The Association of Fit-Fat Index with Incident Diabetes in Japanese Men: A Prospective Cohort Study

Robert A. Sloan\(^1\), Susumu S. Sawada\(^2\), Lee I-Min\(^3,4\), Yuko Gando\(^2\), Ryoko Kawakami\(^5\), Takashi Okamoto\(^6\), Koji Tsukamoto\(^6\) & Motohiko Miyachi\(^2\)

Type 2 diabetes is increasing globally and in Asia. The purpose of this study was to examine the association of a fit-fat index (FFI) with diabetes incidence among Japanese men. In total 5,014 men aged 18–64 years old, who had an annual health check up with no history of major chronic disease at baseline from 2002 to 2009 were observed. CRF was estimated via cycle ergometry. Overall, 7.6% of the men developed diabetes. The mean follow-up period was 5.3 years. Hazard ratios, 95% confidence intervals and P trend for diabetes incidence were obtained using the Cox proportional hazards model while adjusting for confounding variables. High FFI demonstrated lower risk 0.54 (0.36–0.82) compared to low BMI 0.63 (0.44–0.90), low WHtR 0.64 (0.41–1.02), and High CRF 0.72 (0.51–1.03). FFI showed a marginally stronger dose response relationship across quartiles (P (trend) = 0.001) compared to BMI (P (trend) = 0.002), WHtR (P (trend) = 0.055), and CRF (P (trend) = 0.005). Overall, both fitness and fatness play independent roles in determining diabetes incidence in Japanese men. FFI may be a more advantageous physical fitness measure because it can account for changes in fitness and/or fatness.

According to officials at the International Diabetes Federation, the prevalence of diagnosed and undiagnosed Type 2 diabetes (herein diabetes) in Japanese adults is 11\(^%\). Concomitantly obesity and physical inactivity prevalence are reported to be 3.5\(^%\) and 38\(^%\), respectively\(^7\). To slow the rise, the Japanese Ministry of Health, Labor and Welfare is making efforts aimed at reducing metabolic syndrome and increasing participation rates for medical screening. Though beneficial, such interventions tend to use more traditional health care approaches rather than health promotion strategies designed to identify and act upon earlier stage risk. Phenotypically, Asian populations have greater predisposition towards diabetes, because they tend to store more visceral adiposity and have less muscle mass for a given body mass index (BMI)\(^5\). To complement current efforts, practical upstream approaches targeting components of health-related physical fitness are also needed to help identify and lower diabetes risk.

Cardiorespiratory fitness (CRF) and waist-to-height-ratio (WHtR) are objective components of fitness and fatness linked to diabetes risk\(^4,5\). CRF is an indicator of habitual moderate-to-high intensity aerobic physical activity and depends on the combined function of respiratory, cardiovascular, and musculoskeletal systems\(^6,7\). Moreover, prediabetic individuals with higher CRF levels have lower mortality risks, regardless of fatness levels\(^8\). Unlike other anthropometric measures, WHtR uses a standard boundary value (<0.50) across phenotype, ethnicity, gender, and age, allowing for better comparability between populations\(^8\). Although BMI and WHtR are correlated, they are different. WHtR is a surrogate measure of visceral adiposity, and BMI is a surrogate measure of total lean and fat mass. Investigators have also proposed WHtR as a better screening tool than waist circumference and BMI for adult cardiometabolic risks\(^5\).

Epidemiological and experimental studies have indicated fitness and fatness have independent roles in delaying or preventing the onset of diabetes\(^9,10\). Findings from systematic reviews of clinical trials have shown diet and/or exercise impact fatness, which in turn may affect diabetes incidence. Conversely, diet and/or exercise may affect diabetes incidence independent of fatness. Notably, the use of self-reported diet and exercise is a limitation across trials\(^11,12\). Researchers investigating biological mechanisms suggested fitness and fatness can impact the...
onset of diabetes across an array of mechanisms by varying degrees, depending on intensity, type, and duration of the intervention. Therefore, researchers have called for more investigations to focus on the combined influences of fitness and fatness.

Considering the evidence for varying levels of fitness and fatness to impact diabetes incidence, researchers have begun investigating the utilization of a comprehensive fit-fat index (FFI) on health outcomes. FFI quantifies a given degree of CRF for a given degree of WHtR. Less fit individuals are not always more fit and conversely fitter individuals are not always less fat. A less fit/less fat individual may have the same risk as a more fit/more fat individual.

To date, no researchers have investigated the independent or combined relationship of objectively measured CRF and WHtR with diabetes incidence in an Asian population. We examine the association of FFI as it relates to diabetes incidence in a prospective cohort study of Japanese men. We hypothesized high FFI would associate with lower diabetes incidence better than high fitness or low fatness.

**Results**

The average follow-up period was 5.3 years (ranging 1 to 7 years); 7.6% of the men developed incident diabetes, and 17.5% of the men reported a family history of diabetes. Compared with nondiabetic men, the men who developed diabetes tended to be older, with lower fitness, higher fatness, higher systolic blood pressure, higher prevalence of family history, and were smokers (Table 1). Overlap of the quartiles is due to FFI being correlated with fit fat variables (Supplementary Table 1). Independent associations between fitness and fatness covariates, and diabetes incidence are shown in Table 2; total man-years and cases were included. High FFI demonstrated lower diabetes incidence better than fit/lean and fitter/fatter individuals. The magnitude and direction of association was marginally stronger between FFI and diabetes incidence. Diabetes incidence was also independently associated with age, systolic blood pressure, smoking behavior, and family history (Supplementary Table 1).

**Discussion**

The current prospective cohort study was used to investigate the associations between fitness and fatness with diabetes incidence in a large cohort of healthy Japanese men from baseline. Consistent with the literature, our findings indicated fitness and fatness are useful in showing the probability of diabetes incidence, but combined fitness and fatness offered a slightly more refined risk marker.

To the best of our knowledge, this is the first study to evaluate the associations between objectively measured CRF and WHtR with diabetes incidence in an Asian population. We hypothesized high FFI would associate with lower diabetes incidence better than high fitness or low fatness.

| Characteristics                  | All participants | Diabetes | Nondiabetic | P value |
|----------------------------------|------------------|----------|-------------|---------|
| n                                | 5,014            | 351      | 4,663       | —       |
| Age (years)                      | 48.5 ± 8.1       | 49.9 ± 5.8 | 48.4 ± 8.2  | <0.001  |
| FFI (ml/kg/min)                  | 79.4 ± 20.0      | 70.8 ± 16.7 | 80.0 ± 20.0 | <0.001  |
| CRF (ml/kg/min)                  | 38.6 ± 7.6       | 36.0 ± 6.6 | 38.8 ± 7.6  | <0.001  |
| WHtR                             | 0.49 ± 0.04      | 0.52 ± 0.05 | 0.49 ± 0.04  | <0.001  |
| BMI (kg/m²)                      | 23.7 ± 2.9       | 25.0 ± 3.4 | 23.6 ± 2.8  | <0.001  |
| Systolic blood pressure (mmHg)   | 125.4 ± 14.4     | 130.7 ± 15.2 | 125.0 ± 14.2 | <0.001  |
| Current smokers, n (%)           | 2,410 (48.0)     | 196 (55.8) | 2,214 (47.5) | 0.003   |
| Current drinkers, n (%)          | 4,309 (85.9)     | 298 (84.9) | 4,011 (86.0) | 0.577   |
| Family history of diabetes, n (%)| 879 (17.5)       | 88 (25.1)  | 791 (17.0)  | <0.001  |

Table 1. Baseline Characteristics of Participants. FFI: Fit-Fat Index (METs ÷ WHtR), CRF: Cardiorespiratory Fitness, WHtR: Waist-to-Height Ratio (Waist cm ÷ Height cm), BMI: Body Mass Index. Data are means ± SD, unless otherwise specified.
Chronic adaptions to physical activity may improve CRF and/or visceral adiposity without changes to anthropometric indices, inflammation, and excess free fatty acids. Notably, in our study we found men within the second quartile with higher BMI to have lower incidence of diabetes than those in the fourth quartile (Low BMI). This was likely due to the effects of confounding factors. Furthermore, in a separate study, Hsieh and colleagues found 46% of normal BMI Japanese men to be at higher risk because they had elevated WHtR levels. These types of inconsistencies may provide argument for the use of a more comprehensive measure such as FFI.

Though fitness and fatness are commonly linked to diabetes, the causal biological mechanisms are not entirely understood. Chronic adaptions to physical activity may improve CRF and/or visceral adiposity without changes to anthropometric indices, inflammation, and excess free fatty acids. Biochemical and structural adaptations to habitual physical activity may occur in obese and nonobese individuals, resulting in adaptations in peripheral skeletal muscle glucose metabolism, hepatic function, adipose tissue, insulin action, inflammation, and HbA1c. Reduction of visceral fatness may reduce HbA1c, insulin resistance, inflammation, and excess free fatty acids.

The strengths of our study included the use of valid and objective measures at baseline and follow-up, such as blood glucose, CRF, waist girth, height, and weight. Although CRF was estimated, previous studies have shown a high correlation between laboratory measured CRF and the submaximal Astrand Ryhming protocol. The generalizability of the findings was limited, because participants were Japanese men, ages 18 to 64 years old, working at the same company. Conversely, the homogeneity of the sample strengthened the internal validity of our findings by limiting demographic confounders. In future studies, we plan to test the relevancy of FFI for diabetes risks in women. CRF, WHR and BMI data were obtained during baseline examination; therefore, we cannot account for changes during the follow-up period that were not considered. We were also not able to account for any related medical therapy that may have impacted diabetes incidence. Lastly, the average follow-up of 5.3 years may have been too short to detect the potential impact of fitness and fatness over time.

### Methods

#### Participants

The research ethics committee of the National Institutes of Biomedical Innovation, Health and Nutrition (NIBIOHN) approved the current study methodology, protocol, and procedures. The health examinations were done under Japanese Industrial Safety and Health Law. All information from the health examinations was used only in aggregate form without reference to or disclosure of individual information.

#### Table 2. Adjusted hazard ratios of diabetes incidence by fitness and fatness factors.

| Potential risk factors | n     | Man-years | Cases | Age-adjusted HR (95% CIs) | Multivariable-adjusted P for trend | P value |
|------------------------|-------|-----------|-------|---------------------------|-----------------------------------|---------|
| FFI                    |       |           |       |                           |                                   |         |
| 1st quartile (Low)     | 1,254 | 5,919     | 149   | 1.00 (Referent)           | 1.00 (Referent)                   |         |
| 2nd quartile           | 1,251 | 6,572     | 91    | 0.60 (0.46–0.78)          | 0.77 (0.59–1.02)                  | 0.068   |
| 3rd quartile           | 1,257 | 6,836     | 70    | 0.46 (0.35–0.62)          | 0.67 (0.49–0.92)                  | 0.013   |
| 4th quartile (High)    | 1,252 | 7,321     | 41    | 0.29 (0.21–0.42)          | 0.54 (0.36–0.82)                  | 0.003   |
|                        |       |           |       | P for trend < 0.001       | P for trend = 0.001               |         |
| CRFb                   |       |           |       |                           |                                   |         |
| 1st quartile (Low)     | 1,301 | 6,113     | 149   | 1.00 (Referent)           | 1.00 (Referent)                   |         |
| 2nd quartile           | 1,255 | 6,729     | 84    | 0.57 (0.44–0.75)          | 0.67 (0.51–0.88)                  | 0.005   |
| 3rd quartile           | 1,376 | 7,532     | 68    | 0.44 (0.33–0.58)          | 0.57 (0.42–0.77)                  | <0.001  |
| 4th quartile (High)    | 1,082 | 6,274     | 50    | 0.44 (0.32–0.61)          | 0.72 (0.51–1.03)                  | 0.073   |
|                        |       |           |       | P for trend < 0.001       | P for trend = 0.005               |         |
| WHRc                   |       |           |       |                           |                                   |         |
| 1st quartile (High)    | 1,248 | 6,170     | 152   | 1.00 (Referent)           | 1.00 (Referent)                   |         |
| 2nd quartile           | 1,218 | 6,312     | 83    | 0.55 (0.42–0.72)          | 0.76 (0.56–1.03)                  | 0.072   |
| 3rd quartile           | 1,258 | 6,807     | 72    | 0.47 (0.35–0.62)          | 0.75 (0.53–1.06)                  | 0.098   |
| 4th quartile (Low)     | 1,290 | 7,359     | 44    | 0.30 (0.21–0.42)          | 0.65 (0.41–1.02)                  | 0.059   |
|                        |       |           |       | P for trend < 0.001       | P for trend = 0.055               |         |
| BMI                    |       |           |       |                           |                                   |         |
| 1st quartile (High)    | 1,252 | 6,551     | 153   | 1.00 (Referent)           | 1.00 (Referent)                   |         |
| 2nd quartile           | 1,255 | 6,640     | 72    | 0.43 (0.33–0.57)          | 0.52 (0.39–0.70)                  | <0.001  |
| 3rd quartile           | 1,254 | 6,681     | 65    | 0.40 (0.30–0.54)          | 0.55 (0.40–0.75)                  | <0.001  |
| 4th quartile (Low)     | 1,253 | 6,776     | 61    | 0.38 (0.28–0.51)          | 0.63 (0.44–0.90)                  | 0.011   |
|                        |       |           |       | P for trend < 0.001       | P for trend = 0.002               |         |
the current study, a de-identified limited data set was collected used and approved by the NIBIOHN. A detailed description of the methods and protocols used in this investigation is already published, new additions or variations have been stated.

The participants were employees of a company that supplies natural gas to the greater Tokyo area. The Japan Industrial Safety and Health Law officials require all employees undergo annual health examinations. The participants were 6,884 workers who underwent a health examination and graded exercise test between April 2002 and March 2003. Females were excluded from the current study because of the small number of female participants (n = 831). Also, 540 men with diabetes were excluded, along with 499 males based on a lack of data regarding potential confounders. As participants in the current study, a total of 5,014 men, ages 18 to 64 years old, were followed until March 2009. The company to which the participants belonged has adopted the mandatory retirement system, which has been introduced by many companies in Japan. In this system, the employment relationship is automatically completed when the worker’s age reaches a specific age (this company: 60 years). However, after retirement, there is another system to employ workers as part-time employees until 65 years of age based on their wishes. Most workers continue to work until 65 years of age. On the other hand, some workers retire at the age of 50 years or older, utilizing systems to promote early retirement, such as a system for job-change to affiliated companies and redundancy pay system. Thus, the study participants were to retire between 50 and 65 years of age (n = 1,902) during the follow-up period. At the point of retirement, follow-up was discontinued (censored case).

Health Examination. The annual health examinations, including objective measurements of height, body weight, and blood pressure occurred between April 2002 and March 2003. An automated sphygmomanometer measured the resting blood pressure with the participant in a sitting position. Furthermore, we investigated the potential confounders regarding diabetes development of the participants, including cigarette smoking, alcohol intake, and family history of diabetes, using a self-administered questionnaire.

Determination of Diabetes Incidence. Diabetes incidence was determined based on health examinations conducted annually from April 2002 to March 2009. The criteria for the diagnosis of diabetes were based on the diagnostic guidelines of the American Diabetes Association and the Japan Diabetes Society. Participants with fasting blood glucose levels exceeding 7.0 mmol/L (126 mg/dL) were regarded as having diabetes. The fasting condition was confirmed by a verbal confirmation. From 2007, hemoglobin A1c (HbA1c; NGSP) levels were also used to determine the year in which diabetes was developed. As with fasting blood glucose levels, when employees exhibited HbA1c levels of ≥6.5% (48 mmol/mol), the year in which they had developed diabetes. Furthermore, using a questionnaire administered during examinations, we asked whether a physician had made a diagnosis of diabetes. If more than one of the criteria were met, the year of the earliest episode was indicated as the year of diabetes development.

Cardiorespiratory fitness. The estimated maximal oxygen uptake (ml/kg/min), which is an index of CRF, was measured with a submaximal exercise test on a cycle ergometer (Monark Exercise AB, Vansbro, Sweden). The exercise test was composed of a maximum of three steps, each lasting 4 min, with increased resistance in each step. The heart rate was measured based on the R-R interval on the electrocardiogram. The target heart rate was established as 85% of age-predicted maximum heart rate (220 minus age in years). The load was increased 37 watts per step until the target heart rate was reached. CRF was estimated using the Åstrand-Ryhming nomogram and Åstrand age-correction factors. The method of estimating CRF used in the current study has been shown to strongly correlate with results determined using a direct method, according to comparative studies. A detailed description of the protocol has been already published pertaining to this cohort.

Anthropometric measures. The height and body weight of all participants were measured at health examinations conducted between April 2002 and March 2003. A scale was used to measure the body weight with the participants in light clothing and with shoes removed. The body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters (kg/m²). Waist circumference was measured at the top of the right iliac crest with a nonelastic tape measure to the nearest 0.1 cm. WHtR was calculated by dividing waist circumference (in cm) by height in cm.

Fit-Fat index. Fit-fat index (FFI) represents the combination of CRF as the estimated VO²max and WHtR (VO²max ÷ WHtR) expressed in the form of a quotient. Higher scores are considered better and generally range from ~30 to 150 on a continuous scale. FFI compares individuals beyond independent or joint categories for CRF and WHtR (i.e., Unfit/lean, 32 ml/kg/min ÷ 0.45 WHtR = 70 FFI; Fit/ Fat 38.5 ml/kg/min ÷ 0.55 WHtR = 70 FFI). Depending on the type of CRF test, FFI can also be determined by dividing maximum metabolic equivalent (MET) by WHtR.

Statistical Analysis. We compared baseline characteristics of participants with and without diabetes incidence. We showed the mean and standard deviation for continuous variables and the percentage for category variables. Also, we compared both groups using a t-test for continuous variable and Fisher’s exact test for categorical variables, as appropriate. Cox proportional hazards models were used to estimate independent effects across quartiles of fitness and fatness on diabetes incidence. Fitness fatness variables were correlated (Supplementary Table 1), therefore all models were designed to mitigate overadjustment bias and multicollinearity. Each model was adjusted for age, systolic blood pressure, cigarette smoking, alcohol intake, and family history of diabetes. CRF and WHtR models were adjusted for respectively and included BMI. FFI and BMI models were adjusted for respectively and did not include CRF. The lowest quartile was used as the reference group for FFI and CRF models, and the highest quartile was used as the reference group for WHtR and BMI models. In separate analyses, Cox proportional hazards models were used to estimate independent effects across confounders (Supplementary Table 2).
The proportionality assumption of the models was tested using a log-minus-log plot; no evidence of violation was found. The Statistical Package for Social Science (SPSS) software was used for statistical analysis (SPSS, Inc., Chicago, Illinois, USA). In the analysis, \( p \) values < 0.05 were two-sided and were considered statistically significant.

### Data Availability
The data that support the findings of this study are available from Tokyo Gas Co, Ltd. but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of Tokyo Gas Co, Ltd.

### Conclusions
In summary, our findings add to and expand upon the dearth of evidence regarding the combined relationship of objectively measured fitness and fatness with diabetes risk. Using practical methods of physical fitness assessment, we found FFI to be a more useful etiological marker of diabetes incidence in a large cohort of Japanese men. In future studies, researchers should examine FFI utility among women, other health outcomes, and in experimental investigations.

### References
1. Federation, I. D. IDF Diabetes Atlas (2015).
2. Organization, W. H. (WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland 2016).
3. Nazare, J. A. et al. Ethnic influences on the relations between abdominal subcutaneous and visceral adiposity, liver fat, and cardiometabolic risk profile: the International Study of Prediction of Intra-Abdominal Adiposity and Its Relationship With Cardiometabolic Risk/Intra-Abdominal Adiposity. *Am J Clin Nutr* 96, 714–726, https://doi.org/10.3945/ajcn.112.053578 (2012).
4. Ross, R. et al. Importance of Assessing Cardiorespiratory Fitness in Clinical Practice: A Case for Fitness as a Clinical Vital Sign: A Scientific Statement From the American Heart Association. *Circulation* 134, e653–e699, https://doi.org/10.1161/CIR.0000000000004061 (2016).
5. Browning, L. M., Hisheh, S. D. & Ashwell, M. A systematic review of waist-to-height ratio as a screening tool for the prediction of cardiovascular disease and diabetes: 0.5 could be a suitable global boundary value. *Nutr Res Rev* 23, 247–269, https://doi.org/10.1017/S0954422210000144 (2010).
6. Medicine, A. C. o s. ACSM’s Guidelines for Exercise Testing and Prescription. 10th edn, (Wolters Kluwer Health, 2017).
7. Colberg, S. R. et al. Physical Activity/Exercise and Diabetes: A Position Statement of the American Diabetes Association. *Diabetes Care* 39, 2065–2079, https://doi.org/10.2337/dc16-1728 (2016).
8. McAuley, P. A. et al. Fitness, fatness, and survival in adults with prediabetes. *Diabetes Care* 37, 529–536, https://doi.org/10.2337/dci13-1347 (2014).
9. Ashwell, M., Gunn, P. & Gibson, S. Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: systematic review and meta-analysis. *Obes Rev* 13, 275–286, https://doi.org/10.1111/obr.12002 (2012).
10. Zaccardi, F. et al. Cardiorespiratory fitness and risk of type 2 diabetes mellitus: A 23-year cohort study and a meta-analysis of prospective studies. *Atherosclerosis* 243, 131–137, https://doi.org/10.1016/j.atherosclerosis.2015.09.016 (2015).
11. Fogedholm, M. Physical activity, fitness and fatness: relations to mortality, morbidity and disease risk factors. A systematic review. *Obes Rev* 11, 202–221, https://doi.org/10.1111/j.1467-789X.2009.00653.x (2010).
12. Sloan, R. A. et al. A Fit-Fat Index for Predicting Incident Diabetes in Apparently Healthy Men: A Prospective Cohort Study. *PLoS One* 11, e0157703, https://doi.org/10.1371/journal.pone.0157703 (2016).
13. Balk, E. M. et al. Combined Diet and Physical Activity Promotion Programs to Prevent Type 2 Diabetes Among Persons at Increased Risk: A Systematic Review for the Community Preventive Services Task Force. *Ann Intern Med* 163, 437–451, https://doi.org/10.7326/M15-0452 (2015).
14. Howells, L., Musadqag, B., McKay, A. J. & Majeed, A. Clinical impact of lifestyle interventions for the prevention of diabetes: an overview of systematic reviews. *BMJ Open* 6, e013806, https://doi.org/10.1136/bmjopen-2016-013806 (2016).
15. Bassuk, S. S. & Manson, J. E. Epidemiological evidence for the role of physical activity in reducing risk of type 2 diabetes and cardiovascular disease. *J Appl Physiol (1985)* 99, 1193–1204, https://doi.org/10.1152/japplphysiol.00160.2005 (2005).
16. Tchernev, A. & Despres, J. P. Pathophysiology of human visceral obesity: an update. *Physiol Rev* 93, 359–404, https://doi.org/10.1152/physrev.00033.2011 (2013).
17. Despres, J. P. et al. Abdominal obesity and the metabolic syndrome: contribution to global cardiometabolic risk. *Arterioscler Thromb Vasc Biol* 28, 1039–1049, https://doi.org/10.1161/ATVBAHA.107.159228 (2008).
18. Weinstein, A. R. & Sesso, H. Joint effects of physical activity and body weight on diabetes and cardiovascular disease. *Exerc Sport Sci Rev* 34, 10–15 (2006).
19. LaMonte, M. J. B. S. Physical activity, cardiopulmonary fitness, and adiposity contributions to disease risk, *Curr Opin Clin Nutr Metab Care* 9, 540–546 (2006).
20. Loprinzi, P. D. Comparative evaluation of red blood cell distribution width and high sensitivity C-reactive protein in predicting all-cause mortality and coronary heart disease mortality. *Int J Cardiol* 223, 72–73, https://doi.org/10.1016/j.ijcard.2016.08.156 (2016).
21. Loprinzi, P. D. & Edwards, M. K. CVD-related Fit-Fat Index on inflammatory-based CVD biomarkers. *Int J Cardiol* 223, 284–285, https://doi.org/10.1016/j.ijcard.2016.08.194 (2016).
22. Frith, E. & Loprinzi, P. D. The protective effects of a novel fitness-fatness index on all-cause mortality among adults with cardiovascular disease. *Clin Cardiol* 40, 469–473, https://doi.org/10.1002/ccd.22679 (2017).
23. Frith, E. & Loprinzi, P. D. Fitness Fatness Index and Alzheimer-specific mortality. *Eur J Intern Med* 42, 51–53, https://doi.org/10.1016/j.ejim.2017.04.015 (2017).
24. Sloan, R., Sawada, S. S., Martin, C. K. & Haaland, B. Combined association of fitness and central adiposity with health-related quality of life in healthy Men: a cross-sectional study. *Health Qual Life Outcomes* 13, 188, https://doi.org/10.1186/s12955-015-0385-3 (2015).
25. Kawakami, R. et al. Reference values for cardiopulmonary fitness and incidence of type 2 diabetes. *J Epidemiol* 24, 25–30 (2014).
26. Jae, S. Y. et al. Fitness, Body Habitus, and the Risk of Incident Type 2 Diabetes Mellitus in Korean Men. *Am J Cardiol* 117, 585–589, https://doi.org/10.1016/j.amjcard.2015.11.046 (2016).
27. Kawahara, K. et al. Association of cardiopulmonary fitness and overweight with risk of type 2 diabetes in Japanese men. *PLoS One* 9, e98508, https://doi.org/10.1371/journal.pone.0098508 (2014).
28. Fisch, S. D., Yoshimaga, H. & Muto, T. Waist-to-height ratio, a simple and practical index for assessing central fat distribution and metabolic risk in Japanese men and women. *Int J Obes Relat Metab Disord* 27, 610–616, https://doi.org/10.1038/sj.ijo.0802259 (2003).
29. Lin, X. et al. Effects of Exercise Training on Cardiorespiratory Fitness and Biomarkers of Cardiometabolic Health: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Am Heart Assoc. 4, https://doi.org/10.1161/JAHA.115.002014 (2015).
30. Teraslinna, P., Ismail, A. H. & MacLeod, D. F. Nomogram by Astrand and Ryhming as a predictor of maximum oxygen intake. J Appl Physiol. 21, 513–515 (1966).
31. Sawada, S. S., Lee, I. M., Muto, T., Matuszaki, K. & Blair, S. N. Cardiorespiratory fitness and the incidence of type 2 diabetes: Prospective study of Japanese men. Diabetes Care 26, 2918–2922 (2003).
32. Expert Committee on the, D. and Classification of Diabetes, M. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 26(Suppl 1), S5–20 (2003).
33. Kuzuya, T. et al. Report of the Committee on the classification and diagnostic criteria of diabetes mellitus. Diabetes Res Clin Pract 55, 65–85 (2002).
34. Astrand, P. O. & Ryhming, I. A nomogram for calculation of aerobic capacity (physical fitness) from pulse rate during sub-maximal work. J Appl Physiol 7, 218–221 (1954).
35. Astrand, I. Aerobic work capacity in men and women with special reference to age. Acta Physiol Scand Suppl 49, 1–92 (1960).
36. Cink, R. E. & Thomas, T. R. Validity of the Astrand-Ryhming nomogram for predicting maximal oxygen intake. Br J Sports Med 15, 182–185 (1981).
37. O'brien, R. M. A Caution Regarding Rules of Thumb for Variance Inflation Factors. Quality & Quantity 41, 673–679, https://doi.org/10.1007/s11135-006-9018-6 (2007).

Acknowledgements
We thank the Tokyo Gas Health Promotion Centre physicians and staff for their support.

Author Contributions
Study design: R.S., S.S.S., Acquisition of data: S.S.S., T.O., K.T., Analysis: R.S., S.S.S., Y.G., R.K., Interpretation: R.S., S.S.S., I.M.L., M.M., Drafting: R.S., S.S.S., I.M.L., Revising: ALL Final approval: ALL.

Additional Information
Supplementary information accompanies this paper at https://doi.org/10.1038/s41598-017-18898-3.

Competing Interests: The authors declare that they have no competing interests.

Publisher's note: Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit http://creativecommons.org/licenses/by/4.0/.

© The Author(s) 2018