

The effects of initial and subsequent adiposity status on diabetes mellitus

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• Diabetes Mellitus is a major global public health challenge

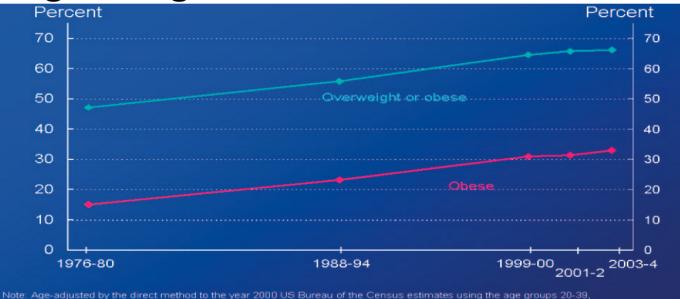








 As an important risk factor for DM, Obesity is rising throughout the world



- 40-59 and 60-74 years. Overweight defined as BMI>=25; Obesity defined as BMI>=30.
- Therefore, obesity-related DM is a large public







 There is recent evidence showing that becoming a non-obese adult could reverse the adverse effects of childhood obesity on DM

The NEW ENGLAND JOURNAL of MEDICINE

#### ORIGINAL ARTICLE

Childhood Adiposity, Adult Adiposity, and Cardiovascular Risk Factors

Markus Juonala, M.D., Ph.D., Costan G. Magnussen, Ph.D.,

Cardiovascular and Metabolic Risk

### Childhood Size and Life Course Weight Characteristics in Association With the Risk of Incident Type 2 Diabetes







 There is also evidence demonstrating that weight loss could reduce the subsequent risk RESEARCH REPORT

Overweight and obesity and weight change in middle aged men: impact on cardiovascular disease and diabetes

S Goya Wannamethee, A Gerald Shaper, Mary Walker

J Epidemiol Community Health 2005;59:134–139. doi: 10.1136/jech.2003.015651

JECH Online First, published on July 13, 2010 as 10.1136/jech.2009.097964

Research report

Association of weight change in different periods of adulthood with risk of type 2 diabetes in Japanese men and women: the Japan Public Health Center-Based Prospective Study

Akiko Nanri,<sup>1</sup> Tetsuya Mizoue,<sup>1</sup> Yoshihiko Takahashi,<sup>2</sup> Yumi Matsushita,<sup>1</sup> Mitsuhiko Noda,<sup>2</sup> Manami Inoue,<sup>3</sup> Shoichiro Tsugane,<sup>3</sup> for the Japan Public Health Center-based Prospective Study Group

S Goya Wannamethee, A Gerald Shaper, Mary Walker

Center-based Prospective Study Group



J Epidemiol Community Health 2005;59:134–139. doi: 10.1136/jech.2003.015651





 However, it has not been clearly established whether becoming non-obese could reverse the adverse effects of initial obesity on DM in adulthood.









- 1. Study population
- A group of 711 participants in an urban community , located in Chengdu, Sichuan province, China.









- 2. Data collection
- The data were collected in 1992 and then again in 2007 from this group.
- In both of the years, the medical professionals did a survey of cardiovascular disease (CVD) risk factors including the standardized questionnaire, physical examination and laboratory tests.







- 2. Data collection
- The questionnaire included sex, age, and CVD risk factors, such as smoking status, alcohol consumption levels and physical activity.
- The physical examination included measurement of blood pressure, height, weight, and so on.
- Laboratory tests included measurement of fasting plasma glucose (FPG), fasting serum total cholesterol (TC), lowdensity lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG).







- 3. Related definition
- 1). Hypertension: SBP ≥140 mmHg, or DBP ≥90 mmHg, and/or those receiving antihypertensive medications;
- 2). Diabetes mellitus: self-reported history or a fasting plasma glucose ≥7.0 mmol/L;
- 3). Smoking: average cigarette consumption ≥ 1 /day;
- 4). Alcohol intake: average intake of alcohol  $\geq$  50g/ day;
- 5). Physically active: excise one or more times per week, and more than 20 min each time;
- 6). Overweight or obese:  $BMI \ge 25 \text{ kg/m}^2$







### 4. Classification of adiposity status

24 subjects were excluded because they were diagnosed of DM in 1992; only 687 participants have complete data. According to both the 1992 and 2007 BMI status, the participants were categorized into 4 groups:

- Group I: constantly normal BMI
- Group II: turning to be overweight or obese
- Group III: turning to have normal BMI
- Group IV: constantly overweight or obese







### 4. Classification of adiposity status

Total:687 male: 58.1% 48.1±6.2 in 1992

412 persons 1992: BMI < 25 2007: BMI < 25	or obese) 88 persons 1992: BMI < 25 2007: BMI ≥ 25
Group III (turning normal BMI) 58 persons 1992: BMI ≥ 25 2007: BMI < 25	Group II (constant overweight or obese) 129 persons 1992: BMI ≥ 25 2007: BMI ≥ 25

Group I (constant normal BMI) Group II (turning overweight







### • Characteristics of participants in 1992 and 2007 according to the adiposity status

Variable	Group I $(n=412)$	Group II (n=88)	Group III $(n=58)$	Group IV (n=129)	p value
Sex (male)	248 (60.2)	50 (56.8)	31 (53,4)	70 (54.3)	0.553
Characteristics of partici	pants in 1992				
Age (years)	$47.9 \pm 6.2^{11}$	$47.4 \pm 6.3^{III}$	$50.4 \pm 6.1^{1,11,1V}$	$48.5 \pm 6.0^{111}$	0.014
BMI (kg/m <sup>2</sup> )	$21.8 \pm 1.9^{II-IV}$	$23.6 \pm 1.1^{1,111,111}$	$26.1 \pm 0.9^{1,11,1V}$	$27.3 \pm 1.8^{I-III}$	< 0.001
SBP (mm Hg)	$112.2 \pm 14.1^{IIIV}$	$114.1 \pm 16.2^{IIIV}$	$121.6 \pm 15.7^{1.11}$	$119.0 \pm 16.5^{UI}$	< 0.001
DBP (mm Hg)	$72.3 \pm 8.6^{IILIV}$	$73.7 \pm 10.2^{111.1V}$	77.6±8.8 <sup>1,11</sup>	$76.3 \pm 9.1^{1.11}$	< 0.001
TC (mmol/L)	$4.5 \pm 0.8^{11}$	$4.5 \pm 0.9$	$4.7 \pm 0.7^{1.1V}$	$4.5 \pm 0.8^{11}$	0.102
HDL-C(mmol/L)	$1.3 \pm 0.2^{111,1V}$	$1.2 \pm 0.3$	$1.2 \pm 0.2^{I}$	$1.2 \pm 0.2^{1}$	0.001
TG (mmol/L)	1.8 (1.4, 2.2) <sup>IIUV</sup>	1.7 (1.4, 2.3) <sup>IIUV</sup>	2.3 (1.8, 3.3) <sup>LII</sup>	2.1 (1.7, 2.7) <sup>1,11</sup>	< 0.001
LDL-C (mmol/L)	$2.3 \pm 0.8$	$2.3 \pm 0.8$	$2.3 \pm 0.9$	$2.2 \pm 0.9$	0.444
FPG (mmol/L)	$4.2 \pm 0.7$	$4.3 \pm 0.7$	$4.3 \pm 0.6$	$4.3 \pm 0.8$	0.837
Smoking	159 (38.6)	35 (39.8)	15 (25.9)	39 (30.2)	0.103
Alcohol intake	51 (12.4)	11 (12.5)	5 (8.6)	20 (15.5)	0.608
Physical activity	86 (20.9)	24 (27.3)	8 (13.8)	28 (21.7)	0.274
Hypertension	50 (12.1) <sup>IV</sup>	17 (19.3)	12 (20.7)	25 (19.4) <sup>1</sup>	0.063
Characteristics of partici	pants in 2007				
Age (years)	$62.9 \pm 6.2^{11}$	$62.4 \pm 6.3^{111}$	$65.4 \pm 6.1^{1.11.11}$	$63.5 \pm 6.0^{111}$	0.014
BMI (kg/m <sup>2</sup> )	$21.8 \pm 2.1^{II-IV}$	$26.3 \pm 1.6^{I,III,IV}$	$23.6 \pm 1.3^{1.11.1V}$	$27.8 \pm 2.4^{I-III}$	< 0.001
SBP (mm Hg)	$132.0 \pm 18.2^{IIIV}$	$133.5 \pm 20.1$ <sup>IIUV</sup>	$144.5 \pm 18.0^{1.0}$	$140.2 \pm 19.1^{10}$	< 0.001
DBP (mm Hg)	$77.9 \pm 10.0^{111.1V}$	$79.2 \pm 10.4^{11}$	$83.1 \pm 9.7^{1.11}$	$81.2 \pm 9.2^{1}$	< 0.001
TC (mmol/L)	$5.0 \pm 0.9^{111}$	$4.9 \pm 0.9$	$4.7 \pm 0.9^{I}$	$4.9 \pm 1.0$	0.177
HDL-C (mmol/L)	$1.5 \pm 0.3^{II-IV}$	$1.3 \pm 0.3^{1}$	$1.4 \pm 0.3^{I}$	$1.3 \pm 0.3^{1}$	< 0.001
TG (mmol/L)	1.4 (1.1, 2.0) <sup>II-IV</sup>	1.7 (1.3, 2.3) <sup>I,IV</sup>	$1.4(1.1, 2.6)^{I}$	1.8 (1.4, 2.5) <sup>1,11</sup>	< 0.001
LDL-C (mmol/L)	$3.0 \pm 0.8$	$3.1 \pm 0.8$	$2.8 \pm 0.8^{IV}$	$3.1 \pm 0.8^{11}$	0.171
FPG (mmol/L)	$4.9 \pm 1.5^{111.1V}$	$5.0 \pm 1.3$	$5.4 \pm 1.8^{1}$	$5.3 \pm 1.7^{1}$	0.008
Smoking	119 (28.9)	24 (27.3)	12 (20.7)	29 (22.5)	0.354
Alcohol intake	54 (13.1)	10 (11.4)	5 (8.6)	18 (14.0)	0.739
Physical activity	239 (58.0)	51 (58.0)	37 (63.8)	74 (57.4)	0.853
Hypertension	178 (43.2) <sup>III,IV</sup>	44 (50.0) <sup>IILIV</sup>	42 (72.4) <sup>1,11</sup>	86 (66.7) <sup>1,11</sup>	< 0.001
DM	33 (8.0) <sup>III,IV</sup>	6 (6.8) <sup>III,IV</sup>	13 (22.4) <sup>1,11</sup>	22 (17.1) <sup>I,II</sup>	< 0.001







 Unadjusted cumulative incidence of DM during the follow-up according to the adiposity status groups

DM	33 (8.0) <sup>III,IV</sup>	6 (6.8) <sup>III,IV</sup>	13 (22.4) <sup>1,11</sup>	22 (17.1) <sup>1,11</sup>	<0.001
Hypertension	178 (43.2) <sup>III,IV</sup>	44 (50.0) <sup>III,IV</sup>	42 (72.4) <sup>I,II</sup>	86 (66.7) <sup>I,II</sup>	< 0.001
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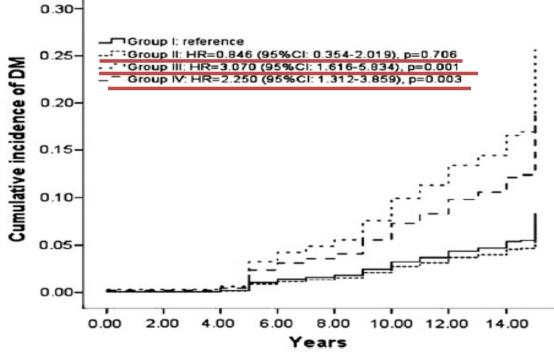
The cumulative incidence of DM was 8.0% for group I, 6.8% for group II, 22.4% for group III and 17.1% for group IV, respectively. The cumulative incidence of DM was significantly higher in groups III and IV than in groups I and II (all p values < 0.05)







 Unadjusted cumulative incidence of DM: With group I as reference, groups III and IV had a significant two to three-fold increased DM risk; However, it was not significantly different between groups I and II, as well as between groups III and IV









### Multivariate-adjusted hazards ratio of DM:

	Group I	Group II (n=88)		Group III (n=58)		Group IV (n=129)	
	(n=412)	HR (95% CI)	p value	HR (95% CI)	p value	HR (95% CI)	p value
Model 1	1.0	0.864 (0.362-2.063)	0.742	2.871 (1.497-5.507)	0.002	2.258 (1.315-3.879)	0.003
Model 2	1.0	0.843 (0.352-2.016)	0.701	2.812 (1.464-5.401)	0.002	2,217 (1.289-3.815)	0.004
Model 3	1.0	0.792 (0.331-1.898)	0.602	2.114 (1.045-4.278)	0.037	1.869 (1.071-3.263)	0.028
Model 4	1.0	0.818 (0.341-1.962)	0.653	2.231 (1.087-4.579)	0.029	1.855 (1.049–3.279)	0.034

Model 1: adjusted for age and sex.

Model 2: adjusted for age, sex and the history of hypertension.

**Model 3**: adjusted for age, sex, the history of hypertension and lipids (including TC, HDL-C, TG and LDL-C).

**Model 4**: adjusted for age, sex, SBP, DBP, TC, HDL-C, TG, LDL-C, FPG and the history of hypertension.



After adjustment of all the covariates, the risk was only slightly reduced







• Relative risks of overweight or obesity in 1992 and 2007 in predicting DM.

	Overweight or obesity in 1992, RR (95% CI)	Overweight or obesity in 2007, RR (95% CI)	p value <sup>a</sup>	p value <sup>b</sup>
Model 1	2.722 (1.664-4.451)		< 0.001	
Model 2		1.366 (0.828-2.252)		0.222
Model 3	3.127 (1.755-5.571)	0.763 (0.421-1.381)	< 0.001	0.371
Model 4	2.100 (1.214-3.633)		0.008	
Model 5	2.347 (1.244-4.428)	0.807 (0.436-1.492)	0.008	0.494

Model 1 included the status of overweight or obesity in 1992.

Model 2 included the status of overweight or obesity in 2007.

**Model 3** included the status of overweight or obesity in 1992 and 2007. **Model 4** included age, sex, SBP, DBP, TC, HDL-C, TG, FPG, LDL-C, and the history of hypertension, as well as the status of overweight or obesity in 1992.

**Model 5** included age, sex, SBP, DBP, TC, HDL-C, TG, FPG, LDL-C, and the history of hypertension, as well as the status of overweight or obesity in 1992 and 2007.







To assess the effects of baseline adiposity status on the new onset of DM, logistic regression models were used to estimate the relative risks (RRs).

With the initial adiposity status in 1992 and the subsequent adiposity status in 2007 included in the model, as well as other confounders, the results showed that the initial adiposity status could predict the cumulative incidence of DM, contrary to the subsequent adiposity status. The associations between the initial adiposity status and the cumulative incidence of DM were enhanced after adjustment for the subsequent adiposity status and other confounders.







### **Evidence from other studies**

- Some previous studies have shown that initial weight change might have a larger impact on DM incidence than recent weight change. And our results
- also showed that initial overweight or obesity in adulthood could predict
- the development of DM independently of subsequent overweight or obesity.
- Epidemiology/Health Services/Psychosocial Research ORIGINAL ARTICLE

### Short-Term Weight Change and the Incidence of Diabetes in Midlife

Results from the Australian Longitudinal Study on Women's Health

### Weight Cycling and the Risk of Developing Type 2 Diabetes among Adult Women in the United States

Alison E. Field, \*† JoAnn E. Manson,  $\ddagger$  Nan Laird, ¶ David F. Williamson,  $\ddagger$  Walter C. Willett, \$ and Graham A. Colditz \$

#### IСМI

Long-term influences of body-weight changes, independent of the attained weight, on risk of impaired glucose tolerance and Type 2 diabetes

E. Black, C. Holst\*, A. Astrup, S. Toubro, S. Echwald, † O. Pedersen + and T. I. A. Sørensen\*§

Monique A. M. Jacobs-van der Bruggen, Annemieke Spijkerman, Pieter H. M. van Baal, Caroline A. Baan\*, Edith J. M. Feskens, H. Susan J. Picavet, Daphne L. van der A, and W. M. Monique Verschuren

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Initially submitted October 19, 2009; accepted for publication April 16, 2010.







### **Evidence from other studies**

 Although many studies have shown that weight loss is associated with significantly reduced DM, these current studies suggest that weight status plays a larger role in diabetes risk than do changes in weight.

#### Intentional Weight Loss and 13-Year Diabetes Incidence in Overweight Adults

| Julie C. Will, PhD, David F. Williamson, PhD, Earl S. Ford, MD, MPH, Eugenia E. Calle, PhD, and Michael J. Thun, MD

J Epidemiol Community Health 2000;54:596-602

Relation of weight gain and weight loss on subsequent diabetes risk in overweight adults

Helaine E Resnick, Paola Valsania, Jeffrey B Halter, Xihong Lin

Overweight and obesity and weight change in middle aged men: impact on cardiovascular disease and diabetes

S Goya Wannamethee, A Gerald Shaper, Mary Walker

J Epidemiol Community Health Services/Psychosocial Research

#### Weight Change and Duration of Overweight and Obesity in the Incidence of Type 2 Diabetes

S. Goya Wannamethee, phd A. Gerald Shaper, frcp besity is well recognized as an important risk factor for type 2 diabetes





Population-Based Prevention of Obesity: The Need for Comprehensive Promotion of Healthful Eating, Physical Activity, and Energy Balance: A Scientific Statement From American Heart Association Council on Epidemiology and Prevention, Interdisciplinary Committee for Prevention (Formerly the Expert Panel on Population and Prevention Science)

Committee for Prevention (rormerly the Expert rate: on ropanion and contents) Science) Shiriki K. Kumanyika, Eva Obarzanek, Nicolas Stettler, Ronny Bell, Alison E. Field, Stephen P. Fortmann, Barry A. Franklin, Matthew W. Gillman, Cora E. Lewis, Walker Carlos Poston II, June Stevens and Yuling Hong







### Conclusion

- Our findings showed that a change from initial overweight or obesity to a normal BMI, as compared with the subjects who persist with overweight or obesity, would not be associated with a reduced risk of DM in adulthood.
- On the other hand, the risks of DM among the subjects with initially normal BMI who became overweight or obese subsequently were similar to those who were never overweight or obese.
- Initial BMI status might play a larger role in DM risk than do changes in BMI in adulthood.
- Once the subjects are overweight or obese in adulthood, they are at high risk for DM to a certain extent, as compared with the subjects who are never overweight or obese, even succeeding in weight loss.
- Keeping weight in the normal BMI range should be emphasized in the public for preventing DM.













