



# Protocol and Rationale for the Russian-Japanese “Tackle Obesity and Metabolic Syndrome Outcome by Diet, Activities and Checking Body Weight Intervention” (RJ-TOMODACHI) Randomized Controlled Trial

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**Background:** The prevalence of obesity in Russia has increased sharply since the mid-1990s. Interestingly, the prevalence of obesity in Japan is lower than in many Western countries. Japan has implemented different types of weight control programs using a smart device to monitor patients remotely. New health promotion methods from Japan are now being used in Russia. The Russian-Japanese “Tackle Obesity and Metabolic Syndrome Outcome by Diet, Activities and Checking Body Weight Intervention” (RJ-TOMODACHI) study aims to evaluate a preventive intervention using Japanese health monitoring technology in reducing excess body weight, compared with standard care, in Russia.

**Methods and Results:** The trial is a single-center, 3-armed, parallel group randomized controlled trial conducted among overweight/obese adults. It has been designed to compare the effectiveness of 2 newly developed interventions against standard care for 6 months. Participants in the low- and high-intensity intervention groups will have 3 and 6 consultations over the study period, respectively. In all, 260 adults were screened at baseline; 65 did not participate in the trial for various reasons. The remaining 195 people were randomized into 3 groups (high-intensity intervention, n=73, low-intensity, n=73; standard care group, n=49).

**Conclusions:** The trial protocol has been designed so that the methodology can be adapted for use in Russia.

**Key Words:** Obesity; Preventive counseling; Remote health monitoring; RJ-TOMODACHI study

Chronic non-communicable diseases (NCDs) are the leading cause of death in Russia and worldwide.<sup>1,2</sup> Obesity is closely associated with other risk factors for chronic NCDs,<sup>3</sup> particularly hypertension.<sup>4</sup> These risk factors also determine the occurrence of cardiovascular diseases, cancer, and diabetes.<sup>5</sup> Currently, approximately one-quarter of adult men and one-third of adult women in Russia are obese.<sup>4</sup>

Japan has the greatest longevity in the world,<sup>6</sup> and the prevalence of obesity among the Japanese population is significantly lower than in Russia. Although the prevalence

of obesity has been increasing in Japan in recent decades, government-led prevention programs in Japan have started to reverse the obesity epidemic since 2008. All health insurers in Japan must provide a lifestyle modification program for metabolic syndrome after health checkups. As part of the initial counseling in this program, participants set personalized goals: 3–5% reductions in body weight (BW) and a 3-cm reduction in waist circumference (WC).<sup>7</sup> A previous study showed greater improvements in body mass index (BMI), WC, and blood pressure (BP) among program participants than non-participants over a period of 3 years.<sup>8</sup>

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**Table 1. Study Schedules for the High- and Low-Intensity Intervention and Standard Care Groups**

	Visit					
	1	2	3	4	5	6
<b>High-intensity intervention</b>						
Time relative to 1st visit		2 weeks later	1 month later	2 months later	3 months later	6 months later
Information registration form	+	+	+	+	+	+
Consultation on diet	+	+	+	+	+	+
Anthropometry	+	+	+	+	+	+
Laboratory examination	+				+	+
Receipt of self-monitoring devices	+					
Analysis of food diaries, check of self-monitored data, and self-monitored data		+	+	+	+	+
Return of self-monitoring devices						+
<b>Low-intensity intervention</b>						
Time relative to 1st visit		3 months later	6 months later			
Information registration form	+	+	+			
Consultation on diet	+	+	+			
Anthropometry	+	+	+			
Laboratory examination	+	+	+			
Receipt of self-monitoring devices	+					
Analysis of food diaries, check of self-monitored data, and self-monitored data		+	+			
Return of self-monitoring devices			+			
<b>Standard care group</b>						
Time relative to 1st visit		3 months later	6 months later			
Information registration form	+		+			
Consultation on diet	+		+			
Anthropometry	+	+	+			
Laboratory examination	+		+			

Effective preventive counseling involves motivating participants to have a healthier lifestyle. This process can be facilitated by monitoring patients' health conditions using smart devices such as smartphone apps,<sup>9,10</sup> and these interventions have been shown to improve people's health behavior.<sup>11</sup> This kind of technology has been developed in Japan and is recommended for self-monitoring as part of the government-led prevention program. In the present study, some of the self-monitoring technologies used as part of the prevention program in Japan are being trialed for use in Russia.

The aim of the Russian-Japanese "Tackle Obesity and Metabolic Syndrome Outcome by Diet, Activities and Checking Body Weight Intervention" (RJ-TOMODACHI) study is to evaluate the effects of a preventive intervention program using monitoring technologies developed in Japan in reducing excess BW compared with standard care in Russia.

## Methods

### Study Design

The RJ-TOMODACHI study is a single-center, 3-armed, parallel group randomized controlled trial conducted with overweight/obese adults. The trial has been designed to compare the effectiveness of 2 newly developed interventions against standard care over a period of 6 months.

### Participants

**Inclusion Criteria** To be eligible for enrollment in the study, patients have to fulfill the following criteria: age

25–60 years, BMI  $\geq 27$  kg/m<sup>2</sup> and  $< 37$  kg/m<sup>2</sup>, living in Moscow or the Moscow region, Internet access (any type), and providing written informed consent.

**Exclusion Criteria** Patients with cardiovascular disease (coronary artery disease, hypertension with BP  $> 180/120$  mmHg, a history of stroke, chronic heart failure [New York Heart Association Class III–IV]), diseases requiring a special diet, Type 1 or Type 2 diabetes, hyper- or hypothyroidism, cancer, dementia, a history of bariatric surgery, or those who are pregnant are excluded from the study. In addition, those taking medications that could affect BW, those who have to take frequent business trips, and shift workers are excluded from the study.

The presence exclusion criteria was determined at the time of screening.

### Recruitment and Screening Procedures

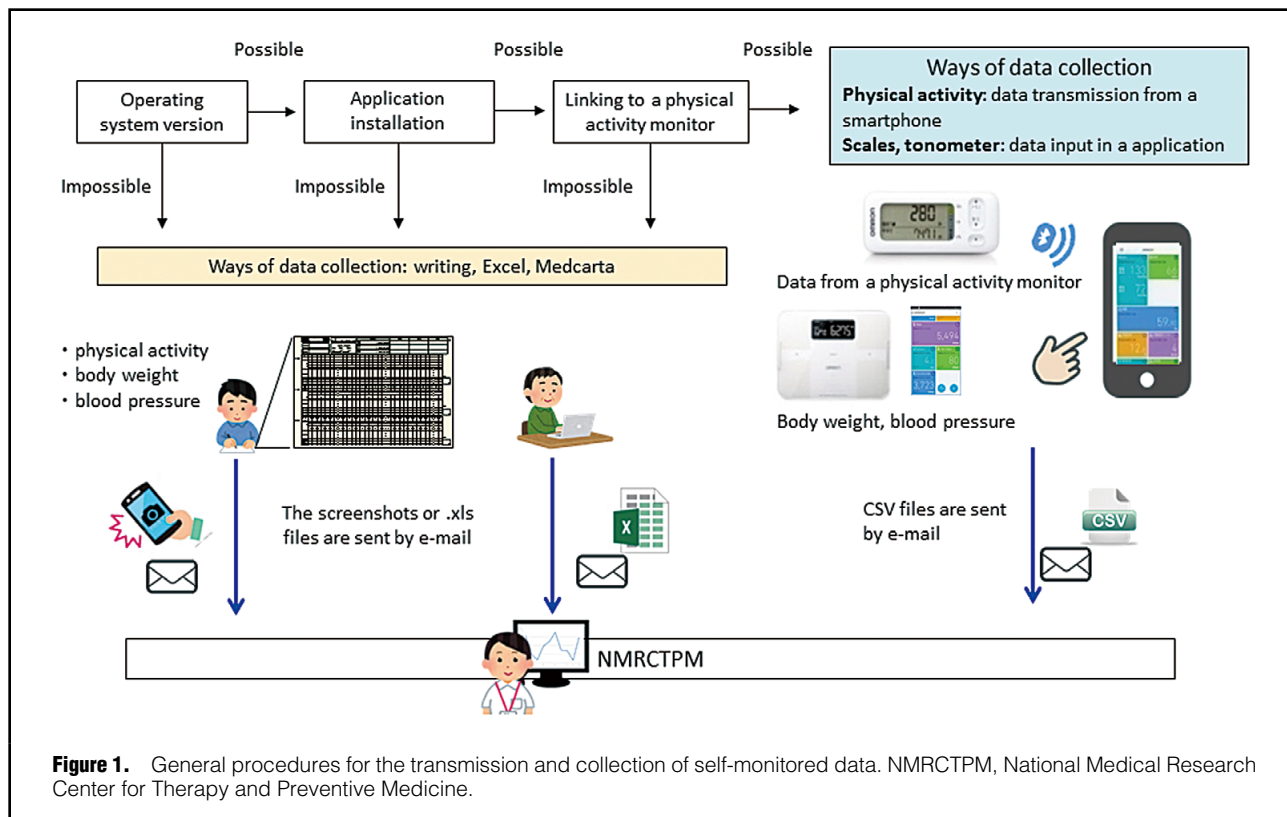
Several methods were used to recruit potential participants, including regular announcements on social media and on the official website of the National Medical Research Center for Therapy and Preventive Medicine (NMRCTPM) of Russia, as well as printed advertisements near the main entrances of 2 NMRCTPM buildings.

A direct telephone line was booked for the entire recruitment period.

As part of the recruitment process, subjects were screened during physician consultations to assess their eligibility based on the inclusion and exclusion criteria.

### Anthropometry Measurements

Anthropometric measurements were performed with par-



participants wearing light clothing, without shoes or head dress, using standardized methods and equipment. Height was measured to the nearest 0.5 cm using a stadiometer. BW was measured to the nearest 0.1 kg with a calibrated scale. WC (the distance around the smallest part of the patient's waist, just above the belly button) was measured using a measuring tape.

### BP and Heart Rate Measurements

BP and pulse measurements were conducted on the right arm using an automatic digital device (INME-01; Institute of Nanotechnologies of Microelectronics [INME], Moscow, Russia). BP and pulse were measured 3 times in seated participants with their arm level with their heart. The mean of 2 measurements, excluding the first of the 3 measurements, was calculated and used in analyses.

### Screening Laboratory Tests

The laboratory tests performed included clinical blood analysis (hemoglobin, erythrocyte, color index, leukocyte, erythrocyte sedimentation rate, common urine analysis [protein, glucose, ketones], lipid profile [total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, very low-density lipoprotein cholesterol, triglyceride]) and biochemical tests (fasting plasma glucose, HbA1c, creatinine, uric acid, total protein, ALT, AST, and TSH). All blood analyses were performed using the ARCHITECT analyzer (Abbott, Abbott Park, IL, USA).

After all measurements and tests, participants were invited for a consultation, at which time they were either included in the study or received recommendations based on the results of the screening.

### Randomization Procedure

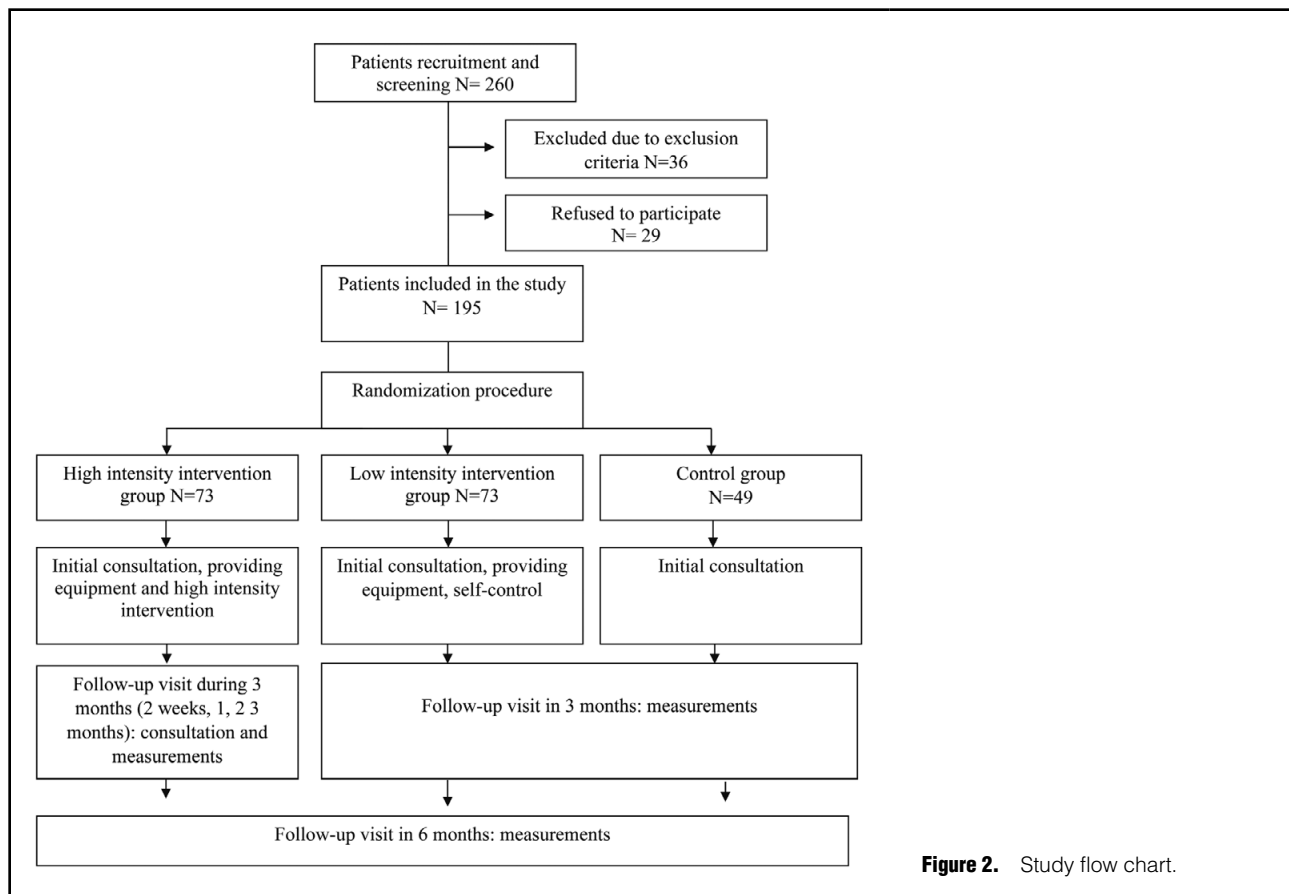
Randomization was computer generated in randomized blocks using software developed by Japanese researchers and Zenbe Co. (<http://www.zenbe.jp/>, accessed October 17, 2019). The randomization procedure was conducted at the NMRCTPM by a researcher not affiliated with the treatment, who preserved allocation anonymity, randomly separating individuals into a standard care control group, a low-intensity intervention group and a high-intensity intervention group at a ratio of 3:2:2. The researchers in charge of conducting the intervention will be informed of participants' allocated group before the participants start their lifestyle modification.

### Standard Survey at the Start of the Trial

The information and registration form contains different sections to allow for the collection of information regarding sociodemographic characteristics, history, and physical activity, an assessment of the risk factor (smoking, alcohol consumption) profile, and a food frequency questionnaire (Supplementary File 1).<sup>12-14</sup>

### Interventions in the High- and Low-Intensity Intervention Groups

It is planned that participants in the high-intensity intervention group will have 6 visits during the study period (Table 1). At each visit, a nurse will measure BW, BMI, BP, hip circumference, and WC. Blood and urine samples will be obtained 3 times for testing. All participants of this group will receive self-assessment devices, as detailed below. Participants will send weekly data from their devices (Figure 1) and will keep a food diary for review at subsequent consultations.



It is planned that participants in the low-intensity intervention group will have 3 visits (at 3 and 6 months; **Table 1**). The participants in this group will undergo an initial consultation, anthropometry measurements, and laboratory tests, and will receive equipment for self-assessment during their first visit. Participants in this group collect data and will keep a food diary for review at their next visit.

Participants in the standard care group will have 3 visits (**Table 1**). These participants will not receive any equipment for self-assessment.

### Self-Assessment Devices Used in the Study

Participants in the high- and low-intensity intervention groups will receive a tonometer (M6 Comfort Digital Tonometer; OMRON Healthcare, Kyoto, Japan), an activity monitor (HJA-405T; OMRON Healthcare), and a body composition monitor (BF214; OMRON Healthcare) for self-monitoring at home (see **Supplementary File 2**). Before the equipment is given out, participants will be trained in how to use it and how to input information into the self-control diary.

### Data Monitoring, Data Collection, and Providing Feedback

Study participants can choose the way they provide self-monitored data to the consulting physician from 3 options (**Supplementary File 2**). RJT18App is a smartphone application to promote behavior change through self-monitoring of BP, BW, and levels of physical activity.

The general procedures for data collection are shown in **Figure 1**.

Self-monitoring data received from the high-intensity intervention group are analyzed by consultants once a week. The participants then consult with physicians using individual e-mails with support messages.

Self-monitoring data received from the low-intensity group are collected and analyzed by consultants after 3 and 6 months of follow-up during face-to-face visits.

### Prevention Counseling

Details regarding prevention counseling are provided in **Supplementary File 3**. On the first visit, the negative consequences of obesity are explained to all participants. Individual recommendations are based on personal characteristics and dietary assessments.

To assess participants' actual diet and drinking regimen, specialists analyze participants' diets over the 2–3 days before their first visit or over 2–3 days of a typical diet if the diet in the days before the first visit was atypical. A 24-h food questionnaire is used to collect this information. Food behavior is also investigated. Detailed instructions for dietary counseling have been prepared (**Supplementary File 3**) and all investigators were trained to provide this counseling.

Very detailed and precise goal setting to decrease calorie intake is provided to all participants.

The intervention includes the development of individual action plans for diet and physical activity for the entire study period, as well as for each week throughout the study period.

	HIG (n=73)	LIG (n=73)	CG (n=49)	Total (n=195)	P value
Age (years)	47.2±7.8	45.8±9.1	47.6±8.1	46.8±8.4	0.431
Male sex	9 (12.3)	10 (13.7)	2 (4.1)	21 (10.8)	
Body weight (kg)	88.5±11.0	87.1±10.1	85.7±7.6	87.3±9.9	0.342
WC (cm)	96.3±7.8	97.0±9.5	95.3±8.6	96.3±8.6	0.472
BMI (kg/m <sup>2</sup> )	32.2±2.7	32.1±2.5	33.1±7.8	32.4±4.5	0.577
SBP (mmHg)	124.7±14.5	128.4±13.6	126.2±14.2	126.4±14.1	0.288
DBP (mmHg)	82.4±12.9	85.2±9.6	82.8±13.4	83.5±11.9	0.344
TC (mmol/L)	5.7±1.0	5.5±0.9	5.6±1.2	5.6±1.0	0.381
HDL-C (mmol/L)	1.5±0.5	1.4±0.3	1.5±0.5	1.5±0.5	0.588
LDL-C (mmol/L)	3.7±1.0	3.5±0.8	3.5±1.0	3.9±0.9	0.372
VLDL-C (mmol/L)	0.6±0.3	0.6±0.3	0.7±0.3	0.6±0.3	0.150
TG (mmol/L)	1.3±0.7	1.3±0.9	1.5±0.8	1.4±0.8	0.347

Values are given as the mean±SD or as n (%). BMI, body mass index; CG, control group; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; HIG, high-intensity intervention group; LDL-C, low-density lipoprotein cholesterol; LIG, low-intensity intervention group; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; VLDL-C, very low density lipoprotein cholesterol; WC, waist circumference.

### Statistical Analysis

Data collected will be located only in the NMRCTPM in Russia. Statistical analyses will be performed by statisticians in the NMRCTPM based on the statistical analysis plan. Intention-to-treat (ITT) analysis will be performed to construct analysis datasets.

The primary endpoints are: (1) the percentage change in BW from 0 to 3 and 6 months; and (2) the proportion of participants achieving a weight loss of >3% from their initial weight.

Secondary endpoints include obesity parameters, including BMI, WC (continuous), and the proportion of participants who lost ≥5% of their initial weight (binary), among others described in the statistical analysis plan (**Supplementary File 4**).

Primary endpoints will be analyzed using non-parametric Kruskal-Wallis or Wilcoxon tests or analysis of variance. The level of significance will be set to 1.7% based on the Bonferroni method for comparing 3 groups in the main analysis and to 0.05% for other analyses.

**Sample Size** The sample size was calculated using the SAS version 9.4 (SAS Institute, Cary, NC, USA), based on the outcome variable “change in weight” of individuals. Under the settings of 90% power, a significance level of 1.7%, and a mean (±SD) difference among the 3 groups of 2±3 kg, a sample size of 150 individuals (n=50 in each group) was determined. Considering sample losses in the intervention groups, the final sample size was set to 200 individuals, 75 in each of the 2 intervention groups and 50 in the control group.

### Ethical Considerations and Trial Registration

This study conforms to the ethical provisions of the Helsinki Declaration and the protocol was approved by the ethics committee of the NMRCPM (protocol 03–03/18 from 25/05/2018). This study is registered with the UMIN Clinical Trial Registry (ID: UMIN000033792).

### Results

During the screening process, 260 potential participants (225 [86.5%] women, 35 [13.5%] were men) were evaluated

(**Figure 2**). After screening, 36 people (13.8%) were excluded based on the inclusion and exclusion criteria, and 29 people (11.2%) declined to take part in the study (after reading the information provided). The remaining 195 people (75%) were randomized into 3 groups. The mean age of the participants was 46.8 years (range 40–54 years; **Table 2**). BMI varied from 29.5 to 34.4 kg/m<sup>2</sup> (mean 32.4 kg/m<sup>2</sup>).

### Discussion

The interventions in this study were developed according to the key features for behavior change: individual goal setting, self-monitoring, and support using remote health monitoring devices.

In Japan, similar interventions were effective in realizing nationwide obesity prevention programs.<sup>15</sup> In Russia, there is an opportunity to implement nationwide prevention interventions as a part of the screening process of the adult population. Each adult in Russia has an opportunity to undergo comprehensive health screening primarily focused on NCDs and their risk factors. After screening, extended preventive counseling is provided by trained medical staff in special preventive primary care settings. So, the technology developed in this study can be implemented across the whole country if its effectiveness is demonstrated.

### Conclusions

This study could be of interest to an international audience for several reasons. First, it is an example of international collaboration and the adaptation of prevention interventions from one country to another. Second, these are novel interventions in terms of data monitoring and feedback, with participants having a choice using a smartphone app or web-based methods or even simply sending in a Microsoft (Bellevue, WA, USA) Excel file. Third, comparing 2 types of interventions with standard care will enable the effect of providing equipment, together with the interventions and preventive counseling, on diet and physical activity to be estimated.

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### Disclosures

Y.M. is a member of *Circulation Reports*' Editorial Team. The other authors have no conflicts of interest to declare.

### IRB Information

This study was conducted in accordance with the ethical provisions of the Declaration of Helsinki and the study protocol was approved by the ethics committee of the National Medical Research Center for Therapy and Preventive Medicine (NMRCTPM) of Russia (Protocol no. 03-03/18 from 25 May 2018). This study is registered with the UMIN Clinical Trial Registry (ID: UMIN000033792).

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### Supplementary Files

Please find supplementary file(s);  
<http://dx.doi.org/10.1253/circrpt.CR-20-0042>