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**Current review of intervention studies on obesity and the role of physical activity in weight control**

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**Abstract**

Obesity is a major public health problem, both globally and in Japan. A nationwide approach targeting metabolic syndrome has routinely been conducted in Japan since April 2008; however, the obesity statistics have not improved. Promotion of physical activity is one anti-obesity strategy. Numerous observational studies have revealed inverse associations between obesity and physical activity; however, these results have not always been conducted as randomized controlled trials (RCTs) that can provide the highest level of evidence. Therefore, this review looks at RCTs in the field of obesity and physical activity worldwide. The Diabetes Prevention Program and the Look AHEAD study are representative RCTs in this field. A guideline for the management of overweight and obesity among U.S. adults has recently been updated using a systematic review of good- or fair-quality RCTs, but a comprehensive, systematic review of RCTs in Japan has not yet been undertaken. This review seeks to fill this gap. Overall, we only found 10 RCTs that met the three inclusion criteria ([1] intervention study on obesity, [2] overweight or obese Japanese participants, and [3] RCT) and did not meet the exclusion criterion (study protocol without results). Based on our review results, it is strongly suggested that more RCTs in this field be conducted in Japan.

**Keywords**: randomized controlled trial, intervention studies, evidence, weight loss, diet, exercise

**Introduction**

Obesity is a major public health problem, both globally and domestically. It is a risk factor for cancer1, cardiovascular disease2, coronary heart disease3,4, and diabetes3. Furthermore, obesity is associated with increased mortality5. In Japan, people typically have a lower body mass index (BMI) than people in other high-income countries; however, the mean BMI of men increased from 22.1 kg/m2 to 23.5 kg/m2 and that of women increased from 21.3 kg/m2 to 23.3 kg/m2 between 1980 and 20086. A nationwide health screening and intervention program specifically targeting metabolic syndrome7 has been routinely conducted in Japan since April 2008; however, the obesity statistics have not improved8.

Promotion of physical activity is one anti-obesity strategy. The American College of Sports Medicine Position Stand9 recommends a minimum of 150 min/week of moderate-intensity physical activity to prevent significant weight gain and reduce associated chronic disease risk factors. According to the position stand, cross-sectional and prospective studies have indicated that weight maintenance after weight loss has improved with a reported physical activity level of >250 min/week; however, no evidence from well-designed randomized controlled trials (RCTs) exists to judge the effectiveness of physical activity for the prevention of weight regain after weight loss.

Here, cross-sectional and prospective studies are categorized as observational studies. Observational studies aim to show an association between Exposure X and Outcome Y. On the other hand, an intervention study aims to demonstrate the causality of Exposure X (operated by an intervention) with Outcome Y. Such studies include the one-arm (single-arm) trial, non-RCT, and RCT. There are sometimes discrepancies between observational and intervention studies. In general, RCT is a study design that can provide the highest level of evidence (Fig. 1).

Taking the aforementioned topic as an example, observational studies indicate that physical activity (Exposure X) is associated with weight maintenance after weight loss (Outcome Y). For instance, the National Weight Control Registry (NWCR)10 is the largest longitudinal prospective study of individuals who reported to be successful in long-term weight loss maintenance. The participants must have lost a minimum of 13.6 kg (30 lb) and must have maintained that weight loss for at least 1 year. An NWCR-based report10 showed that the amount of physical activity was 2,621 ± 2,252 kcal/week; thus, over-
all NWCR participants were extremely physically active.

Another study, the Nurses’ Health Study II\textsuperscript{11)}, is an ongoing prospective study of 116,608 female nurses aged 25-42 years who responded to a mailed questionnaire in 1989. Follow-up questionnaires have been mailed biennially. One report based on this cohort study\textsuperscript{11)} investigated the duration and type of activity required to prevent weight regain over 6 years among women who lost >5% of their baseline body weight (n=4,558). As a result, an increase of 30 min/day in total discretionary activity over 6 years was associated with less weight regain, particularly among overweight women. Increased jogging or running was associated with less weight regain than was increased brisk walking or other activities. Therefore, observational studies indicate that a high level of physical activity is important to maintain intentional weight loss. However, no RCTs could demonstrate the causality of increasing physical activity (Exposure X operated by an intervention) with maintenance of weight loss (Outcome Y). A few previous studies tested this hypothesis\textsuperscript{12,13). One study\textsuperscript{12)} examined the effect of varying durations and intensities of exercise on weight loss in overweight women during a 24-month period. Two hundred one overweight and obese women were randomly assigned to one of 4 behavioral weight loss intervention groups based on physical activity energy expenditure (1,000 vs. 2,000 kcal/week) and intensity (moderate vs. vigorous). They were also told to reduce dietary intake to between 1,200 and 1,500 kcal/day. Consequently, weight loss did not differ among the 4 groups. This might have been the result of lack of adherence to the prescribed intensity during this study. In fact, a post-hoc analysis showed that individuals sustaining a loss of >10% of initial body weight at 24 months reported performing more physical activity (1,835 kcal/week or 275 min/week) compared to those who sustained a weight loss of less than 10% of initial body weight. Another study\textsuperscript{13)} examined the effects of different prescribed doses of physical activity on weight change. Two hundred seventy-eight overweight adults were randomly assigned to one of 3 groups: the self-help group (SELF); the MOD-PA group, which was prescribed 150 min/week of physical activity; or the HIGH-PA group, which was prescribed 300 min/week of physical activity, without interventions promoting a reduction in energy intake. As a result, percent of weight change over 18 months did not differ among the 3 groups, despite the existence of significant differences in physical activity among the groups. A post-hoc analysis showed that individuals losing >3% of their baseline weight became significantly more physically active (18-month change: 161.9 ± 252.6 min/week) than those remaining within ±3% (78.2 ± 162.6 min/week) and those gaining >3% (74.7 ± 274.3 min/week) of their baseline weight. Therefore, intervention studies indicate that a prescribed physical activity intervention does not influence weight loss outcome; however, those who successfully sustain their weight loss are more physically active.

As just described, associations from observational studies are not always demonstrated by RCTs that can provide the highest level of evidence. Therefore, this review focused on RCTs in the field of obesity worldwide that included physical activity as a related factor. The other purpose was to systematically review RCTs conducted in Japan and show the current Japanese situation concerning the field of obesity and physical activity.

**Narrative review of RCT worldwide**

**Diabetes Prevention Program.** One representative RCT with lifestyle modification is the Diabetes Prevention Program (DPP)\textsuperscript{14). This RCT was designed to compare the effectiveness on the onset of diabetes among a placebo control group, a group treated with metformin, and a group that received a lifestyle intervention. The study participants were 3,234 adults in the United States who were at high risk for developing type 2 diabetes and were randomly assigned to one of three groups (1082 to the placebo, 1073 to the metformin, and 1079 to the lifestyle group). The goals for the participants in the lifestyle intervention group were to achieve and maintain a weight loss of at least 7% of initial body weight through a healthy

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**Fig. 1** Level of evidence.

- **Systematic Reviews**
- **Randomized Controlled Trials**
- **Cohort Studies**
- **Case Control Studies**
- **Case Report or Case Series**
- **Expert Opinions**
- **Animal and Laboratory Studies**

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Low

High
low-calorie, low-fat diet, and to engage in physical activity of moderate intensity for at least 150 min/week.

The curriculum was composed of 16 lessons over 24 weeks covering diet, exercise, and behavioral modification. At the end of the curriculum, 50% of the participants in the lifestyle intervention group had achieved the goal of ≥7% weight loss, and 74% had met the goal of ≥150 min/week of physical activity. Overall, the participants were followed for an average of 2.8 years. Participants assigned to the lifestyle intervention group had much greater weight loss and a greater increase in physical activity than did participants assigned to either the metformin or the placebo group. The average weight loss was 0.1, 2.1, and 5.6 kg in the placebo, metformin, and lifestyle intervention groups, respectively. Diabetes incidence was 58% lower in the lifestyle intervention group and 31% lower in the metformin group than in the placebo group, and it was 39% lower in the lifestyle intervention group than in the metformin group. Therefore, lifestyle intervention was demonstrated to reduce the incidence of diabetes much more than did metformin.

From the DPP research group, various important findings were reported. In a 3.2-year follow-up, the impact on hypertension, dyslipidemia, and cardiovascular disease (CVD) events were assessed, along with the effects on metabolic syndrome. Lifestyle intervention improved hypertension and dyslipidemia compared to the placebo and metformin; however, no differences in CVD events were observed among the three groups. Incidence of metabolic syndrome was reduced by 41% in the lifestyle group and by 17% in the metformin group compared with the placebo group. In a 10-year follow-up, participants in the lifestyle group returned to near their baseline weight, and there were no significant group differences in weight loss. However, diabetes incidence was reduced by 34% in the lifestyle group and by 18% in the metformin group compared with the placebo group.

Look AHEAD study. Look AHEAD (Action for Health in Diabetes) was a National Institutes of Health (NIH)-funded clinical trial, conducted in 16 centers in the United States, that investigated the long-term (up to 13.5 years) effects of an intensive lifestyle intervention (ILI) delivered over 4 years in 5,145 overweight and obese individuals with type 2 diabetes. The participants who were 45-74 years of age and had a BMI ≥25 were randomized to one of 2 groups: the ILI group, which was designed to achieve and maintain weight loss through decreased caloric intake and increased physical activity, and a control group that was given diabetes support and education (DSE). The primary outcome was time to incidence of a major CVD event.

At 1 year, participants assigned to the ILI group lost an average of 8.6% of their initial body weight vs. 0.7% in the DSE group. Averaged across 4 years, ILI could produce sustained weight loss (6.15% vs. 0.88%, in ILI and DSE, respectively) and improvements in fitness, glycemic control, and CVD risk factors. At a median follow-up of 9.6 years, weight loss was greater in the ILI than the DSE group (6.0% vs. 3.5%, respectively), and improvements in most CVD risk factors were observed. However, the primary outcome, a composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for angina during a maximum follow-up of 13.5 years, occurred in 403 ILI patients and 418 DSE patients. The hazard ratio was 0.95 (95% confidence interval, 0.83 to 1.09). As a result, the trial ended early on the basis of futility analysis.

Although there was no significant difference between the ILI and DSE groups in terms of cardiovascular morbidity and mortality, other benefits of the lifestyle intervention were identified. At 1 year, moderate weight loss reduced the incidence of urinary incontinence in women and men. Sleep apnea was improved at 1 year, and the effect persisted for 4 years. At 4 years, the ILI group was significantly more likely to experience partial or complete remission of type 2 diabetes. At 8 years, ILI showed long-term benefits on mobility function: better scores of physical performance battery, faster 20-m and 400-m walk speeds, and a reduced incidence of very high-risk chronic kidney disease. ILI reduced the risk of developing depression and preserved physical health-related quality of life over the observation period for a median of 9.6 years. In addition, ILI participants had fewer hospitalizations, fewer medications, and lower healthcare costs, compared to DSE over 10 years. Therefore, the importance of ILI cannot be denied.

Other representative RCTs. The abovementioned RCTs were conducted on a very long-term basis. Most RCTs were not so long in duration. The Dose-Response to Exercise in postmenopausal Women (DREW) trial was a representative RCT that examined the effects of 50%, 100%, and 150% of the NIH Consensus Panel physical activity recommendations (4, 8, and 12 kcal/kg per week in energy expenditure, respectively), compared to a no-exercise control group, on cardiorespiratory fitness in sedentary, overweight, or obese postmenopausal women with elevated blood pressure. Four hundred sixty-four participants were randomly assigned to 1 of the 4 groups during a 6-month study period. After adjusting for covariates, the exercise intervention groups increased their peak VO2 by 4.2%, 6.0%, and 8.2% in the 4, 8, and 12 kcal/kg per week groups, respectively, compared to the control group. Although there were no significant differences between the groups for body weight and other health outcomes, the DREW study demonstrated a graded dose-response change in fitness across levels of exercise training in overweight and obese women.

Another recent, good-quality RCT was a one-year intensive lifestyle intervention study consisting of diet and physical activity for severely obese adults (BMI >35).
This study recruited 130 participants and assigned them into 2 intervention groups. One group had a diet and physical activity intervention for the entire 12 months (initial-activity group). The other had the identical dietary intervention, but with a physical activity intervention that was delayed for 6 months (delayed-activity group). At 6 months, both intervention groups had lost a significant amount of body weight, but the initial-activity group lost significantly more weight in the first 6 months compared to the delayed-activity group (10.9 kg vs. 8.2 kg). At 12 months, weight loss was similar for the 2 groups (12.1 kg vs. 9.9 kg), and no significant difference was observed.

Recently, an updated guideline for the management of overweight and obesity in adults was published by the American College of Cardiology, the American Heart Association Task Force on Practice Guidelines, and the Obesity Society. According to the guideline, the principle components of an effective comprehensive lifestyle intervention include: [1] the prescription of a moderately reduced-calorie diet; [2] a program of increased physical activity; and [3] the use of behavioral strategies to facilitate adherence to diet and physical activity recommendations. The comprehensive lifestyle intervention is designed to induce an energy deficit of ≥500 kcal/day. This deficit is often achieved by prescribing an energy intake of 1,200 to 1,500 kcal/day for women and 1,500 to 1,800 kcal/day for men and by prescribing increased physical activity (such as brisk walking) for ≥150 min/week, which is equal to ≥30 min/day most days of the week. Higher levels of physical activity, approximately 200-300 min/week, are also recommended to maintain lost weight or minimize weight regain in the long term (>1 year). The behavioral strategies include regular self-monitoring of food intake, physical activity, and body weight. The strength of evidence for these strategies was reported to be high from a systematic review of good- or fair-quality RCTs.

Current review of RCTs in Japan

A systematic review was conducted to summarize RCTs on obesity and physical activity in Japan. Published studies up to August 2015 were identified from PubMed. The search terms used included (“obes*” OR “overweight” OR “over weight” OR “weight loss” OR “weight reduction” OR “weight maintenance” OR “weight control”) AND (“randomized controlled trial” OR “randomized trial” OR “clinical trial” OR “randomised controlled trial” OR “randomised trial”) in the title and abstract, and (“physical activity” OR “exercise” OR “physical training” OR “fitness” OR “physical performance” OR “physical capability”) among all fields. The initial search identified 1,654 articles. In the second search, (Japan*) was added to the search terms for the search of all fields. The second search identified only 28 articles. The authors (YN and HS) independently assessed the eligibility of the studies for inclusion according to the following criteria: [1] intervention study on obesity, [2] overweight or obese Japanese participants, and [3] RCT. In addition, study protocols without results that were identified were excluded. Eighteen articles were excluded, and the remaining 10 articles are summarized in Table 1.

The best quality RCT seemed to be the Zensharen Study for the Prevention of Lifestyle Diseases Group. This study was a multi-center RCT that recruited overweight individuals with impaired fasting glucose levels and investigated the effectiveness of lifestyle modification on type 2 diabetes incidence. Six hundred forty-one participants were randomly assigned into one of two groups: an intervention and a control group. All the participants were individually instructed to reduce their total energy intake and increase physical activity, aiming at a 5% loss of baseline weight through the help of nurses, dieticians, physical therapists, and physicians. Participants in the intervention group were invited to a series of follow-up visits and worked toward their goals by using self-monitoring sheets for recording body weight, pedometer counts, and how close they came to attaining their goals. Mean weight reduction during the first 12 months was 2.5 kg in the intervention group and 1.1 kg in the control group. The proportion of participants who achieved a 5% loss of baseline weight was significantly higher in the intervention group at 12, 24, and 36 months. In the overall analysis, the adjusted hazard ratio for type 2 diabetes in the intervention group was 0.56 (95% confidence interval, 0.36-0.87). This RCT demonstrated that lifestyle modifications could prevent type 2 diabetes incidence among overweight Japanese people with impaired fasting glucose levels.

Sapporo Fitness Club Trial was an RCT that tested the effects of exercise at a fitness club on CVD risk factors. Participants were recruited based on the results from a database of the Sapporo Health Promotion Center, and 561 overweight Japanese with CVD risk factors were randomized into one of two groups - an intervention and control group - after lifestyle counseling. Participants in the intervention group received a membership to a fitness club (one of 5 designated clubs) for 6 months. Participants in the control group did not receive the membership for the first 6 months, but they could receive the same benefits in the second 6 months. The exercise group exercised at fitness clubs an average of 2.6 times per week. A significant between-group difference was observed in body weight loss (-1.88 kg and -0.28 kg, in intervention and control groups, respectively), and a marginally significant difference was observed in systolic blood pressure reduction (-8.30 mm Hg and -6.17 mm Hg, respectively). This RCT demonstrated that exercising at a fitness club improved CVD risk factors in overweight Japanese individuals with multiple CVD risk factors.

The Saku Control Obesity Program was a 1-year lifestyle intervention for weight loss based on a behavioral...
### Table 1. Summary of randomized controlled trials on obesity and physical activity in Japan.

| Study                     | Participants (sex, age, BMI) | Follow-up (months) | Intervention arms                                                                 | Weight change (kg) |
|---------------------------|-----------------------------|--------------------|-----------------------------------------------------------------------------------|--------------------|
| Adachi Y et al., 2007<sup>34</sup> | 205 (F, 46 yr, 26.1)        | 7                  | 1: computer tailored advice with self monitoring  
2: computer tailored advice only  
3: self-help booklet with self monitoring  
4: self-help booklet only             | 1: -2.9  
2: -2.2  
3: -1.6  
4: -1.4 (n=183) |
| Nishijima H et al., 2007<sup>35</sup> | 561 (234M/327F, 67 yr, 26.4) | 6                  | 1: exercise 2-4 times/week at a fitness club  
2: lifestyle-modification advice          | 1: -1.88  
2: -0.28 (n=501) |
| Tanaka M et al., 2010<sup>36</sup> | 51 (M, 46 yr, 26.2)         | 7                  | 1: booklet and computer tailored advice  
2: booklet only                           | 1: -2.4  
2: -1.6 |
| Takada A et al., 2011<sup>37</sup> | 97 (32M/65F, 46 yr, 25.7)   | 6                  | 1: telephone and mail support  
2: self help                              | 1: -2.1  
2: -0.6 (n=47, 4 months) |
| Saito T et al., 2011<sup>38</sup> | 641 (143M/498F, 49 yr, 27.0) | 36                 | 1: frequent intervention at least 9 times for 36 months  
2: lifestyle-modification advice          | 1: -2.5  
2: -1.1 (12 months) |
| Nakade M et al., 2012<sup>39</sup> | 235 (116M/119F, 54 yr, 30.6) | 24                 | 1: individual-based counseling and mail support  
2: no support for 1 year                  | 1: -4.5  
2: -0.1 (n=226, 12 months) |
| Nanri A et al., 2012<sup>40</sup> | 102 (M, 53 yr, 25.8)        | 6                  | 1: lifestyle modification 4 times for 3 months  
2: standard health guidance               | 1: -2.01  
2: -0.28 |
| Sakurai R et al., 2013<sup>41</sup> | 66 (15M/51F, 62 yr, 25.4)   | 3                  | 1: exercise, diet, hot bathing  
2: exercise, diet  
3: hot bathing  
4: health class                            | 1: -2.4  
2: -0.6  
3: +0.9  
4: +0.3 |
| Nakata Y et al., 2014<sup>42</sup> | 188 (43M/145F, 51 yr, 28.9) | 30                 | 1: group-based support for 6 months (9 times)  
2: single lecture and educational materials (2 times)  
3: single lecture (1 time)                 | 1: -7.7  
2: -4.7  
3: -2.9 (6 months)<sup>43</sup>  
1: -3.3  
2: -3.3 (n=125, 30 months) |
| Tanaka S et al., 2014<sup>43</sup> | 200 (M, 42 yr, 27.0)        | 6                  | 1: dietary intervention and dairy delivery  
2: dietary intervention                     | 1: -1.1  
2: -2.6 |

BMI, body mass index; M, male; F, female.
approach. Participants were recruited at the Saku Health Dock Center in Nagano Prefecture, and 235 overweight and obese adults were randomly assigned to one of two groups: an intervention or a wait-list control group. Participants in the intervention group received an initial 30-min individual counseling session at baseline, followed up by 20-min group sessions concerning effective exercise provided by registered dieticians and exercise instructors at 1, 3, 6, and 9 months. During the months between the 5 face-to-face sessions, the participants recorded their progress for the previous month and their new plans for the following month, and mailed their records to the dieticians. The dieticians checked these and sent back comments to each participant. One year later, results showed that the intervention group lost significantly more weight than the control group (-5.0 kg vs. +0.1 kg for men, and -3.9 kg vs. -0.2 kg for women, respectively). And, at a 1-year follow-up to the intervention period, it was seen that the intervention group maintained significantly lower weight. This RCT demonstrated that the behavioral approach led to weight loss and maintenance of weight loss through diet and behavior modification.

Nakata et al. focused on providing educational materials (textbooks, notebooks, and a pedometer) and implementing group-based support as effective individual components of a weight loss program. Participants were recruited through newspaper advertisements, and 188 overweight and obese adults were randomly assigned into one of three groups: control group, moderate intervention group, or intensive intervention group. All participants received an initial motivational lecture. The energy intake goals were 1,200 and 1,600 kcal/day for women and men, respectively, and the increased energy expenditure goal was 1,000 kcal/week. Participants in the moderate and intensive intervention groups also received the educational materials and a lecture on how to use them. Only participants in the intensive intervention group received group-based support at weeks 2, 4, 6, 10, 14, 18, and 22, during which a trained staff member gave lectures and two other staff members reviewed participants’ notebooks and advised them on their diet and other lifestyle-related factors.

During the 6-month intervention period, the participants in the control, moderate, and intensive intervention groups reduced their weight by 2.9, 4.7, and 7.7 kg, respectively. All differences between groups were significant. A follow-up exam 2 years later showed the amount of weight lost in the moderate and intensive intervention groups to be the same (3.3 kg). Secondary analysis using the data of those who completed the study (n=100) revealed that the participants in the highest quartile of percentage of weight lost significantly increased their step counts and moderate-to-vigorous physical activity compared to the lowest quartile group. This RCT demonstrated that group-based support was an effective component of a weight loss program, but the effect seemed to disappear within 2 years. In addition, it was suggested that increasing physical activity is a crucial factor for successful weight loss maintenance.

The other studies found in our literature review focused on computer tailored advice, telephone and mail support, tailor-made lifestyle modification, hot bathing and dairy delivery. Although all RCTs provided valuable findings, RCTs in this specific field in Japan were quite limited. For instance, no RCTs compared diet plus exercise with diet only. Our research group published related articles, but these studies were not RCTs. As a result, no RCTs in Japan were found to be eligible for a recent systematic review comparing the efficacy of diet plus exercise with diet only.

Conclusions

The RCT is a study design that can provide an extraordinarily high level of evidence. There are many RCTs in the world, and good quality ones are utilized for making guidelines or systematic reviews. Regrettably, RCTs in the field of obesity and physical activity in Japan are quite limited. Ideally, Japanese national guidelines should be based on RCTs conducted in Japan. Accordingly, it is strongly suggested that more RCTs in this field be conducted in Japan.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this article.

References

1) Renehan AG, Tyson M, Egger M, Heller RF and Zwahlen M. 2008. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 371: 569-578.
2) Arnlöv J, Ingelsson E, Sundström J and Lind L. 2010. Impact of body mass index and the metabolic syndrome on the risk of cardiovascular disease and death in middle-aged men. Circulation 121: 230-236.
3) Bogers RP, Bemelmans WJ, Hoogenveen RT, Boshuizen HC, Woodward M, Knekt P, van Dam RM, Hu FB, Visscher TL, Menotti A, Thorpe RJ Jr, Jamrozik K, Calling S, Strand BH and Shipley MJ; for the BMI-CHD Collaboration Investigators. 2007. Association of overweight with increased risk of coronary heart disease partly independent of blood pressure and cholesterol levels: a meta-analysis of 21 cohort studies including more than 300,000 persons. Arch Intern Med 167: 1720-1728.
4) Tirosh A, Shai I, Afek A, Dubnov-Raz G, Ayalon N, Gordon B, Derazne E, Tzar D, Shamis A, Vinker S and Rudich A. 2011. Adolescent BMI trajectory and risk of diabetes versus coronary disease. N Engl J Med 364: 1315-1325.
5) Flegal KM, Kit BK, Orpana H and Graubard BI. 2013. Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. JAMA 309: 71-82.
6) Finucane MM, Stevens GA, Cowan MJ, Danaei G, Lin JK, Paciorek CJ, Singh GM, Gutierrez HR, Lu Y, Bahalim AN, Farzadfar F, Riley LM and Ezzati M; Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Body Mass Index). 2011. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9·1 million participants. Lancet 377: 557-567.

7) Kohro T, Furai Y, Mitsutake N, Fujii R, Morita H, Oku S, Ohe K and Nagai R. 2008. The Japanese national health screening and intervention program aimed at preventing worsening of the metabolic syndrome. Int Heart J 49: 193-203.

8) Ministry of Health, Labour and Welfare: Final assessment of Healthy Japan 21 (in Japanese). [http://www.mhlw.go.jp/stf/houdou/2r9852000001r5gc-att/2r9852000001r5np.pdf] Accessed August 31, 2015.

9) Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JO and Wyatt HR. 2008. Physical activity patterns in the National Weight Control Registry. Obesity (Silver Spring) 16: 153-161.

10) Mekary RA, Feskanich D, Hu FB, Willett WC and Field AE. 2010. Physical activity in relation to long-term weight maintenance after intentional weight loss in premenopausal women. Obesity (Silver Spring) 18: 167-174.

11) Jakicic JM, Marcus BH, Lang W and Janney C. 2008. Effect of exercise on 24-month weight loss maintenance in overweight women. Arch Intern Med 168: 1550-1559.

12) Jakicic JM, Otto AD, Lang W, Semler L, Winters C, Polizen K and Mohr KI. 2011. The effect of physical activity on 18-month weight change in overweight adults. Obesity (Silver Spring) 19: 100-109.

13) Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA and Nathan DM; Diabetes Prevention Program Research Group. 2002. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 346: 393-403.

14) Ratner R, Goldberg R, Haffner S, Marcovina S, Orchard T, Fowler S and Temprosa M; Diabetes Prevention Program Research Group. 2005. Impact of intensive lifestyle and metformin therapy on cardiovascular disease risk factors in the diabetes prevention program. Diabetes Care 28: 888-894.

15) Orchard TJ, Temprosa M, Goldberg R, Haffner S, Ratner R, Marcovina S and Fowler S; Diabetes Prevention Program Research Group. 2005. The effect of metformin and intensive lifestyle intervention on the metabolic syndrome: the Diabetes Prevention Program randomized trial. Ann Intern Med 142: 611-619.

16) Diabetes Prevention Program Research Group, Knowler WC, Fowler SE, Hamman RF, Christophi CA, Hoffman HJ, Brenneman AT, Brown-Friday JO, Goldberg R, Venditti E and Nathan DM. 2009. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet 374: 1677-1686.

17) Ryan DH, Espeland MA, Foster GD, Haffner SM, Hubbard VS, Johnson KC, Kahn SE, Knowler WC and Yanovski SZ; Look AHEAD Research Group. 2003. Look AHEAD (Action for Health in Diabetes): design and methods for a clinical trial of weight loss for the prevention of cardiovascular disease in type 2 diabetes. Control Clin Trials 24: 610-628.

18) Look AHEAD Research Group, Pi-Sunyer X, Blackburn G, Brancati FL, Bray GA, Bright R, Clark JM, Curtis JM, Espeland MA, Foreyt JP, Graves K, Haffner SM, Harrison B, Hill JO, Horton ES, Jakicic J, Jeffery RW, Johnson KC, Kahn S, Kelley DE, Kitabchi AE, Knowler WC, Lewis CE, Maschak-Carey BJ, Montgomery B, Nathan DM, Patricio J, Peters A, Redmon JB, Reeves RS, Ryan DH, Safford M, Van Dorsten B, Wadden TA, Wagenknecht L, Wesche-Thobaben J, Wing RR and Yanovski SZ. 2007. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the Look AHEAD trial. Diabetes Care 30: 1374-1383.

19) Look AHEAD Research Group and Wing RR. 2010. Long-term effects of a lifestyle intervention on weight and cardiovascular risk factors in individuals with type 2 diabetes mellitus: four-year results of the Look AHEAD trial. Arch Intern Med 170: 1566-1575.

20) Look AHEAD Research Group, Wing RR, Bolin P, Brancati FL, Bray GA, Clark JM, Coday M, Crow RS, Curtis JM, Egan CM, Espeland MA, Evans M, Foreyt JP, Ghazarian S, Gregg EW, Harrison B, Hazuda HP, Hill JO, Horton ES, Hubbard VS, Jakicic JM, Jeffery RW, Johnson KC, Kahn SE, Kitabchi AE, Knowler WC, Lewis CE, Maschak-Carey BJ, Montez MG, Murillo A, Nathan DM, Patricio J, Peters A, Pi-Sunyer X, Pownall H, Rebourassin D, Regensteiner JG, Rickman AD, Ryan DH, Safford M, Wadden TA, Wagenknecht LE, West DS, Williamson DF and Yanovski SZ. 2013. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. N Engl J Med 369: 145-154.

21) Phelan S, Kanaya AM, Subak LL, Hogan PE, Espeland MA, Wing RR, Burgio KL, DiLillo V, Gorin AA, West DS and Brown JS; Look AHEAD Research Group. 2012. Weight loss prevents urinary incontinence in women with type 2 diabetes: results from the Look AHEAD trial. J Urol 187: 939-944.

22) Breyer BN, Phelan S, Hogan PE, Rosen RC, Kitabchi AE, Wing RR and Brown JS; Look AHEAD Research Group. 2014. Intensive lifestyle intervention reduces urinary incontinence in overweight/obese men with type 2 diabetes: results from the Look AHEAD trial. J Urol 192: 144-149.

23) Foster GD, Borradaille KE, Sanders MH, Millman R, Zammit G, Newman AB, Wadden TA, Kelley D, Wing RR, Pi-Sunyer FX, Rebourassin D and Kuna ST; Sleep AHEAD Research Group of Look AHEAD Research Group. 2009. A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the Sleep AHEAD study. Arch Intern Med 169: 1619-1626.

24) Kuna ST, Rebourassin DM, Borradaille KE, Sanders MH, Millman RP, Zammit G, Newman AB, Wadden TA, Jakicic JM, Wing RR, Pi-Sunyer FX and Foster GD; Sleep AHEAD Research Group of the Look AHEAD Research Group. 2013. Long-term effect of weight loss on obstructive sleep apnea severity in obese patients with type 2 diabetes. Sleep 36: 641-649.

25) Gregg EW, Chen H, Wagenknecht LE, Clark JM, Dehanty LM, Bantle J, Pownall HJ, Johnson KC, Safford MM, Kitabchi AE, Pi-Sunyer FX, Wing RR and Bertoni AG; Look
AHEAD Research Group. 2012. Association of an intensive lifestyle intervention with remission of type 2 diabetes. *JAMA* 308: 2489-2496.

27) Houston DK, Leng X, Bray GA, Hergenroeder AL, Hill JO, Jakicic JM, Johnson KC, Neiberg RH, Marsh AP, Rejeski WJ and Kritchevsky SB; Action for Health In Diabetes (Look AHEAD) Movement and Memory Ancillary Study Research Group. 2015. A long-term intensive lifestyle intervention and physical function: the look AHEAD Movement and Memory Study. *Obesity (Silver Spring)* 23: 77-84.

28) Look AHEAD Research Group. 2014. Effect of a long-term behavioural weight loss intervention on nephropathy in overweight or obese adults with type 2 diabetes: a secondary analysis of the Look AHEAD randomised clinical trial. *Lancet Diabetes Endocrinol* 2: 801-809.

29) Rubin RR, Wadden TA, Bahnson JL, Blackburn GL, Brancait FL, Bray GA, Coday M, Crow SJ, Curtis JM, Dutton G, Egan C, Evans M, Ewing L, Faulconbridge L, Foreyt J, Gassou S, Gregg EW, Hazuda HP, Hill JO, Horton ES, Hubbard VS, Jakicic JM, Jeffery RW, Johnson KC, Kahn SE, Knowler WC, Lang W, Lewis CE, Montez MG, Murillo A, Nathan DM, Patricio J, Peters A, Pi-Sunyer X, Pownall H, Rejeski WJ, Rosenthal RH, Ruelas V, Toledo K, Van Dorsten B, Vitalins M, Williamon D, Wing RR, Yanovski SZ and Zhang P; Look AHEAD Research Group. 2014. Impact of intensive lifestyle intervention on depression and health-related quality of life in type 2 diabetes: the Look AHEAD Trial. *Diabetes Care* 37: 1544-1553.

30) Espeland MA, Glick HA, Bertoni A, Brancait FL, Bray GA, Clark JM, Curtis JM, Egan C, Evans M, Foreyt JP, Ghazarian S, Gregg EW, Hazuda HP, Hill JO, Hire D, Horton ES, Hubbard VS, Jakicic JM, Jeffery RW, Johnson KC, Kahn SE, Killeen T, Kitabchi AE, Knowler WC, Krisa A, Lewis CE, Miller M, Montez MG, Murillo A, Nathan DM, Nyenwe E, Patricio J, Peters AL, Pi-Sunyer X, Pownall H, Redmond JB, Rushing J, Ryan DH, Safford M, Tsai AG, Wadden TA, Wing RR, Yanovski SZ and Zhang P; Look AHEAD Research Group. 2014. Impact of an intensive lifestyle intervention on use and cost of medical services among overweight and obese adults with type 2 diabetes: the action for health in diabetes. *Diabetes Care* 37: 2548-2556.

31) Church TS, Earnest CP, Skinner JS and Blair SN. 2007. Effects of different doses of physical activity on cardiorespiratory fitness among sedentary, overweight or obese postmenopausal women with elevated blood pressure: a randomized controlled trial. *JAMA* 297: 2081-2091.

32) Goodpaster BH, Delany JP, Otto AD, Hollman J, South-Paul JE, Thomas SB, Brown J, McTigue K, Bushnell SW and Yamabuki K. 2004. Target value of intraabdominal fat area for improving coronary heart disease risk factors. *Obes Facts* 4: 222-228.

33) Jensen MD, Ryan DH, Apovian CM, Ard JD, Comuzzie AG, Donato KA, Hu FB, Hubbard VS, Jakicic JM, Kushner RF, Loria CM, Milen BE, Nonas CA, Pi-Sunyer FX, Stevens J, Stevens VJ, Wadden TA, Wolfe BM, Yanovski SZ, Jordan HS, Kendall KA, Luz LJ, Mentor-Marcel R, Morgan LC, Trisolini MG, Wnek J, Anderson JL, Halperin JL, Albert NM, Bozkurt B, Brindis RG, Curtis LH, DeMets D, Hochman JS, Kovacs RJ, Ohman EM, Pressler SJ, Sellek FW, Shen WK, Smith SC Jr and Tomaselli GF. 2014. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation* 129: S102-S138.

34) Adachi Y, Sato C, Yamatsu K, Ito S, Adachi K and Yamagami T. 2007. A randomized controlled trial on the long-term effects of a 1-month behavioral weight control program assisted by computer tailored advice. *Behav Res Ther* 45: 459-470.

35) Nishijima H, Satake K, Igarashi K, Morita N, Kanazawa N and Okita K. 2007. Effects of exercise in overweight Japanese with multiple cardiovascular risk factors. *Med Sci Sports Exerc* 39: 926-933.

36) Tanaka M, Adachi Y, Adachi K and Sato C. 2010. Effects of a non-face-to-face behavioral weight-control program among Japanese overweight males: a randomized controlled trial. *Int J Behav Med* 17: 17-24.

37) Takada A, Nakamura R, Furukawa M, Takahashi Y, Nishimura S and Kosugi S. 2011. The relationship between weight loss and time and risk preference parameters: a randomized controlled trial. *J Biosoc Sci* 43: 481-503.

38) Saito T, Watanabe M, Nishida J, Iizumi T, Oomura M, Takagi T, Fukunaga R, Bandai Y, Tajima N, Nakamura Y and Ito M; for the Zensharen Study for Prevention of Lifestyle Diseases Group. 2011. Lifestyle modification and prevention of type 2 diabetes in overweight Japanese with impaired fasting glucose levels: a randomized controlled trial. *Arch Intern Med* 171: 1352-1360.

39) Nakade M, Iba N, Suda N, Morita A, Miyachi M, Sasaki S, Watanabe S and SCOP Group. 2012. Behavioral change during weight loss program and one-year follow-up: Saku Control Obesity Program (SCOP) in Japan. *Asia Pac J Clin Nutr* 21: 22-34.

40) Nannri A, Tomita K, Matsushita Y, Ichikawa F, Yamamoto M, Nagafuchi Y, Kakumoto Y and Mizoue T. 2012. Effect of six months lifestyle intervention in Japanese men with metabolic syndrome: randomized controlled trial. *J Occup Health* 54: 215-222.

41) Sakurai R, Fujiwara Y, Saito K, Fukaya T, Kim MJ, Yasunaga M, Kim H, Ogawa K, Tanaka C, Tsuoda N, Muraki E, Suzuki K, Shinkai S and Watanabe S. 2013. Effects of a comprehensive intervention program, including hot bathing, on overweight adults: a randomized controlled trial. *Geriatr Gerontol Int* 13: 638-645.

42) Nakata Y, Okada M, Hashimoto K, Harada Y, Sone H and Tanaka K. 2014. Weight loss maintenance for 2 years after a 6-month randomized controlled trial comparing education-only and group-based support in Japanese adults. *Obes Facts* 7: 376-387.

43) Tanaka S, Uenishi K, Ishida H, Takami Y, Hosoi T, Kadowaki T, Orimo H and Ohashi Y. 2014. A randomized intervention trial of 24-wk dairy consumption on waist circumference, blood pressure, and fasting blood sugar and lipids in Japanese men with metabolic syndrome. *J Nutr Sci Vitaminol (Tokyo)* 60: 305-312.

44) Nakata Y, Okada M, Hashimoto K, Harada Y, Sone H and Tanaka K. 2011. Comparison of education-only versus group-based intervention in promoting weight loss: a randomized controlled trial. *Obes Facts* 4: 222-228.

45) Tanaka K, Okura T, Shigematsu R, Nakata Y, Lee DJ, Wee SW and Yamabuki K. 2004. Target value of intraabdominal fat area for improving coronary heart disease risk factors.
46) Okura T, Nakata Y, Lee DJ, Ohkawara K and Tanaka K. 2005. Effects of aerobic exercise and obesity phenotype on abdominal fat reduction in response to weight loss. *Int J Obes (Lond)* 29: 1259-1266.

47) Nakata Y, Okura T, Matsuo T and Tanaka K. 2009. Factors alleviating metabolic syndrome via diet-induced weight loss with or without exercise in overweight Japanese women. *Prev Med* 48: 351-356.

48) Schwingshackl L, Dias S and Hoffmann G. 2014. Impact of long-term lifestyle programmes on weight loss and cardiovascular risk factors in overweight/obese participants: a systematic review and network meta-analysis. *Syst Rev* 3: 130.