Impact of Physical Activity on Glycemic Control and Insulin Resistance: A Study of Community-dwelling Diabetic Patients in Eastern China

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Abstract

Objective The aim of this study was to evaluate the relationship of various intensities of physical activity with glycemic control and insulin resistance in eastern China.

Methods A population-based, cross-sectional study was conducted in eastern China. The subjects included 604 community-dwelling people. The participants were classified as insufficiently active (IA); sufficiently active (SA) and very active (VA) according to the International Physical Activity Questionnaire (IPAQ). Insulin sensitivity was assessed using the homeostasis model assessment of insulin resistance (HOMA-IR). Related social, biological, lifestyle factors and clinical characteristics were recorded and used as potential confounders.

Results The cohort of 604 type 2 diabetes patients were classified according to the activity level: 107 subjects who were classified as IA, 329 met the criteria for SA, and the rest were VA. The proportion of obese patients, smokers, patients with hypertension, and the body weight, body mass index (BMI), waist circumference, hemoglobin A1c protein (HbA1c), and 2-h postprandial blood glucose (2hPG) were significantly lower in the SA and VA groups than in the IA group ($p < 0.05$ or 0.01). The SA group had lower levels of fasting blood glucose (FPG) and HOMA-IR than the IA and VA groups ($p < 0.05$ or 0.01). HOMA-IR was positively correlated with FPG, 2hPG, HbA1c, waist circumference and BMI. HOMA-IR was negatively correlated with the total walking activity ($p < 0.05$). After adjusting for FPG, 2hPG, HbA1c, waist circumference and BMI among the groups, a partial correlation analysis showed a correlation between HOMA-IR and the total walking activity.

Conclusion Physical activity is a significant factor regarding glycemic control and insulin sensitivity, although SA and walking may be superior to VA for ameliorating insulin sensitivity.

Key words: exercise, insulin resistance, HOMA-IR, diabetes

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Introduction

Type 2 diabetes (T2DM) is a worldwide health problem. The latest data revealed that the prevalence of diabetes and prediabetes among Chinese adults has reached 9.7% and 15.5%, respectively (1). Because China has more than 92 million adults with diabetes, as reported in 2010, it is considered one of the countries with the largest diabetes burden. Diabetes is characterized by the development of specific mi-

crovascular complications and a high incidence of accelerated atherosclerosis. The costs of T2DM are enormous with comorbid risks of cardiovascular disease, blindness, kidney disease, and neuropathy. Effective treatment in diabetic patients can achieve long-term beneficial effects in regards to the risks of these complications.

Physical exercise is a very effective method of T2DM treatment and prevention. Physical activity influences several aspects of T2DM, including blood glucose concentrations, insulin resistance, blood pressure, blood lipids, body weight,

and body fat distribution (2-5). The International Physical Activity Questionnaire (IPAQ) is widely used in physical activity studies around the world. The long form of the IPAQ measures the frequency, duration, and intensity of physical activity in 4 domains: work, transport, domestic and garden, and leisure time. Studies have shown acceptable validity and reliability of the IPAQ for use in population-based studies of physical activity (6).

The positive impact of exercise for improving glucose control in T2DM is widely accepted in the literature and clinical teaching. Most studies suggest that exercise can prevent diabetes (7-9) and improve glucose metabolism in diabetes (10, 11). Some studies have suggested that vigorous exercise was more effective (12-15), while others suggested low-moderate-intensity exercise could be better (16, 17). However, there is a current lack of evidence in regard to which level of intensity or which form of exercise is more favorable on blood glucose metabolism and insulin resistance.

The most commonly used parameters to measure glucose control are fasting blood glucose (FPG), 2-h postprandial blood glucose (2hPG) and hemoglobin A1c protein (HbA1c). The homeostasis model assessment of insulin resistance (HOMA-IR) was developed for application in large epidemiologic investigations (18) and has been widely used to evaluate insulin resistance.

Thus, in this study, we examined the relationships between the levels of total physical activity (including walking measures) and glucose metabolism and insulin resistance among community-dwelling people with T2DM in eastern China.

Materials and Methods

Subjects

This study is a population-based, cross-sectional study among Chinese people in Hangzhou, China. The study included 604 T2DM patients who were diagnosed using the criteria for diagnosis and classification of diabetes (WHO 1999) from January 2010 to July 2010. All patients were aged 30 years or older and lived in private households. The sample population did not include people who lived in institutions (e.g., hospitals and nursing homes); 282 men (46.7%, 33-91 years of age) and 322 women (53.3%, 33-90 years of age) were selected to participate in the study. Informed consent was obtained from each individual. Permission to conduct the study was granted by the Ethics Committee of the Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University.

Physical activity assessment

All participants were interviewed by specialists who used a standard questionnaire for the study. To estimate the physical activity status, the long version of the IPAQ was used. The original English version of the IPAQ was trans-

lated to Chinese. To calculate the physical activity scores, only activities lasting at least 10 minutes were taken into account, and questions referred to the previous 7 days. According to the IPAQ, we assessed the frequency (times per week), duration (minutes per time) and intensity of physical activity. The internationally accepted protocol was used to evaluate the weekly calorie expenditure expressed as metabolic equivalents per week (MET/week). Energy expenditure was expressed as metabolic equivalents multiplied by time in minutes per week (MET×min/week), one MET was defined as $3.5 \text{ mL O}_2 \times \text{kg}^{-1} \times \text{min}^{-1}$. The items in the IPAQ are structured to provide separate domain-specific scores for work, transportation, domestic and garden time and leisure time domains. According to the IPAQ scoring protocol, MET×min/week of specific activity (walking or moderate intensity activity or vigorous intensity activity) was computed by multiplying the MET value of a particular activity (sitting was set to 1 equivalent, 3.3 for walking, 4.0 for moderate intensity activity, and 8.0 for vigorous intensity activity) with minutes spent in the activity. The total physical activity score was calculated, as well as separate scores for each of the 4 physical activity domains. The IPAQ has been previously validated and its values could be classified into three categories: insufficiently active (IA; <600 MET×min/week); sufficiently active (SA; 600-3,000 MET/min/week); and very active (VA; >3,000 MET×min/week). The amount of sitting was calculated as follows: sitting total min/week = (weekday sitting min×5 weekdays) + (weekend day sitting min×2 weekend days).

Demographic and clinical characteristics

In addition to the physical activity status, the study questionnaire included age, gender, family status (married, divorced, widowed), financial status (average annual income during the last year), occupational status, and education level. Current smokers were defined as those who smoked at least one cigarette per day or stopped cigarette smoking during the past 12 months. Former smokers were defined as those who had stopped smoking for more than one year.

Blood pressure (BP), height, weight, and waist circumference were measured by trained researchers. The body mass index (BMI) was calculated as weight (in kilograms) divided by standing height (in meters squared). Waist circumference was measured on bare skin during midrespiration between the 10th rib and the iliac crest. Obesity was defined as a BMI >28 kg/m². BP was taken using a standard mercury sphygmomanometer two times on the right arm of subjects who had been sitting down for 10 minutes, and the mean of two measurements was used for analyses. The BP levels greater or equal to 140/90 mmHg or patients on antihypertensive medication were classified as hypertensive. Hypercholesterolemia was defined as low-density lipoprotein cholesterol levels ≥2.56 mmol/L or patients on treatment.

Blood samples were obtained after a 12-hour fast and analyzed to assess the HbA1c, total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-c), low-density

Table 1. Demographic and Clinical Characteristics of All Participants ($\bar{x}\pm$ SD).

	Physical Activity Status			f value	p value
	IA (n=107)	SA (n=329)	VA (n=168)		
Man/Woman	57/50	154/175	71/97	/	0.077
Obesity (%)	30.84	11.85	20.24	/	<0.001
Smokers (%)	23.36	12.77	20.24	/	0.014
Hypertension (%)	78.50	66.26	63.10	/	0.022
Hypercholesterolemia (%)	69.16	70.21	71.43	/	0.919
Mean age	68.57 $\pm$ 10.95	67.78 $\pm$ 9.23	66.14 $\pm$ 7.89*	2.690	0.069
Body weight (kg)	68.86 $\pm$ 12.31	65.35 $\pm$ 10.35**	65.19 $\pm$ 10.02**	4.962	0.007
Height (m)	1.62 $\pm$ 0.89	1.62 $\pm$ 0.89	1.62 $\pm$ 0.71	0.100	0.905
BMI (kg/m ²)	26.06 $\pm$ 3.93	24.84 $\pm$ 2.88**	24.80 $\pm$ 3.54**	6.246	0.002
Waist circumference (cm)	91.32 $\pm$ 11.21	87.43 $\pm$ 9.43**	85.43 $\pm$ 10.91**#	11.006	<0.001
Systolic BP (mmHg)	152.54 $\pm$ 24.41	153.42 $\pm$ 82.96	143.35 $\pm$ 20.23	1.427	0.241
Diastolic BP (mmHg)	82.31 $\pm$ 14.89	80.37 $\pm$ 12.81	80.81 $\pm$ 12.70	0.831	0.436
Triglyceride (mmol/L) †	0.45 $\pm$ 0.56	0.34 $\pm$ 0.60	0.28 $\pm$ 0.64*	2.372	0.094
Total cholesterol (mmol/L)	5.28 $\pm$ 1.13	5.11 $\pm$ 1.08	5.08 $\pm$ 0.87	1.281	0.278
LDL-c (mmol/L)	3.14 $\pm$ 0.97	2.98 $\pm$ 0.96	2.94 $\pm$ 0.80	1.565	0.210
HDL-c (mmol/L)	1.30 $\pm$ 0.33	1.35 $\pm$ 0.32	1.38 $\pm$ 0.34	1.555	0.212
HbA1c (%)	7.25 $\pm$ 1.50	6.77 $\pm$ 1.14**	6.83 $\pm$ 1.29**	5.928	0.003
Fasting plasma glucose (mmol/L)	8.58 $\pm$ 2.41	8.00 $\pm$ 2.21*	8.45 $\pm$ 2.65#	3.445	0.033
2-h postprandial plasma glucose (mmol/L)	15.47 $\pm$ 5.38	14.33 $\pm$ 5.04*	13.76 $\pm$ 5.14**	3.630	0.027
Fasting plasma insulin (mmol/L)	6.69 $\pm$ 2.66	6.37 $\pm$ 2.54	6.49 $\pm$ 2.86	0.601	0.549
2-h postprandial plasma insulin (mmol/L)	25.81 $\pm$ 14.57	27.87 $\pm$ 18.48	24.73 $\pm$ 16.86	1.954	0.143
HOMA-IR †	0.82 $\pm$ 0.50	0.71 $\pm$ 0.48*	0.75 $\pm$ 0.55	2.032	0.132

Data are expressed as the means $\pm$ SD.

*p<0.05, **p<0.01 for the comparisons between SA or VA vs. IA.

#p<0.05, ##p<0.01 for the comparisons between VA vs. SA.

† Triglyceride levels and the HOMA-IR were logarithmically transformed to the natural logarithm prior to analysis.

lipoprotein-cholesterol (LDL-c) and triglycerides (TG) levels. The subjects ingested a solution containing 75 g of dextrose, and venous blood samples were obtained at 0 and 120 min for the determination of the plasma glucose (FPG and 2hPG) and plasma insulin (Fins and 2hins) levels. Insulin resistance was assessed as calculated using the HOMA-IR approach (glucose $\times$ insulin/22.5).

Statistical analysis

Continuous variables are presented as the mean values $\pm$ standard deviation (SD), and categorical variables are presented as the absolute and relative frequencies. Due to the skewness, we logarithmically transformed HOMA-IR and triglyceride levels to the natural logarithm in the analyses. Non-normally distributed data are presented as the medians and interquartile ranges, (P25-P75). Multiple groups of normally distributed continuous variables were analyzed by one-way analysis of variance (ANOVA); comparisons were analyzed by a t-test for dependent samples. For asymmetric continuous variables, the tested hypotheses were analyzed using the Kruskal-Wallis test. Associations between the categorical variables were tested using contingency tables and the chi-square test. Correlations between the continuous or discrete variables were tested by calculating Pearson's or Spearman's correlation coefficients. A partial correlation analysis was used to examine the relationships between the HOMA-IR and physical activity. All statistical evaluations were carried out using the SPSS version 13.0 for Windows software program. p values <0.05 were considered to be statistically significant.

Results

Clinical and biochemical characteristics

All patients were classified according to their activity level; 107 subjects were classified as IA, 329 met the criteria for SA, and the remaining were VA. There were no significant differences in the distribution of gender, systolic BP, diastolic BP, TC, LDL-c, HDL-c, Fins, and 2hins among all groups (p>0.05 for all). The proportions of obese subjects, smokers, subjects with hypertension, and the body weight, BMI, waist circumference, HbA1c, and 2hPG were significantly lower in the SA and VA groups than in the IA group (p<0.05 or 0.01). The SA group had lower levels of FPG and HOMA-IR than the IA and VA groups (Table 1). The results showed that activity has beneficial effects on the body weight, BP, HbA1c, and 2hPG. The results indicate that sufficiently active exercise was the optimal level for improving glucose metabolism and insulin sensitivity in T2DM.

Weekly energy expenditure and sitting time

According to the IPAQ scoring protocol, MET $\times$ min/week of specific activity was computed by multiplying the MET value of a particular activity (3.3 for walking, 4.0 for moderate intensity activity, and 8.0 for vigorous intensity activity) with minutes spent in the activity. The total sitting time was calculated as follows: sitting total min/week = (weekday sitting min $\times$ 5 weekdays) + (weekend day sitting min $\times$ 2 weekend days). The SA and VA groups had higher levels of

Table 2. Weekly Energy Expenditure and Sitting Time of All Participants.

	Physical Activity Status			p value
	IA	SA	VA	
Total Physical (MET×min/week)	297.0(0~462.0)	2,052.0(1,400.3~2,646.0)	4,044.0(3,486.0~5,116.1)	<0.001
Total Walking (MET×min/week)	0 (0~346.5)	1,188.0(627.0~1,386.0)	1,534.5(990.0~2,310.0)	<0.001
Total Moderate (MET×min/week)	0 (0~0)	1,260.0(360.0~1,260.0)	2,520.0(1,687.5~3,202.5)	<0.001
Total Vigorous (MET×min/week)	0 (0~0)	0(0~0)	0 (0~0)	0.001
Total Sitting (min/week)	2,520.0(2,040.0~4,200.0)	1,680.0(1,260.0~2,100.0)	1,260.0(840.0~2,100.0)	<0.001

Data are expressed as the M, P25-P75.

*p<0.05, **p<0.01 for the comparisons between SA or VA vs. IA.

#p<0.05, ##p<0.01 for the comparisons between VA vs. SA.

Figure. The relationship between the total walking time and Ln HOMA in participants (Coefficient of partial correlation=-0.094, p=0.022).

total physical, total walking, total moderate and total vigorous activity ($p<0.01$) than the IA group. The total sitting time was significantly lower in the SA and VA groups than in the IA group ($p<0.001$, Table 2).

Relationships between the HOMA-IR and physical activity

According to Pearson's or Spearman's correlation analyses, the HOMA-IR was positively correlated with the FPG, 2hPG, HbA1c, waist circumference and BMI. The HOMA-IR was negatively correlated with total walking activity ($p<0.05$). Total physical, total moderate, total vigorous activity, total sitting time, HbA1c, proportions of smokers, patients with hypertension, patients with hypercholesterolemia, gender and age were not correlated with the HOMA-IR ($p>0.05$ for all). After adjusting for the FPG, 2hPG, HbA1c, waist circumference and BMI among the groups, the partial correlation analysis still showed a correlation between the

HOMA-IR and total walking activity (coefficient of partial correlation=-0.094, $p=0.022$; Figure). These results showed that the walking activity significantly contributed to increased insulin sensitivity more than the other energy expenditure forms.

Discussion

As a result of progressive industrialization, Westernized eating habits, and a sedentary lifestyle, Chinese people recently tend to demonstrate a decline in their level of physical activity. These changes in lifestyle appear to have an impact on the increasing obesity problem in the country and may subsequently lead to insulin resistance (19). Insulin resistance, considered by some to be the underlying cause of metabolic syndrome, is an important factor in the etiology of T2DM (20), and physical activity is a core component of T2DM prevention programs (21, 22).

Nearly all studies have shown that exercise can improve glucose metabolism and increase insulin sensitivity. However, there is currently a lack of sufficient evidence as to which intensity level or what forms of exercise are more favorable on improving blood glucose metabolism and insulin resistance. Assah et al. (23) and Ekelund et al. (24) reported that moderate- to vigorous-intensity physical activity have favorable effects on insulin resistance, although light-intensity physical activity had no such effect. However, Cooper et al. (25) suggested that moderate- and vigorous-intensity physical activity were not associated with clustered metabolic risk after accounting for sedentary time. On the other hand, Gando et al. (26) showed that light-intensity physical activity was inversely associated with insulin resistance in elderly Japanese women. Another study demonstrated that the frequency of exercise is an influential factor more likely to underlie the beneficial effects of aerobic training, suggesting that the repetition of exercise sessions may be more important than longer or more intense sessions (27).

Our study also emphasized that activity has beneficial effects on body weight, BP, glucose metabolism and insulin sensitivity. The major finding of the present study was that the SA group had lower levels of FPG and HOMA-IR than the IA and VA groups. These results indicate that sufficient active exercise was the optimal level for improving glucose metabolism and insulin in T2DM. It has also been previously reported that when moderate-intensity and vigorous-intensity exercise were compared at the same volume (low-volume / moderate-intensity vs. low-volume / vigorous-intensity), the moderate-intensity exercise was more effective, implying that there is some aspect of moderate-intensity exercise training that has more beneficial effects on insulin action than vigorous exercise (28). The SA group could have a greater increase in insulin sensitivity even after exercise withdrawal, which is significantly different from the VA group (29).

A further analysis showed that the relationship between the HOMA-IR and total walking activity remained significant after adjusting for other differences among the groups. These results showed that walking activity significantly contributed to increase insulin sensitivity more than the other energy expenditure forms. Previous studies showed that walking exercise has been proposed to be a less expensive alternative with a good clinical outcome (30). In elderly patients, joint disease and/or degeneration of myotendinous structures become apparent when physical activity levels are increased. Thus, walking may be the most suitable mode of exercise.

In conclusion, physical activity is a significant factor regarding glycemic control and insulin sensitivity, although SA and walking may be superior to VA for improving insulin sensitivity.

The authors state that they have no Conflict of Interest (COI).

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References

1. Yang W, Lu J, Weng J, et al. Prevalence of diabetes among men and women in China. *N Engl J Med* **362**: 1090-1101, 2010.
2. Colberg SR, Sigal RJ, Fernhall B, et al. Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement executive summary. *Diabetes Care* **33**: 2692-2696, 2010.
3. Sigal RJ, Kenny GP, Wasserman DH, et al. Physical activity/exercise and type 2 diabetes. *Diabetes Care* **27**: 2518-2539, 2004.
4. Sigal RJ, Kenny GP, Wasserman DH, et al. Physical activity/exercise and type 2 diabetes: a consensus statement from the American Diabetes Association. *Diabetes Care* **29**: 1433-1438, 2006.
5. Hwang MH, Kim S. Type 2 Diabetes: Endothelial dysfunction and Exercise. *J Exerc Nutrition Biochem* **18**: 239-247, 2014.
6. Craig CL, Marshall AL, Sjoström M, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc* **35**: 1381-1395, 2003.
7. Hill JO, Stults J, Wyatt HR, et al. Physical activity in prevention and management of obesity and type-2 diabetes. *Nestle Nutr Workshop Ser Clin Perform Programme* **11**: 183-191; discussion 191-196, 2006.
8. Laaksonen DE, Lindstrom J, Lakka TA, et al. Physical activity in the prevention of type 2 diabetes: the Finnish diabetes prevention study. *Diabetes* **54**: 158-165, 2005.
9. Gill JM, Cooper AR. Physical activity and prevention of type 2 diabetes mellitus. *Sports Med* **38**: 807-824, 2008.
10. Keyserling TC, Samuel-Hodge CD, Ammerman AS, et al. A randomized trial of an intervention to improve self-care behaviors of African-American women with type 2 diabetes: impact on physical activity. *Diabetes Care* **25**: 1576-1583, 2002.
11. Trenell MI, Hollingsworth KG, Lim EL, et al. Increased daily walking improves lipid oxidation without changes in mitochondrial function in type 2 diabetes. *Diabetes Care* **31**: 1644-1649, 2008.
12. Slentz CA, Duscha BD, Johnson JL, et al. Effects of the amount of exercise on body weight, body composition, and measures of central obesity: STRRIDE--a randomized controlled study. *Arch Intern Med* **164**: 31-39, 2004.
13. Krishnan S, Rosenberg L, Palmer JR. Physical activity and television watching in relation to risk of type 2 diabetes: the Black Women's Health Study. *Am J Epidemiol* **169**: 428-434, 2009.
14. Williams PT. Vigorous exercise, fitness and incident hypertension, high cholesterol, and diabetes. *Med Sci Sports Exerc* **40**: 998-1006, 2008.
15. Williams PT, Franklin B. Vigorous exercise and diabetic, hypertensive, and hypercholesterolemia medication use. *Med Sci Sports Exerc* **39**: 1933-1941, 2007.
16. Gando Y, Yamamoto K, Murakami H, et al. Longer time spent in light physical activity is associated with reduced arterial stiffness in older adults. *Hypertension* **56**: 540-546, 2010.
17. Slentz CA, Tanner CJ, Bateman LA, et al. Effects of exercise training intensity on pancreatic beta-cell function. *Diabetes Care* **32**: 1807-1811, 2009.
18. Matthews DR, Hosker JP, Rudenski AS, et al. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* **28**: 412-419, 1985.
19. James WP. The epidemiology of obesity: the size of the problem. *J Intern Med* **263**: 336-352, 2008.
20. Reusch JE. Current concepts in insulin resistance, type 2 diabetes mellitus, and the metabolic syndrome. *Am J Cardiol* **90**: 19G-26G,

- 2002.
21. Henson J, Yates T, Biddle SJ, et al. Associations of objectively measured sedentary behaviour and physical activity with markers of cardiometabolic health. *Diabetologia* **56**: 1012-1020, 2013.
22. Wijndaele K, Orrow G, Ekelund U, et al. Increasing objectively measured sedentary time increases clustered cardiometabolic risk: a 6 year analysis of the ProActive study. *Diabetologia* **57**: 305-312, 2014.
23. Assah FK, Brage S, Ekelund U, Wareham NJ. The association of intensity and overall level of physical activity energy expenditure with a marker of insulin resistance. *Diabetologia* **51**: 1399-1407, 2008.
24. Ekelund U, Brage S, Griffin SJ, Wareham NJ. Objectively measured moderate- and vigorous-intensity physical activity but not sedentary time predicts insulin resistance in high-risk individuals. *Diabetes Care* **32**: 1081-1086, 2009.
25. Cooper AJ, Brage S, Ekelund U, et al. Association between objectively assessed sedentary time and physical activity with metabolic risk factors among people with recently diagnosed type 2 diabetes. *Diabetologia* **57**: 73-82, 2014.
26. Gando Y, Murakami H, Kawakami R, et al. Light-intensity physical activity is associated with insulin resistance in elderly Japanese women independent of moderate-to vigorous-intensity physical activity. *J Phys Act Health* **11**: 266-271, 2014.
27. Umpierre D, Ribeiro PA, Schaan BD, et al. Volume of supervised exercise training impacts glycaemic control in patients with type 2 diabetes: a systematic review with meta-regression analysis. *Diabetologia* **56**: 242-251, 2013.
28. Houmard JA, Tanner CJ, Slentz CA, et al. Effect of the volume and intensity of exercise training on insulin sensitivity. *J Appl Physiol* **96**: 101-106, 2004.
29. Bajpeyi S, Tanner CJ, Slentz CA, et al. Effect of exercise intensity and volume on persistence of insulin sensitivity during training cessation. *J Appl Physiol* **106**: 1079-1085, 2009.
30. Praet SF, van Rooij ES, Wijtvliet A, et al. Brisk walking compared with an individualised medical fitness programme for patients with type 2 diabetes: a randomised controlled trial. *Diabetologia* **51**: 736-746, 2008.