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Association between lifestyle and metabolic syndrome incidence of workers in northern Okinawa, Japan: A cohort study

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ABSTRACT

In Japan, specific health checkups were implemented to prevent metabolic syndrome (MetS) and cardiovascular diseases in April 2008. This study aimed to clarify the relationship between lifestyle factors and the MetS incidence to understand how the disease can be prevented and to improve the public health policy.

A retrospective cohort study was conducted using the specific health checkup data of 2,781 workers. Lifestyle factors were assessed using lifestyle-related items in the general health questionnaire included in the specific health checkups. The hazard ratio values for the incidence of MetS according to lifestyle-related items were determined from the data of the specific health checkup for 12 years. The Cox proportional hazard survival model was used to evaluate hazard ratio values after adjusting for confounding factors. The limitations of this research method are discussed using a target trial emulation framework which investigates problems such as biases in observational studies.

The crude incidence rates per 1,000 person-years of MetS in women and men were 15.25 and 47.58, respectively. Three dietary lifestyle-related factors, namely "Eating snacks and sweet beverages other than breakfast, lunch, and dinner," "Eating faster than others," and "Skipping breakfast at least three times a week," were identified, with the hazard ratio values 1.262 (95 % confidence interval [CI] 1.032–1.542, p = 0.023), 1.220 (95 % CI 1.032–1.442, p = 0.020) and 1.189 (95 % CI 1.012–1.397, p = 0.036), respectively.

These results suggest that lifestyle improvements related to extracted lifestyle-related items contribute to the prevention of MetS.

1. Introduction

Metabolic syndrome (MetS) is defined as a combination of risk factors such as obesity, hypertension, dyslipidemia, hyperglycemia, and other metabolic disorders, and is one of the causes of cardiovascular disease (Gami et al., 2007; Takeuchi et al., 2005). In Japan, due to the dramatic increase in cardiovascular disease, a specific health checkup to prevent MetS and cardiovascular disease has been conducted since April 2008 for people aged 40–74 years. Recently, approximately 30 million people (29,935,810 people [2019]: 47.7 % of Japan's 40–74 years old population) have undergone a specific health checkup.

At the time of a specific health checkup, a general health questionnaire containing lifestyle-related items was undertaken. The questions are based on lifestyle-related items associated with obesity and diabetes, as described by previous studies (Sakurai et al., 2012; Willi et al., 2007; Otsuka et al., 2006; Waki et al., 2005; Sasaki et al., 2003; Craig et al., 1989). However, studies on the relationship between lifestyle-related items and the incidence of MetS using the general health questionnaire of a specific health checkup are limited (Tsutatani et al., 2017).

The transition of the nationwide prevalence of MetS (2008–2019) remained almost constant from 14.4 % to 15.8 %. Thus, it is important to consider the effective utilization of lifestyle-related items in general health questionnaires to lower the prevalence of MetS. We conducted a retrospective cohort study for 12 years on the relationship between the incidence of MetS and lifestyle-related items using the results of specific health checkups of workers enrolled in the Employee Health Insurance. We also examined the limitations of the research method applied in this study using the framework of target trial emulation (TTE) which

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investigates problems such as biases in observational studies (García-Albéniz et al., 2017; Hernán and Robins, 2016).

The purpose of this study was to identify important information related to the incidence of MetS from lifestyle-related items in the general health questionnaire of the specific health checkup and to consider the effective utilization of these items for improving the public health policy.

2. Methods

2.1. Specific health checkup

In Japan, under the initiative of the Japanese Ministry of Health, Labor and Welfare, a specific health checkup has been conducted since April 1, 2008, focusing on the prevention of metabolic syndrome and cardiovascular disease. Specified health checkups are conducted once a year for people aged 40–74 years who have some kind of medical insurance. If MetS or MetS reserve group (Pre-MetS) is diagnosed, health guidance for 3 months (MetS: monthly guidance and evaluation by physical measurements and blood test after 3 months; Pre-MetS: one guidance and evaluation by physical measurements and blood test after 3 months) is carried out. In addition, when only central obesity (waist circumference ≥ 85 cm in men, ≥ 90 cm in women) is determined, information on MetS countermeasures is provided.

2.2. Study design and population

This was a retrospective cohort study using data from specific health checkups conducted at Okinawa North Medical Association Hospital over 12 years, from April 1, 2008, to March 31, 2021. The Okinawa North Medical Association Hospital is one of the core hospitals in northern Okinawa Prefecture. Among the specific health checkup examinees, the workers who were enrolled in the Employee Health Insurance were selected as the research participants (Fig. 1).

The Japanese MetS criteria were used as the diagnostic criteria for MetS. Individuals with central obesity (waist circumference ≥ 85 cm in men, ≥ 90 cm in women) plus at least two of the following three components were defined as MetS: (1) blood pressure ≥ 130/85 mmHg or taking an antihypertensive; (2) fasting plasma glucose (FPG) ≥ 110 mg/dl or medication for diabetes; (3) serum high-density lipoprotein cholesterol (HDL-C) < 40 mg/dl, with or without serum triglyceride ≥ 150 mg/dl, or medication for hyperlipidemia. Individuals with central obesity plus one of the three components were defined as Pre-MetS.

Healthy examinees who did not participate in the specific health checkup during the study period and those with missing data for lifestyle-related items were excluded. The incidence of MetS was observed in this cohort over 12 years.

2.3. Outcome variable

The outcome variable was MetS incidence, which was determined by specific health checkups. Since the date of MetS incidence could not be determined, the central day between the date of diagnosis of MetS and the date of the previous specific health checkup was used as the estimated date of MetS incidence. Person-years were calculated using the estimated date of MetS incidence. The person-years of those who were not diagnosed with MetS and participated in specific health checkups only halfway through the observation period and those who did not develop MetS until the end of the observational period were calculated based on the date of the last participating specific health checkup.

2.4. Explanatory variable

The explanatory variables were sex, age, and nine lifestyle-related items selected from the general health questionnaire for specific health checkups. The lifestyle-related items included the following nine items: (1) "Having an evening meal within 2 h before bedtime 3 days or more per week," (2) "Eating snacks and sweet beverages other than breakfast, lunch and dinner," (3) "Eating faster than others," (4) "Skipping breakfast at least three times a week," (5) "Walking for at least 1 h/day or having equivalent physical activities," (6) "Exercising at least 2 days/week at least 30 min each at an intensity that causes a slight sweat for at least 1 year," (7) "Frequency of drinking," (8) "Regular smoker," (9) "Feeling refreshed after a night's sleep.".

2.5. Adjusted variable

The adjusted variables were sex, age, and nine lifestyle-related items. All explanatory variables were applied to the Cox proportional hazard survival model and analyzed using the forced entry method and

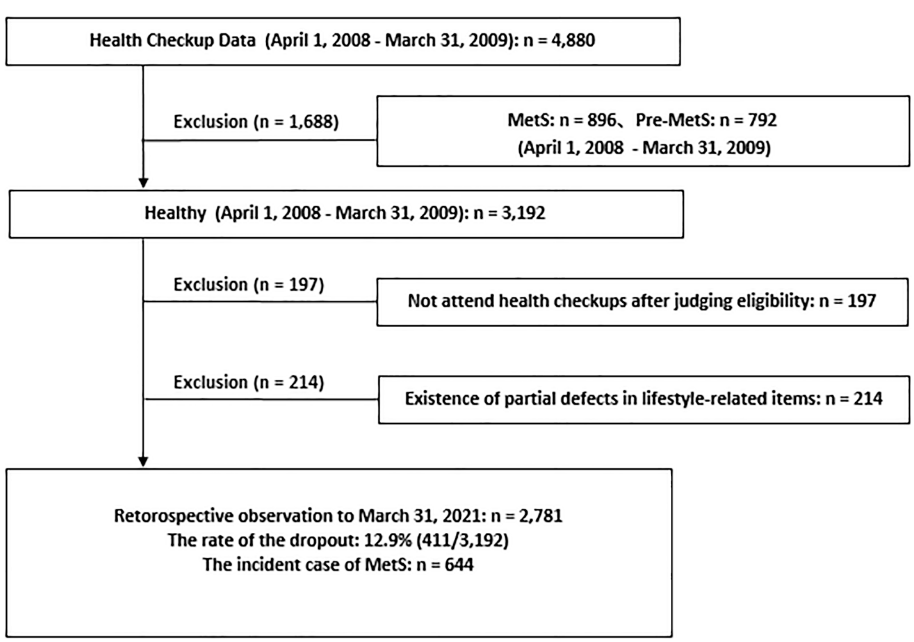

Fig. 1. Study design and selection of study population. (MetS: metabolic syndrome; Pre-MetS: MetS reserve group).

backward stepwise method.

2.6. Statistical analysis

The significance of MetS prevalence by age group was determined using Pearson's chi-square test. The observed person-years were calculated from the estimated incidence dates, and the crude incidence rate per 1,000 person-years was calculated. Hazard ratio values were calculated using the Cox proportional hazard survival model. Applying explanatory variables such as sex, age, and nine lifestyle-related items to the Cox proportional hazard survival model, the hazard ratio values of the explanatory variables by the forced entry method, and the hazard ratio values of the explanatory variables remaining by the backward stepwise method were calculated. A level of α = 0.05 was used to determine the significance of the models and variables. All statistical analyses were performed using the IBM SPSS Statistics ver. 28 (IBM Corp., Armonk, NY, USA).

Ethical approval

This study was approved after being deliberated by the institutional review board of Okinawa North Medical Association Hospital. We confirmed the consent of the participants to anonymize personal information and use data, such as the results of the health checkup for research, in writing and on the website.

3. Results

3.1. Study participants and crude incidence rate of MetS

Based on the specific health checkup examinees (4,880) among workers enrolled in the Employee Health Insurance from April 1, 2008, to March 31, 2009, a total of 3,192 (65.4 %) were healthy, 792 (16.2 %) had Pre-MetS, and 896 (18.4 %) had MetS. The prevalennce rates of MetS were 4.7 %, 27.3 %, and 18.4 % for women, men, and the total population, respectively (Table 1). Sex differences in MetS prevalence rate appeared to be due to sex differences in the prevalence rates of MetS components (obesity, hypertension, hyperlipidemia, and hyperglycemia). The prevalence rates of men and women in the MetS components were obesity (men: 48.5 %; women: 29.4 %), hypertension (men: 33.5 %; women: 21.4 %), and hyperlipidemia (men: 30.4 %; women: 26.5 %) and hyperglycemia (men: 18.9 %; women: 6.7 %). After screening, 2,781 participants in Healthy group were included in the study cohort (Fig. 1). In the study cohort, the total observed person-years were 22,181 person-years, the incident case number was 644 (women: 194; men: 450), and the crude incidence rate per 1,000 person-years was 29.03 (women: 15.25; men: 47.58) (Table 1).

3.2. Hazard ratio value of lifestyle-related items for MetS

Table 2 shows the hazard ratio values for MetS for sex-, age-, and the nine lifestyle-related items. First, we examined the forced entry method, and found significant hazard ratio values for sex, age, and the two lifestyle-related items. Next, sex, age, and three lifestyle-related items related to dietary habits remained significant after the analysis using the

Table 1
MetS rate in specific health checkup examinees (4,880) during the observation initiation period (April 1, 2008-March 31, 2009) and crude incidence rate per 1,000 person- years of MetS in the study cohort (2,781)

MetS rate in specific health checkup examinees (4,880) during April 1, 2008 - March 31, 2009						CIR of MetS in the study cohort (2,781)					
	Age	Healthy	Pre-MetS	MetS	Total		Age	Number of participants	Person-years	Incident cases	CIR
Women**	40-49	822	45	23	890	Women	40-49	729	7,109	80	11.25
		92.4%	5.1%	2.6%	100.0%						
	50-59	755	78	52	885		50-59	661	5,056	100	19.78
		85.3%	8.8%	5.9%	100.0%						
	60-69	120	15	14	149		60-69	92	550	13	23.66
		80.5%	10.1%	9.4%	100.0%						
	70-74	7	1	2	10		70-74	5	10	1	99.64
		70.0%	10.0%	20.0%	100.0%						
	Total	1,704	139	91	1,934		Total	1,487	12,724	194	15.25
		88.1%	7.2%	4.7%	100.0%						
Men**	40-49	675	278	293	1,246	Men	40-49	596	4,774	234	49.02
		54.2%	22.3%	23.5%	100.0%						
	50-59	686	302	409	1,397		50-59	597	4,114	186	45.21
		49.1%	21.6%	29.3%	100.0%						
	60-69	117	68	94	279		60-69	93	536	24	44.78
		41.9%	24.4%	33.7%	100.0%						
	70-74	10	5	9	24		70-74	8	33	6	181.85
		41.7%	20.8%	37.5%	100.0%						
	Total	1,488	653	805	2,946		Total	1,294	9,457	450	47.58
		50.5%	22.2%	27.3%	100.0%						
Total**	40-49	1,497	323	316	2,136	Total	40-49	1,325	11,882	314	26.43
		70.1%	15.1%	14.8%	100.0%						
	50-59	1,441	380	461	2,282		50-59	1,258	9,170	286	31.19
		63.1%	16.7%	20.2%	100.0%						
	60-69	237	83	108	428		60-69	185	1,085	37	34.09
		55.4%	19.4%	25.2%	100.0%						
	70-74	17	6	11	34		70-74	13	43	7	162.68
		50.0%	17.6%	32.4%	100.0%						
	Total	3,192	792	896	4,880		Total	2,781	22,181	644	29.03
		65.4%	16.2%	18.4%	100.0%						

**: P <0.001 by Pearson's chi-square test, relationship between age and metabolic syndrome determination
Abbrevations; MetS: Metabolic Syndrome; Pre-MetS: MetS reserve group; CIR: crude incidence rate per 1,000 person-years

Table 2
Hazard ratio values of lifestyle-related items for MetS by forced entry method and backward stepwise method of Cox regression hazard servival model

lifestyle-related item	Number of participants	Person-years	Incident cases	CIR	Hazard ratio†	95% confidence interval			P-value		Hazard ratio‡	95% confidence interval			P-value	
Sex																
Woman	1,487	12,724	194	130.464	1.000						1.000					
Man	1,294	9,457	450	347.759	2.912	2.407	–	3.522	P < 0.001	++	3.119	2.631	–	3.697	P < 0.001	++
Age																
for every 1 year increase					1.020	1.007	–	1.033	0.002	++	1.019	1.007	–	1.032	0.002	++
Having an evening meal within 2 hours before bedtime 3 days or more per week																
no	1,866	15,119	414	221.865	1.000											
yes	915	7,062	230	251.366	1.032	0.871	–	1.222	0.719							
Eating snacks and sweet beverages other than breakfast, lunch and dinner																
no	2,274	18,239	522	229.551	1.000						1.000					
yes	507	3,942	122	240.631	1.268	1.032	–	1.558	0.024	+	1.262	1.032	–	1.542	0.023	+
Eating faster than others																
No (general or slow)	2,004	16,019	441	220.060	1.000						1.000					
Yes (fast)	777	6,162	203	261.261	1.242	1.049	–	1.472	0.012	+	1.220	1.032	–	1.442	0.020	+
Skipping breakfast at least three times a week																
no	1,869	14,950	403	215.623	1.000						1.000					
yes	912	7,231	241	264.254	1.157	0.980	–	1.367	0.086		1.189	1.012	–	1.397	0.036	+
Walking for at least 1 hour/day or having equivalent physical activities																
no	1,315	10,507	301	228.897	1.000											
yes	1,466	11,674	343	233.970	0.915	0.779	–	1.075	0.280							
Exercising at least 2 days/week at least 30 minutes each at an intensity that cause a slight sweat for at least 1 year																
no	2,102	17,080	469	223.121	1.000											
yes	679	5,101	175	257.732	1.055	0.880	–	1.265	0.562							
Frequency of drinking																
No (never or sometime)	2,176	17,539	452	207.721	1.000											
Yes (everyday)	605	4,642	192	317.355	1.073	0.894	–	1.286	0.450							
Regular smoker																
no	1,825	15,014	349	191.233	1.000											
yes	956	7,168	295	308.577	1.116	0.938	–	1.329	0.216							
Feeling refreshed after a night's sleep																
no	957	7,676	203	212.121	1.000											
yes	1,824	14,505	441	241.776	1.053	0.889		1.246	0.551							

+: P < 0.05; ++: P < 0.01
Hazard ratio†: by forced entry method; Hazard ratio‡: by backward stepwise method
Abbrevations; MetS: Metabolic Syndrome; CIR: crude incidence rate per 1,000 person-years

backward stepwise method considering the influence of confounding factors. The hazard ratio values of sex, age, “Eating snacks and sweet beverages other than breakfast, lunch, and dinner,” “Eating faster than others,” and “Skipping breakfast at least three times a week,” were 3.119 (95 % confidence interval [CI] 2.631–3.697, p < 0.001), 1.019 (95 % CI 1.007–1.032, p = 0.002), 1.262 (95 % CI 1.032–1.542, p = 0.023), 1.220 (95 % CI 1.032–1.442, p = 0.020) and 1.189 (95 % CI 1.012–1.397, p = 0.036), respectively.

4. Discussion

The purpose of this study was to extract items that are statistically significantly related to the incidence of MetS from lifestyle-related items in the general health questionnaire of specific health checkups and to consider the effective utilization of the extracted lifestyle-related items. Three dietary lifestyle-related factors were identified, and their effective utilization was considered for improving the public health policy.

The prevalence of MetS at the start of observation (April 1, 2008 – March 31, 2009) was 18.4 %. According to the Japanese Ministry of Health, Labor, and Welfare, the nationwide prevalence of MetS in 2008 was 14.4 % (number of specific health checkup examinees: 20,192,502; the number with MetS: 2,907,018), and the prevalence of MetS in this study is one of the highest in Japan. The transition of nationwide MetS prevalence (2008–2019) remained almost constant from 14.4 % to 15.8 %. With the dramatic increase in the global prevalence of MetS in recent years, the fact that the prevalence of MetS in Japan remains constant may be inferred as an outcome of specific health checkups (GBD 2015 Obesity collaborators et al., 2017; Wang et al., 2007).

Three dietary lifestyle-related items were identified as statistically significant factors for the incidence of MetS. According to a retrospective cohort study on the relationship between lifestyle-related items and the incidence of MetS in specific health checkups, “Having an evening meal within 2 h before bedtime 3 days or more per week” in men and “Frequency of drinking” in women were considered as statistically significant lifestyle-related items (Tsutatani et al., 2017). The reasons for the difference in our results were thought to be due to the use of the abdominal circumference, which is one of the adjusted variables in the MetS diagnostic criteria, as well as the characteristics of the study population (in our research, the workers at the business establishment).

Several cross-sectional studies have reported an association between snack foods and MetS. Thorp A A et al. showed that TV viewing time and snack food consumption were independently and jointly associated with MetS in Australian women (Thorp et al., 2013). In Japanese workers, Yoshida J et al. recognized that “snacks after dinner” and “dinner immediately before bed” had a significant odds ratio for obesity, which is a component of MetS (Yoshida et al., 2018). Mimiran P et al. conducted an 8.9-year prospective cohort study in the Iranian population, showing snack foods, especially candies and chocolate, increased the risk of MetS among individuals with a low physical activity level (Mirmiran et al., 2021). These studies suggest that snack food intake, along with other lifestyle habits, promotes overconsumption of calories and is a risk of developing MetS.

There are several studies on the relationship between the extracted lifestyle-related item “Eating faster than others” and MetS. Tanihara S et al. showed that fast eating speed increased serum insulin resistance and fasting blood glucose levels, thereby increasing the risk of MetS (Tanihara et al., 2011). Moreover, some studies have shown that fast eating speed causes binge eating and increases postprandial blood glucose (Teo et al., 2020; Tanihara et al., 2011; Rei et al., 2006; Matsuki et al., 2003). These studies suggest that fast eating speed can be a high-risk factor for MetS.

Several studies have shown that skipping breakfast has unhealthy effects on waist circumference, body mass index (BMI), MetS, and circulatory disease (Yokoyama et al., 2016; Kutsuma et al., 2014; Watanabe et al., 2014). Kobayashi F et al. showed that skipping breakfast enhances the post-lunch and post-dinner blood glucose elevation response in healthy individuals (Kobayashi et al., 2014). In patients with type 2 diabetes, skipping breakfast is associated with impaired insulin response and low intact glucagon-like peptide-1 (iGLP-1), which enhances the post-lunch and post-dinner blood glucose elevation response. It has been shown to cause hyperglycemic conditions over time (Jakubowicz et al., 2015). These studies suggest a link between skipping breakfast and MetS.

The number of examinees in the specific health checkup increased from 20,192,502 (2008) to 29,935,810 (2019) nationwide. Accordingly, those who fall under MetS and Pre-MetS have a system in which health guidance is provided, and lifestyle-related items are used for health guidance. However, those in the healthy group did not receive health guidance to prevent MetS incidence using lifestyle-related items. For instance, in 2019, approximately 70 % of the 29,935,810 examinees in the healthy group (about 20 million) completed specific health examinations without receiving health guidance. The implementation of health guidance for the prevention of MetS incidence using the lifestyle-related items extracted in this study for this healthy group can be effective in reducing the constant MetS prevalence rate.

4.1. Limitations

The limitations of this research method were examined using a target trial emulation framework. Among the items to be considered in target trial emulation, the following four items were examined: (1) eligibility, (2) treatment assignment, (3) time zero (timing to start follow-up), and (4) causal contrasts of interest. In a target trial (an ideal randomized controlled trial), participants are first screened based on a series of eligibility criteria, assigned to an intervention group (treatment assignment), and then followed up (time zero). Finally, the outcomes are evaluated (Fig. 2).

In this study, eligibility was performed after treatment assignment and at time zero. If some individuals were lost to follow-up (411 in this study), there might be differences in the rate of follow-up loss between groups with and without lifestyle-related items. For example, when comparing the incidence of MetS by the presence or absence of “Eating faster than others,” there may be more dropouts in the group who responded “Yes” to “Eating faster than others.” This finding suggests that there is a potential selection bias in this study. However, the direction in which this selection bias affects the increase or decrease in the hazard ratio value is unclear. Considering that the dropout rate in this study was low (12.9 %, 411/3,192), the magnitude of the effect of this selection bias seems to be relatively small.

Intention-to-treat and per-protocol effects were examined for causal contrasts of interest in a target trial. It is unclear how long the lifestyle-related items in this study will be maintained after time zero, and it is impossible to evaluate the per-protocol effect. In this study, a modified intention-to-treat analysis was used, excluding those who had only baseline-specific health checkup data. Since the validity of the modified intention-to-treat analysis in a target trial has been confirmed, the analysis in this study appears to be valid (Abraha and Montedori (2010)).

5. Conclusion

A retrospective cohort study was conducted using the results of a 12-year health checkup to clarify the relationship between lifestyle-related items in the questionnaire and MetS incidence. We identified three

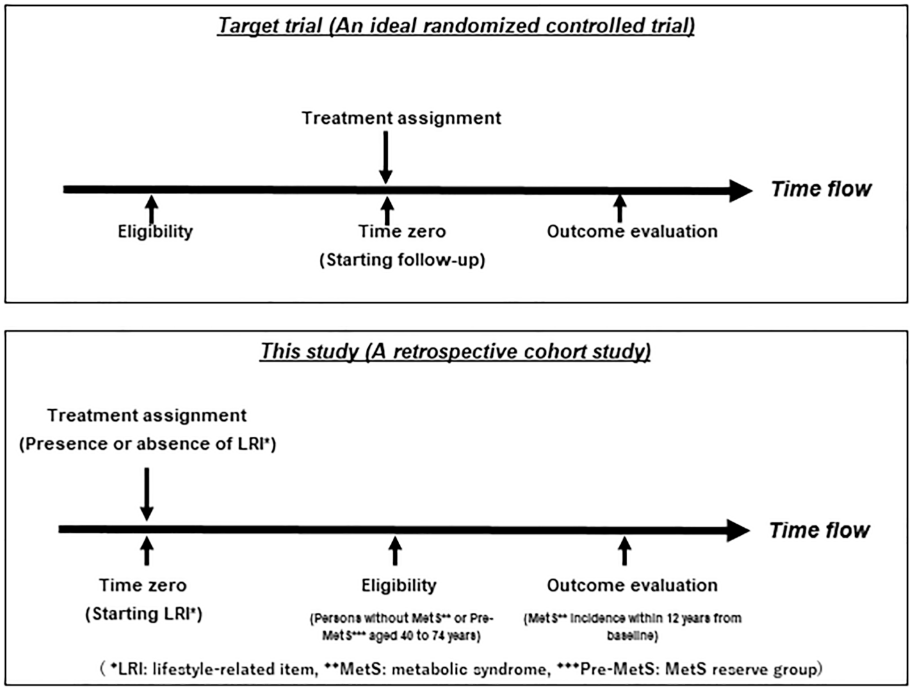

Fig. 2. Time relationship among the main items of the target trial emulation framework.

lifestyle-related items that were significantly associated with the incidence of MetS. These items are like to be effective for the prevention of MetS incidence and the reduction in the prevalence rate of MetS to provide health guidance focusing on healthy groups that are not in the Pre-MetS or MetS conditions at the time of a specific health checkup.

CRediT authorship contribution statement

Takuji Kishimoto: Conceptualization, Data curation, Writing – original draft. **Miwa Churiki:** . **Tatsuya Miyazato:** Data curation. **Akihiro Yamashiro:** Data curation. **Yoshitaka Nagasawa:** Validation. **Hayashi Shokita:** Validation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors do not have permission to share data.

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