was a coordinated approach that can affect the robustness of circadian rhythms. They believed that irregular eating patterns could disrupt the body's metabolism and lead to chronic diseases. Maintenance of TRF intervention without altering nutritional quality and quantity could reverse chronic disease. Thus, their study suggested that maintaining TRF could prevent and treat chronic diseases by stabilizing the circadian clock. (Manoogian & Panda, 2017)

Jamshed and his group conducted a 4-day experiment with 11 overweight adults aged 20-45 years using a randomized crossover method. After comparing and calculating the experimental results, it was found that the blood glucose, cardiometabolic risk factors, hormones and gene expression of whole blood cells was significantly affected in patients who took eTRF to interfere with the eating window time. The results showed that eTRF improved multiple aspects of health. Firstly, improve insulin conduction by reducing the average daily blood sugar and reducing fluctuations to achieve the purpose of blood sugar control. Secondly, this approach improved the circadian patterns of fasting cholesterol, ketones, cortisol, and clock genes. Finally, some research data suggest that eTRF can assist in improving cardiometabolic health, with anti-aging potential. However, they also suggested that further studies are needed to corroborate these results due to the limitations of the target population. (Jamshed et al., 2019)

Chronic disease impact

Different to short-term effects on the human bodies, the next category focuses on chronic diseases.

Christensen and Kirkham conducted research on the effectiveness of TRE in breast cancer (BC) and cardiovascular disease (CVD). Evidence shows that TRE has positive effects on metabolic, cardiovascular and cancer-specific health. Furthermore, they describe the safety and feasibility of implementing TRE in such patients. They mention that short-term fasting has become a practice in Judaism and Islam. Such as fasting, Yom Kippur, etc. A large amount of practical evidence proves that short-term implementation of TRE is a safe method for human health. Therefore, they recommend TRE as a method for the prevention and adjunctive treatment of BC and CVD diseases. (Christensen & Kirkham, 2021)

Gabel and his group conducted a research review on the effect of TRE on body weight and cardiovascular disease risk factors in 2021. Findings showed that TRE intervention had a positive effect in reducing fat mass, blood pressure, triglyceride levels, and markers of oxidative stress compared with a population without meal time restrictions. Therefore, they believe that TRE is a safe dietary intervention to affect obesity and cardiovascular disease. (Gabel et al., 2021)

Świątkiewicz and his group presented quantitative research of the effects of a greater than 14-hour TRE intervention on metabolic, neuroendocrine, inflammatory and oxidative stress and cardiac standard parameters in Polish adults (18-75 years) and is still recruiting participants. The primary objective of the study was to collect large-scale data through the myCircadianClock mobile software to enable a randomized controlled trial to further determine the effect of long-term TRE on cardiometabolic health in the MeTS population. (Świątkiewicz, et al., 2021)

Peters and his group proposed a research protocol for the effects of eTRE (8:00-16:00) and lTRE (13:00-21:00) on parameters such as insulin sensitivity, blood sugar, blood lipids in female obese patients. Its research is to prove 3 expectations. First, they wanted to demonstrate that both modes of eating intervention improved blood sugar, metabolism, insulin sensitivity, and more. Second, they believe that people with diabetes will improve their blood sugar status more effectively than normal people. Human blood pressure, blood triglycerides, total and LDL cholesterol, and sleep quality may decrease. Finally, they hypothesized that the effects of the two different approaches on the body's circadian rhythms may be opposite. (Peters et al., 2021)

Park and his group investigated the effects of 4-week late TRE on body weight and cardiometabolic risk factors in 33 night-worked adults. The results showed that most of the test subjects had a significant reduction in fat mass after 4 weeks. Both fasting insulin and insulin resistance are moving in a positive direction. And there were no significant changes in sleep duration, sleep quality, and psychometric measurements. However, they argue that their study had a small sample size, so the findings cannot yet justify a wider rollout. In addition, they did not assess the dietary intake of the target population before TRE intervention and lacked comparisons of dietary changes before and after TRE intervention. Finally, they did not consider the effect of target population gender on TRE outcomes. (Park et al., 2021)

Since 2008, experts had proposed a problem that eating speed, eating frequency, and food quality might affect the risk of MeTS. Garcidueñas-Fimbres and his group conducted qualitative research on such problem in 2021. They summarised reliable research essays, journals from PubMed and Web of Science as evidence. The evidence showed that children and adults who ate more quickly may increase the risk of MeTS whereas people who eat more frequently may reduce the risk. The diet quality also has an impact on the risk of MeTS. (Garcidueñas-Fimbres et al., 2021)

Charlot and his group summarized the impact and importance of circadian rhythms and lifestyle habits on metabolic health. At the same time, they also proposed three possible limitations of TRE. The first is the restriction of TRE on the eating window. It is because that people need to maintain family, work, and life, it is difficult to adhere to the requirements of the eating window exactly every day. Second, TRE currently is lack of standard protocol rules for setting the optimal time for the eating window. Finally, they mentioned that the effect of TRE may be affected by seasonal factors, so different eating window time rules need to be set for different seasons. They assessed the advantages and disadvantages of TRE for the treatment and prevention of metabolic diseases. (Charlot et al., 2021)

Wilkinson and his group conducted a study on whether TRE/TRF could conflict with drug treatment. The results suggest that TRE has a positive effect on cardiometabolic health in patients with metabolic syndrome. It can help patients enhance drug absorption capacity and accelerate recovery efficiency. At the time, they considered TRE to be an implicitly powerful way of life, and proposed that medical practices could consider formalizing it as a treatment regimen for metabolic syndrome. (Wilkinson et al., 2020)

In the medical field, data on TRE's role in weight loss, cardiometabolic health, and human health are controversial. Schuppelius and his group conducted a clinical experimental study on the effect of TRE on glucose and lipid metabolism. Trial data suggest that TRE has a positive effect on the target population's glucose levels both before and after meals. At the same time, TRE can affect the sensitivity of patients to insulin. They suggest that some studies showing adverse effects of TRE on blood glucose and lipids may be due to different parameter designs. For example, eating window time setting, calorie intake changes, etc. It may also be related to the target population, such as metabolic status, age, gender, etc. Finally, based on the experimental data, they still believe that TRE has a positive effect on the prevention and treatment of glucose and lipid metabolism disorders. (Schuppelius et al., 2021)

Manoogian and his group states that circadian rhythm disturbances can lead to a greatly increased risk of chronic metabolic disease in patients. They concluded that TRE/TRF shortening the daily eating window would contribute to circadian rhythm stabilization. According to the study, they confirmed that the experimental population can reduce the risk of obesity, diabetes, and cardiovascular disease under the intervention of TRE. And, epidemiological studies also advance similar concepts. Extended night fasting can help reduce the risk of chronic disease. However, they also suggested that more separate clinical studies are needed to demonstrate the effect of TRE intervention on the prevention and control of chronic metabolic diseases. (Manoogian et al., 2022)

Future feasibility of TRE

Some studies had used mobile apps for data collection and TRE monitoring. This would make it easier for scientists to recruit large numbers of trial participants via mobile apps in the nearly future.

Phillips and his group used a smartphone app as a tool to study the effects of eating time, unprocessed food, and processed food on metabolism in adults. Data is collected by manually recording parameters such as eating type, eating time, and personnel activities through the APP. The data showed that the 6-month TRE intervention staff lost 1.6% of their body weight. Those who ate a normal diet gained 1.1 percent. They wanted to demonstrate the potential assistance of smart APPs in assisting the implementation of TRE interventions by monitoring and collecting data through smart APPs. And it is proposed that further research is needed on the time setting of TRE intervention for different conditions and different patients' eating windows. (Phillips et al., 2021)

Światkiewicz and his group summarized the TRE pilot study evidence for MeTS through 2021. Multiple studies have demonstrated the feasibility of TRE and its positive effects on body fat, obesity, blood pressure and other issues without changing dietary quantity, quality, exercise factors. They propose future prospects for implementing TRE in the prevention and treatment of MeTS. However, they summarize the following problems faced by TRE. For example, the TRE research participants are different, the sample size is small, the TRE duration is short, and the TRE eating window time setting is different. In addition, they raised the question of the widely fluctuating effect of TRE on glucose and lipid metabolism in the MeTS population. Further research and verification are needed to determine whether long-term TRE has adverse effects in humans. (Światkiewicz, et al., 2021)

Croese and his group conducted a randomized crossover comparative analysis of the effect of TRE on quality of life in obese people. They compared the effects of TRE interventions on human physical functioning, emotional well-being, physical pain, energy changes, social functioning and general health. The results indicated that TRE intervention did not adversely affect quality of life. However, they also suggested that the mood swings in the female sample were more pronounced than those in the males. At the same time, the limitations of TRE intervention time and sample size may affect the accuracy of the conclusions. Further experiments are needed to confirm their findings. (Croese et al., 2021)

The literature review suggests that TRE could bring some health benefits to many diseases. These diseases come from different age groups. For example, obesity is the main problem to be prevented and faced by children and adolescents ($N < 25$). Metabolic syndrome is a major problem in the elderly ($N > 50$). There are also some female diseases for women only that TRE can help. These different diseases and target populations mean that optimum TRE Window time needs to be tailored for different genders, ages and backgrounds in order to avoid adverse effects.

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